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Combined Diphtheria, Tetanus and Acellular Pertussis, Hepatitis B enhanced Inactivated Poliomyelitis and *Haemophilus influenzae* type B vaccine

Infanrix™ hexa

Summary Bridging Report

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1. INTRODUCTION

This summary bridging report integrates the information presented in the two Combined Diphtheria, Tetanus and Acellular Pertussis, Hepatitis B enhanced Inactivated Poliomyelitis and *Haemophilus influenzae* type B vaccine (Infanrix™ hexa) periodic safety update reports (PSURs) covering the two year period from 23 October 2009 to 22 October 2011. Further details are provided below.

Report Number	Dates of Report	Time Period
16	23 October 2010 - 22 October 2011	1 year
15	23 October 2009 - 22 October 2010	1 year

This report presents data on all formulations.

2. WORLDWIDE MARKET AUTHORISATION STATUS

Infanrix™ hexa has been approved in 92 countries (see APPENDIX 1 of PSUR 16).

3. UPDATE ON REGULATORY AUTHORITY OR MANUFACTURER ACTIONS TAKEN FOR SAFETY REASONS

During the period under review, no actions have been taken for safety reasons concerning withdrawal, rejection, suspension or failure to obtain a renewal of a Marketing Authorisation; neither have there been any dosage modifications, changes in target population, formulation changes, restriction on distribution, or clinical trial suspension.

4. CHANGES TO REFERENCE SAFETY INFORMATION

The Reference Safety Information (RSI) in effect at the beginning of the reporting period is the Global Prescriber Information (GPI) of Global Datasheet (GDS) version 9 dated 23 November 2007. Refer to APPENDIX 2A of PSUR 15; the RSI is identified by double-underlining within the GPI.

During the period of this report one new version (version 10) of the RSI was issued. Refer to APPENDIX 2B of PSUR 15; the RSI is identified as grey shaded text within the GPI. In CSI version 10 dated 21 October 2010 the following changes were implemented:

- A warning about the risk of syncope (fainting) after any vaccination was added in the Warnings and Precautions Section: *Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints*.

The following changes were implemented as well in RSI version 10 compared to version 9, although not mentioned in PSUR 15:

- The Company revised the text considered as RSI in the GDS taking into account the fact that any text that refers to 'negative data' or 'no data available' should not be considered as RSI. As a consequence, the following is no longer considered to be RSI:
  - *Dosage and Administration* Section
  - *Interactions* Section (except for the key message related to higher incidence of fever reported with Infanrix™ hexa)
  - *Pregnancy* and *Lactation* Section
  - The sentence *The safety profile presented below is based on data from more than 16 000 subjects* in the Clinical Trials Section.
  - *Overdosage* Section
- Several changes were made to the *Use and Handling* Section:
  - wording regarding reconstitution of the vaccine was clarified
  - paragraph related to Bioset presentation was deleted
  - instructions related to PRTC pre-filled syringe and information related to the vial and vial presentation were added
  - a statement regarding disposal of unused products or waste material was added

5. PATIENT EXPOSURE

5.1. Market Experience

Information on the actual number of people exposed to Infanrix™ hexa in the different countries is not available to the MAH. Therefore, the total patient exposure is approximated by the number of doses distributed which is the most reliable data available with regard to patient exposure for a vaccine in a post-marketing setting.

It is important to note that the sales database from which data are retrieved is an in-house 'living' database and is subject to updates and corrections depending on information provided by GSK local country subsidiaries (e.g. vaccine doses may be returned by subsidiaries to the central warehouse). These constant updates may result in discrepancies between consecutive queries of the database.

During the period covered by this report 24 283 415 doses of Infanrix™ hexa have been distributed. Since launch until the data lock point (DLP) of this report, 72 931 338 doses have been distributed. As vaccination with Infanrix™ hexa can vary between 1 and 4 doses per subject in accordance with local recommendations and compliance with the vaccination schedule, and assuming that one dose distributed corresponds to one dose administered, post-marketing exposure to Infanrix™ hexa during the SBR reporting

period is estimated to be between 6 070 854 and 24 283 415 subjects. The number of subjects exposed since launch until the data lock point of this report is estimated between 18 232 834 and 72 931 338.

6. INDIVIDUAL CASE HISTORIES

A total of 2408 reports meeting ICH E2C PSUR criteria have been received during the period of this report. These reports include all serious and non-serious reports from spontaneous notifications (including published reports), but exclude all non-healthcare professional reports and all non-serious reports received solely from regulatory authorities. In addition, unblinded, serious attributable reports arising from clinical studies, post-marketing surveillance studies, named patient use or solicited reports following use of a GSK product have been included. These cases are presented within the summary tabulation in Appendix 1.

The tabulation shows the MedDRA System Organ Class (SOC), High Level Group Term (HLGT) and Preferred Term (PT), and the number of unique cases for each adverse event.

The total number of cases presented in line listings and summary tabulations in the series of PSURs appended to this summary report is 2388.

It should be noted that the data-set for the summary tabulation differs from the data-sets included in the individual PSURs during the time period given that the summary tabulation in this report contains follow-up information on cases previously included in the PSURs.

7. STUDIES

7.1. Newly-Analysed Studies

Three new corporate studies relevant to the safety of Infanrix™ hexa were completed and analysed during the period of this report.

- **Study #112157 (DTPa-HBV-IPV=Hib-MenC-TT-002 PRI)** A phase II, open-label, randomised, multicentre study to evaluate the safety and immunogenicity of GSK Biologicals‟ DTPa-HBV-IPV/Hib-MenC-TT vaccine co- dministered with GSK Biologicals‟ 10-valent pneumococcal conjugate vaccine in healthy infants when administered as a three-dose primary vaccination course at 2, 3 and 4 months of age.

  The observed incidence of solicited and unsolicited adverse events was in the same range in the 3 groups, i.e. “Hepta” (candidate heptavalent vaccine), “HexaMnC” (Infanrix™ hexa co-administered with conjugate meningococcal vaccine (Menjugate), and “HexaPn” [Infanrix™ hexa co-administered with conjugate pneumococcal vaccine (Synflorix)]; all the vaccines administered in the study were well tolerated. One SAE (thrombocytopenia) reported for a subject in the Hepta

group was considered by the investigator to have a potential causal relationship to vaccination. All serious adverse events reported during the study resolved without sequelae.

- **Study #110142 (10-PN-PD-DIT-027 PRI)** A phase III randomized, single-blind, controlled study to demonstrate the non-inferiority of co-administration of GSK Biological 10-valent pneumococcal conjugate vaccine with Pediacel™ versus coadministration with Infanrix™ hexa, when administered to infants as a three-dose primary vaccination course during the first six months of life and as a booster dose at 11- 13 months of age.

  This study was conducted with 3 parallel groups: "10Pn-Hexa" group received 10Pn-PD-DIT and Infanrix™ hexa, "10Pn-PDC" group received 10Pn-PD-DIT and Pediacel and "Prev-PDC" group received Prevenar and Pediacel. The incidences of grade 3 solicited local and general adverse events were low in all study groups. The percentage of doses followed by unsolicited adverse events was in the same range in all groups. Grade 3 unsolicited adverse events with causal relationship to vaccination were rarely reported. No fatal SAEs were reported in this study up to the data lock point. Up to the data lock point, SAEs after primary vaccination were reported in 32 subjects (17 subjects in the 10Pn-Hexa group, 5 subjects in the 10Pn-PDC group and 10 subjects in the Prev-PDC group).One of these SAEs reported for a subject in the 10Pn-Hexa group (apparent life threatening event) was assessed by the investigator to be causally related to vaccination.

- **Study #111654 (10-PN-PD-DIT-048)** A phase III, multi-centre, double-blind, randomised study to assess the non-inferiority of a commercial lot of GlaxoSmithKline (GSK) Biologicals 10-valent pneumococcal conjugate (10Pn-PD-DiT) vaccine compared to a clinical phase III vaccine lot, when given as a three-dose primary immunization course.

  This study was conducted with 2 parallel groups: the "Clin" group received the phase 3 clinical lot of 10Pn-PD-DIT with Infanrix™ hexa or Infanrix-IPV/Hib and HRV, the "Com" group received the commercial lot of 10Pn-PD-DIT with Infanrix™ hexa or Infanrix-IPV/Hib and HRV. All subjects were concomitantly administered a dose of Infanrix™ hexa. The following results are supportive of an acceptable safety profile of the clinical phase III:

  Unsolicited adverse events:

  The percentage of doses followed by at least one unsolicited symptom in the 31-day postvaccination period was 16.2% in the Clin group and 17.0% in the Com group. The most frequently reported unsolicited AE in each group was upper respiratory tract infection (5.0% in the Clin group and 6.0% in the Com group). The percentage of doses followed by at least one unsolicited symptom considered by the investigator to be causally related to vaccination and the percentage of doses with grade 3 unsolicited AEs in the 31-day post-vaccination period was at most 1.0% in both groups. No grade 3 unsolicited AEs were considered by the investigator to be causally related to vaccination.

Serious adverse events:

No fatal SAEs were reported in this study. A total of 36 non-fatal SAEs were reported for 25 (5.4%) out of 466 vaccinated subjects: 18 subjects (7.7%) in the Clin group and 7 subjects (3.0%) in the Com group. No SAEs were considered by the investigator to be causally related to vaccination. One SAE did not resolve (spinal muscular atrophy) and one SAE (tuberculous meningitis) was still ongoing at the end of this study.

The safety information generated in these studies is consistent with the current safety profile of Infanrix™ hexa.

7.2. Targeted Safety Studies

There were no planned, ongoing or completed targeted safety studies for Infanrix™ hexa.

7.3. Other Safety Studies

The following ongoing studies are not targeted safety studies but were also considered of interest as they may provide useful new information on the safety profile of Infanrix™ hexa:

- **103506 (DTPA-HBV-IPV-118 PRI)** A phase IV, non-randomised, open-label, multi centre study with two parallel groups to assess the immunogenicity and safety of GlaxoSmithKline (GSK) Biologicals combined DTPa-HBV-IPV/Hib vaccine administered as a three-dose primary vaccination course at 2, 4 and 6 months of age in healthy infants in Canada.
- **113948 (DTPA-HBV-IPV-124 PRI)** A phase II, double-blind, randomized, multicentre study to evaluate the safety and immunogenicity of new formulations of GlaxoSmithKline BiologicalsDTPa-HBV-IPV/Hib vaccine when administered to healthy toddlers as a booster dose at 12 to 15 months of age.
- **114843 (DTPA-HBV-IPV-125 BST:124)** A phase II, double-blind, randomized, multicentre study to evaluate the safety and immunogenicity of new formulations of GlaxoSmithKline Biologicals DTPa-HBV-IPV/Hib vaccine when administered to healthy toddlers as a booster dose at 12 to 15 months of age.

7.4. Published Safety Studies

A full review of the literature was conducted during the reporting period. Useful information was published during the period concerning:

- safety and reactogenicity of Infanrix-IPV+Hib and Infanrix hexa (Lim, 2011). Both vaccines were well tolerated and substitution of DTPa-IPV/Hib with Infanrix hexa at Month 5 reduced the number of injections required at this age by one.
- immunogenicity and safety of co-administration of Infanrix hexa with an investigational tetravalent meningococcal serogroups A, C, W-135 and Y-tetanus toxoid conjugate vaccine (ACWW-TT; Knuf, 2011). Pre-specified criteria for non-

inferiority of immunogenicity following co-administration versus separate ACWY-TT and Infanrix hexa administration were reached, and the safety profile of co-administration was similar to that of Infanrix hexa alone.

These studies did not highlight any safety issue.

8. OTHER INFORMATION

8.1. Late-breaking information

One new fatal case (B0762668A) was received after the data lock point as well as new follow-up data for one of the fatal cases (D0072852A) described in *Section 6.5.1 Cases with a Fatal Outcome* of PSUR 16. Refer to *Section 8.2 Late-breaking information* of PSUR 16 for further information about these cases. The latest CIOMS forms for these cases are attached in APPENDIX 5C of PSUR 16.

8.2. Cumulative review of Gaze palsy

In the assessment report (dated 3 March 2010) of PSUR 14, EMA had the following request:

b. During the period of this report 14 cases of gaze palsy have been identified. In ten of the cases, the event was reported in association with concurrent events, mostly convulsions. However, the median TTO is less than one day. In addition, outcome was reported resolved with sequelae in 1 case and unresolved in 1 case. The MAH is requested to provide a detailed cumulative reviewing of cases of Gaze palsy since launch. The events, TTO, outcome and concomitant drugs should be specified

Accordingly, a cumulative review of cases of Gaze palsy diagnosed after Infanrix hexa administration was performed. All spontaneous reports in the GSK worldwide safety database reported from Infanrix hexa launch up to a data lock point of 22 October 2011 were included in the analysis.

Since launch, 70 spontaneous cases of Gaze palsy were received, corresponding to a reporting frequency of 0.10 per 100 000 Infanrix hexa doses distributed. All cases are summarized in Appendix 2, including time to onset, events, outcome and concomitant drugs reported.

In 45/70 cases the event occurred on the same day of vaccination. In all cases Gaze palsy was one of the presenting symptoms of a larger clinical syndrome, i.e. Febrile and non-febrile Convulsion and Hypotonic-hyporesponsive episode (HHE), which are both listed events in the Infanrix hexa reference safety information.

In 43 cases outcome was reported to be ‘Resolved’ or ‘Resolved with sequelae’. In the other cases outcome was either ‘Improved’ (N=1), ‘Unresolved’ (N=6) or ‘Unknown’ (N=20).

The information received with these cases does not provide evidence of a specific safety concern for Gaze Palsy.

9. OVERALL SAFETY EVALUATION AND CONCLUSION

From the review of data received during the reporting period and presented in this report, it has been concluded that the safety profile of Infanrix hexa is adequately reflected in the RSI.

No further amendments to the RSI are considered necessary at this time.

The benefit/risk profile of Infanrix hexa continues to be favourable.

The Company will continue to monitor cases of anaemia haemolytic autoimmune, thrombocytopenia, thrombocytopenic purpura, autoimmune thrombocytopenia, idiopathic thrombocytopenic purpura, haemolytic anemia, cyanosis, injection site nodule, abcess and injection site abscess, Kawasaki's disease, important neurological events (including encephalitis and encephalopathy), Henoch-Schonlein purpura, petechiae, purpura, haematochezia, allergic reactions (including anaphylactic and anaphylactoid reactions), cases of lack of effectiveness as well as fatal cases.

10. REFERENCES

Knuf M, Pantazi-Chatzikonstantinou A, Pfletschinger U *et al*. An investigational tetravalent meningococcal serogroups A, C, W-135 and Y-tetanus toxoid conjugate vaccine co-administered with Infanrix™ hexa is immunogenic, with an acceptable safety profile in 12-23-month-old children. *Vaccine.* 2011 29:25 (4264-4273).

Lim FS, Phua KB, Lee BW *et al*. Safety and reactogenicity of DTPa-HBV-IPV/Hib and DTPa-IPV/I-Hib vaccines in a post-marketing surveillance setting. *The Southeast Asian journal of tropical medicine and public health*. 2011 42:1 (138-147).

APPENDIX 1 : SUMMARY TABULATION OF INFANRIX HEXA ADVERSE EVENTS

SUMMARY TABULATION OF INFANRIX™ HEXA ADVERSE EVENTS

23 OCTOBER 2009 TO 22 OCTOBER 2011

N.B. Events are only considered serious if they fulfil GSK medically serious criteria. GSK medically serious criteria are applied automatically only to events from spontaneous, post-marketing or literature case reports. Events arising from Clinical trial cases are not run against the list of GSK medically serious terms. For this reason events may appear as both serious and non-serious (for further details see section 6.1). It should be noted that the end column of the tabulation presents total of cases with event rather than count of events.

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Anaemia	No	12	0	12
		Bone marrow failure	No	1	0	1
		Hypochromic anaemia	No	2	0	2
		Iron deficiency anaemia	No	2	0	2
		Microcytic anaemia	No	2	0	2
		Pancytopenia	No	2	0	2
	Coagulopathies and bleeding diatheses (excl thrombocytopenic)	Haemorrhagic diathesis	No	2	0	2
	Haemolyses and related conditions	Anaemia haemolytic autoimmune	No	1	0	1
		Jaundice acholuric	No	1	0	1
		Warm type haemolytic anaemia	No	1	0	1
	Platelet disorders	Idiopathic thrombocytopenic purpura	No	11	0	11
		Thrombocytopenia	Yes	15	0	15
		Thrombocytopenic purpura	No	5	0	5
		Thrombocytosis	No	5	0	5
	Red blood cell disorders	Hypochromasia	No	1	0	1
		Microcytosis	No	1	0	1
	Spleen, lymphatic and reticuloendothelial system disorders	Lymphadenopathy	Yes	0	21	21
		Lymph node pain	No	0	1	1
		Splenomegaly	No	2	0	2
	White blood cell disorders	Agranulocytosis	No	1	0	1
		Eosinophilia	No	0	3	3
		Granulocytopenia	No	1	0	1
		Leukocytosis	No	13	0	13
		Leukopenia	No	3	0	3
		Neutropenia	No	7	0	7

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
		White blood cell disorder	No	1	0	1
Cardiac disorders	Cardiac arrhythmias	Arrhythmia	No	0	1	1
		Atrial tachycardia	No	1	0	1
		Bradycardia	No	0	14	14
		Cardiac arrest	No	6	0	6
		Cardio-respiratory arrest	No	1	0	1
		Sinus tachycardia	No	0	1	1
		Supraventricular tachycardia	No	1	0	1
		Tachycardia	No	0	10	10
	Cardiac disorder signs and symptoms	Cardiovascular disorder	No	0	4	4
		Cardiovascular insufficiency	Yes	1	0	1
		Cyanosis	No	90	17	106
	Cardiac valve disorders	Mitral valve incompetence	No	1	0	1
	Heart failures	Cardiac failure	No	1	0	1
		Cardiogenic shock	No	1	0	1
		Cardiopulmonary failure	No	1	0	1
	Myocardial disorders	Cardiomyopathy	No	1	0	1
		Congestive cardiomyopathy	No	1	0	1
	Pericardial disorders	Pericarditis	No	1	0	1
Congenital, familial and genetic disorders	Blood and lymphatic system disorders congenital	Haemophilia	No	1	0	1
	Cardiac and vascular disorders congenital	Atrial septal defect	No	1	0	1
	Metabolic and nutritional disorders congenital	Methylmalonic aciduria	No	1	0	1
	Musculoskeletal and connective tissue disorders congenital	Macrocephaly	No	1	0	1
		Microcephaly	No	2	0	2
		Talipes	No	1	0	1
	Neurological disorders congenital	Cerebral palsy	No	1	0	1
		Congenital neuropathy	No	1	0	1
	Reproductive tract and breast disorders congenital	Hydrocele	No	2	0	2
		Phimosis	No	1	0	1
Ear and labyrinth disorders	External ear disorders (excl congenital)	Auricular swelling	No	0	2	2
		Cerumen impaction	No	0	1	1
	Middle ear disorders (excl congenital)	Tympanic membrane disorder	No	0	1	1
		Tympanic membrane hyperaemia	No	0	2	2
		Tympanic membrane perforation	No	0	2	2
Endocrine disorders	Thyroid gland disorders	Hypothyroidism	No	2	0	2

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
Eye disorders	Eye disorders NEC	Eye disorder	No	0	9	9
		Eyelid disorder	No	0	4	4
		Eye oedema	No	0	1	1
		Eye swelling	No	0	1	1
	Ocular haemorrhages and vascular disorders NEC	Conjunctival haemorrhage	No	0	1	1
	Ocular infections, irritations and inflammations	Conjunctival hyperaemia	No	0	2	2
		Conjunctivitis	No	0	7	7
		Eyelid oedema	Yes	0	5	5
	Ocular neuromuscular disorders	Blepharospasm	No	0	1	1
		Eyelid ptosis	No	0	1	1
		Eye movement disorder	No	0	25	25
		Gaze palsy	No	43	0	43
		Oculogyric crisis	No	3	0	3
		Ophthalmoplegia	No	2	0	2
		Pupils unequal	No	0	1	1
		Strabismus	No	0	4	4
	Retina, choroid and vitreous haemorrhages and vascular disorders	Retinal haemorrhage	No	2	0	2
	Vision disorders	Anisometropia	No	0	1	1
		Astigmatism	No	0	1	1
		Diplopia	No	0	1	1
		Hypermetropia	No	0	1	1
		Vision blurred	No	0	1	1
		Visual acuity reduced	No	0	1	1
		Visual impairment	No	0	2	2
Gastrointestinal disorders	Abdominal hernias and other abdominal wall conditions	Inguinal hernia	No	0	1	1
	Dental and gingival conditions	Gingival bleeding	No	0	2	2
	Gastrointestinal conditions NEC	Gastrointestinal disorder	No	0	2	2
	Gastrointestinal haemorrhages NEC	Haematochezia	No	7	2	9
		Melaena	No	1	0	1
		Rectal haemorrhage	No	4	0	4
	Gastrointestinal inflammatory conditions	Colitis	No	1	0	1
		Enteritis	No	1	0	1
		Gastritis	No	0	1	1
		Gastrointestinal inflammation	No	0	2	2
		Oesophagitis	No	0	1	1
	Gastrointestinal motility and defaecation conditions	Constipation	No	0	4	4
		Diarrhoea	Yes	0	53	53
		Diarrhoea haemorrhagic	No	3	0	3

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
		Frequent bowel movements	Yes	0	1	1
		Gastrointestinal hypomotility	No	0	1	1
		Gastrooesophageal reflux disease	No	1	7	8
		Ileus paralytic	No	2	0	2
		Intestinal dilatation	No	0	1	1
	Gastrointestinal signs and symptoms	Abdominal distension	No	0	6	6
		Abdominal pain	No	0	10	10
		Abdominal pain upper	No	0	1	1
		Abdominal rigidity	No	0	1	1
		Abnormal faeces	No	0	7	7
		Acute abdomen	No	1	0	1
		Dyspepsia	No	0	2	2
		Dysphagia	No	0	1	1
		Faeces discoloured	No	0	6	6
		Flatulence	No	0	6	6
		Gastrointestinal pain	No	0	2	2
		Mucous stools	No	0	2	2
		Nausea	No	0	2	2
		Post-tussive vomiting	No	0	1	1
		Regurgitation	No	0	5	5
		Vomiting	Yes	0	108	108
	Gastrointestinal stenosis and obstruction	Intestinal obstruction	No	1	0	1
		Intussusception	No	4	0	4
	Malabsorption conditions	Coeliac disease	No	0	1	1
	Oral soft tissue conditions	Chapped lips	No	0	4	4
		Cheilitis	No	0	6	6
		Lip disorder	No	0	1	1
		Lip haematoma	No	0	1	1
		Lip oedema	Yes	0	1	1
		Lip swelling	Yes	0	3	3
		Mouth haemorrhage	No	1	3	3
		Oral discharge	No	0	1	1
	Peritoneal and retroperitoneal conditions	Ascites	No	2	0	2
		Peritoneal disorder	No	0	1	1
	Salivary gland conditions	Lip dry	No	0	1	1
		Salivary hypersecretion	No	0	9	9
	Tongue conditions	Glossoptosis	No	0	1	1
		Hypertrophy of tongue papillae	No	0	1	1
		Protrusion tongue	No	0	1	1
		Swollen tongue	Yes	0	1	1
General disorders and administration site conditions	Administration site reactions	Application site discolouration	No	0	1	1
		Injected limb mobility	No	0	4	4

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
		decreased				
		Injection site abscess sterile	No	0	2	2
		Injection site cyst	No	0	2	2
		Injection site dermatitis	Yes	0	1	1
		Injection site discolouration	No	0	22	22
		Injection site eczema	No	0	3	3
		Injection site erythema	Yes	0	190	190
		Injection site extravasation	No	0	11	11
		Injection site haematoma	No	0	14	14
		Injection site haemorrhage	No	0	4	4
		Injection site hypersensitivity	Yes	0	1	1
		Injection site induration	Yes	0	83	83
		Injection site inflammation	No	0	49	49
		Injection site mass	No	0	5	5
		Injection site necrosis	No	1	0	1
		Injection site nodule	No	0	41	41
		Injection site oedema	Yes	0	64	64
		Injection site pain	Yes	0	76	76
		Injection site pallor	No	0	3	3
		Injection site papule	No	0	1	1
		Injection site pruritus	No	0	21	21
		Injection site rash	Yes	0	4	4
		Injection site reaction	No	0	48	48
		Injection site scab	No	0	1	1
		Injection site scar	No	0	1	1
		Injection site swelling	Yes	0	136	136
		Injection site urticaria	No	0	1	1
		Injection site vesicles	Yes	0	7	7
		Injection site warmth	No	0	62	62
		Vaccination site abscess sterile	No	1	0	1
		Vaccination site erythema	Yes	0	1	1
		Vaccination site granuloma	No	0	1	1
		Vaccination site induration	Yes	0	3	3
		Vaccination site oedema	No	0	3	3
		Vaccination site pain	Yes	0	1	1
		Vaccination site reaction	No	0	1	1
		Vaccination site swelling	No	0	2	2
	Body temperature conditions	Hyperpyrexia	No	0	10	10
		Hyperthermia	No	0	8	8
		Hypothermia	No	0	4	4
		Pyrexia	Yes	2	591	593
	Device issues	Needle issue	No	0	1	1
	Fatal outcomes	Death	No	8	0	8
		Sudden death	No	2	0	2
		Sudden infant death syndrome	No	12	0	12
	General system disorders NEC	Abasia	No	0	3	3

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
		Abscess sterile	No	11	0	11
		Asthenia	No	0	16	16
		Chills	No	0	10	10
		Condition aggravated	No	0	3	3
		Developmental delay	No	0	12	12
		Discomfort	No	0	4	4
		Disease recurrence	No	0	1	1
		Enanthema	No	0	1	1
		Extensive swelling of vaccinated limb	Yes	0	29	29
		Face oedema	Yes	0	2	2
		Fatigue	No	0	34	34
		Feeling abnormal	No	0	2	2
		Feeling cold	No	0	3	3
		Feeling hot	No	0	12	12
		Feeling of body temperature change	No	0	1	1
		Feeling of relaxation	No	0	1	1
		Foaming at mouth	No	0	4	4
		Foreign body reaction	No	0	3	3
		Gait deviation	No	0	1	1
		Gait disturbance	No	0	22	22
		Generalised oedema	No	0	1	1
		General physical health deterioration	No	0	18	18
		Granuloma	No	0	5	5
		Ill-defined disorder	No	0	40	40
		Induration	No	0	15	15
		Inflammation	No	0	35	35
		Influenza like illness	No	0	1	1
		Irritability	Yes	0	50	50
		Localised oedema	No	0	1	1
		Local reaction	No	0	4	4
		Local swelling	No	0	8	8
		Malaise	No	0	34	34
		Mucosal inflammation	No	0	1	1
		Mucous membrane disorder	No	0	1	1
		Multi-organ failure	No	1	0	1
		Nonspecific reaction	No	0	2	2
		Oedema	No	0	5	5
		Oedema peripheral	No	0	57	57
		Pain	No	0	40	40
		Swelling	No	0	26	26
		Tenderness	No	0	1	1
		Thirst decreased	No	0	2	2
	Product quality issues	Incorrect product storage	No	0	59	59
		Product quality issue	No	0	33	33
	Therapeutic and nontherapeutic effects (excl	Adverse drug reaction	No	0	1	1

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
	toxicity)					
		Adverse event	No	0	2	2
		Drug ineffective	Yes	0	1	1
		No therapeutic response	Yes	0	7	7
		Therapeutic response decreased	Yes	0	1	1
	Tissue disorders NEC	Cyst	No	0	2	2
		Dysplasia	No	0	1	1
		Fibrosis	No	0	5	5
		Nodule	No	0	3	3
		Ulcer	No	0	1	1
Hepatobiliary disorders	Gallbladder disorders	Cholecystitis	No	1	0	1
	Hepatic and hepatobiliary disorders	Hepatic function abnormal	No	0	2	2
		Hepatomegaly	No	0	1	1
		Hepatosplenomegaly	No	0	2	2
		Hepatotoxicity	No	1	0	1
		Hypertransaminasaemia	No	1	0	1
		Jaundice	No	2	0	2
Immune system disorders	Allergic conditions	Allergy to metals	No	0	1	1
		Allergy to vaccine	Yes	0	1	1
		Anaphylactic reaction	Yes	6	0	6
		Anaphylactic shock	Yes	4	0	4
		Anaphylactoid reaction	Yes	1	0	1
		Drug hypersensitivity	Yes	0	1	1
		Hypersensitivity	Yes	0	29	29
		Milk allergy	No	0	3	3
		Type III immune complex mediated reaction	No	0	2	2
	Immune disorders NEC	Immune system disorder	No	0	2	2
	Immunodeficiency syndromes	Selective IgA immunodeficiency	No	0	1	1
Infections and infestations	Ancillary infectious topics	Transmission of an infectious agent via a medicinal product	No	1	0	1
	Bacterial infectious disorders	Bacterial infection	No	0	3	3
		Bronchitis bacterial	Yes	0	1	1
		Cellulitis	No	9	0	9
		Erysipelas	No	0	2	2
		Escherichia infection	No	0	2	2
		Escherichia urinary tract infection	No	0	3	3
		Gastroenteritis bacterial	No	1	0	1
		Gastroenteritis Escherichia coli	No	1	0	1
		Gastroenteritis staphylococcal	No	1	0	1
		Haemophilus infection	No	0	6	6
		Injection site cellulitis	No	0	2	2

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
		Meningitis haemophilus	No	5	0	5
		Meningitis pneumococcal	No	2	0	2
		Pertussis	No	0	62	62
		Pneumococcal infection	No	0	1	1
		Pneumococcal sepsis	No	0	1	1
		Salmonella sepsis	No	1	0	1
		Salmonellosis	No	0	1	1
		Staphylococcal abscess	No	0	3	3
		Staphylococcal infection	No	0	1	1
		Streptococcal abscess	No	0	2	2
		Streptococcal bacteraemia	No	0	1	1
	Fungal infectious disorders	Fungal skin infection	Yes	0	1	1
	Infections - pathogen unspecified	Abdominal abscess	No	0	1	1
		Abscess	No	0	11	11
		Abscess limb	No	0	1	1
		Acute tonsillitis	Yes	0	2	2
		Bacteraemia	No	2	0	2
		Bone abscess	No	1	0	1
		Bronchitis	Yes	0	12	12
		Bronchopneumonia	No	1	0	1
		Ear infection	No	0	4	4
		Encephalitic infection	No	1	0	1
		Enteritis infectious	No	1	0	1
		Epiglottitis	Yes	1	0	1
		Febrile infection	No	0	1	1
		Gastroenteritis	No	9	0	9
		Groin abscess	No	0	1	1
		Impetigo	No	0	3	3
		Incision site abscess	No	0	7	7
		Infection	No	0	12	12
		Infectious peritonitis	No	1	0	1
		Injection site abscess	No	0	20	20
		Injection site infection	No	0	3	3
		Injection site pustule	No	0	1	1
		Labyrinthitis	No	0	1	1
		Lung infection	No	0	1	1
		Mastoiditis	No	0	1	1
		Meningitis	Yes	4	0	4
		Meningitis aseptic	Yes	2	0	2
		Nasopharyngitis	Yes	0	13	13
		Osteomyelitis	No	2	0	2
		Otitis media	No	0	7	7
		Otitis media acute	No	0	1	1
		Pharyngitis	Yes	0	2	2
		Pneumonia	No	4	0	4
		Pneumonia primary atypical	No	1	0	1
		Purulence	No	0	3	3
		Purulent discharge	No	0	2	2

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
		Pyelonephritis	No	2	0	2
		Rash pustular	Yes	0	3	3
		Respiratory tract infection	Yes	0	6	6
		Rhinitis	Yes	0	17	17
		Sepsis	No	8	0	8
		Septic shock	No	1	0	1
		Soft tissue infection	No	0	2	2
		Sputum purulent	No	0	1	1
		Subdural empyema	No	0	1	1
		Tonsillitis	Yes	0	3	3
		Tracheitis	Yes	0	2	2
		Upper respiratory tract infection	Yes	0	14	14
		Urinary tract infection	No	1	3	4
		Vaccination site abscess	No	2	0	2
		Vaccination site infection	No	0	1	1
		Wound infection	No	0	1	1
	Viral infectious disorders	Bronchiolitis	No	0	2	2
		Croup infectious	No	0	2	2
		Eczema herpeticum	Yes	0	1	1
		Exanthema subitum	No	0	1	1
		Gastroenteritis astroviral	No	1	0	1
		Gastroenteritis norovirus	No	2	0	2
		Gastroenteritis rotavirus	No	11	0	11
		Gastroenteritis viral	No	1	0	1
		Gianotti-Crosti syndrome	No	0	3	3
		H1N1 influenza	No	0	1	1
		Hand-foot-and-mouth disease	No	0	1	1
		Herpes ophthalmic	No	0	1	1
		Herpes simplex	No	0	1	1
		Herpes virus infection	No	0	1	1
		Herpes zoster	Yes	0	2	2
		Measles	No	0	1	1
		Meningitis viral	Yes	1	0	1
		Pneumonia respiratory syncytial viral	No	1	0	1
		Respiratory syncytial virus infection	No	0	2	2
		Rotavirus infection	No	0	1	1
		Varicella	No	0	1	1
		Vestibular neuronitis	No	0	1	1
		Viral infection	No	0	8	8
		Viral rash	Yes	0	3	3
Injury, poisoning and procedural complications	Chemical injury and poisoning	Maternal exposure during pregnancy	No	0	2	2
	Injuries NEC	Arthropod bite	No	0	1	1
		Child maltreatment syndrome	No	0	2	2
		Concussion	No	1	0	1

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
		Contusion	No	0	3	3
		Craniocerebral injury	No	1	0	1
		Fall	No	0	7	7
		Laceration	No	0	1	1
		Soft tissue injury	No	0	1	1
	Medication errors	Accidental exposure	No	0	2	2
		Accidental overdose	No	0	10	10
		Drug administered at inappropriate site	No	0	1	1
		Drug administered to patient of inappropriate age	No	0	97	97
		Drug administration error	No	0	33	33
		Drug dispensing error	No	0	2	2
		Drug prescribing error	No	0	1	1
		Expired drug administered	No	0	15	15
		Inappropriate schedule of drug administration	No	0	161	161
		Incorrect dose administered	No	0	41	41
		Incorrect route of drug administration	No	0	30	30
		Incorrect storage of drug	No	0	43	43
		Medication error	No	0	2	2
		Overdose	No	0	33	33
		Underdose	No	0	38	38
		Wrong drug administered	No	0	78	78
		Wrong technique in drug usage process	No	0	165	165
	Procedural related injuries and complications NEC	Vaccination complication	No	0	25	25
		Vaccination failure	Yes	68	0	68
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Blood pressure decreased	Yes	0	2	2
		Cardiac murmur	No	0	1	1
		Heart rate decreased	No	0	2	2
		Heart rate increased	No	0	6	6
		Heart sounds abnormal	No	0	1	1
		Peripheral pulse decreased	No	0	1	1
		Pulse absent	No	1	0	1
		Pulse pressure decreased	No	0	1	1
		Pulse pressure increased	No	0	1	1
	Enzyme investigations NEC	Blood lactate dehydrogenase increased	No	0	1	1
	Haematology investigations (incl blood groups)	Platelet count decreased	Yes	0	2	2
		White blood cell count increased	No	0	2	2
	Hepatobiliary investigations	Alanine aminotransferase increased	No	1	0	1

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
		Ammonia increased	No	0	1	1
		Aspartate aminotransferase increased	No	2	0	2
		Hepatic enzyme increased	No	1	0	1
		Transaminases increased	No	7	0	7
	Immunology and allergy investigations	Allergy test positive	Yes	0	1	1
		Autoantibody positive	No	0	1	1
		Blood immunoglobulin E increased	No	0	1	1
		Blood immunoglobulin M decreased	No	0	1	1
		Immunology test abnormal	No	0	1	1
	Metabolic, nutritional and blood gas investigations	Blood glucose increased	No	0	1	1
		Blood lactic acid increased	No	0	1	1
		Oxygen saturation decreased	No	0	14	14
	Microbiology and serology investigations	Adenovirus test positive	No	0	1	1
		Bacterial test positive	No	0	1	1
		Bordetella test negative	No	0	1	1
		Bordetella test positive	No	0	2	2
		Clostridium test	No	0	1	1
		Clostridium test negative	No	0	4	4
		Corynebacterium test negative	No	0	4	4
		Cytomegalovirus test positive	No	0	1	1
		Hepatitis B antibody negative	No	0	4	4
		Hepatitis B antibody positive	No	0	1	1
		Hepatitis B antigen positive	No	0	1	1
		Hepatitis B surface antigen positive	No	0	1	1
		Rotavirus test positive	No	0	1	1
		Staphylococcus test positive	No	0	1	1
		Viral test positive	No	0	1	1
	Neurological, special senses and psychiatric investigations	Electroencephalogram abnormal	No	0	2	2
		Reflex test normal	No	0	1	1
	Physical examination topics	Body temperature	No	0	1	1
		Body temperature decreased	No	0	3	3
		Body temperature fluctuation	No	0	1	1
		Body temperature increased	Yes	0	35	35
		Head circumference abnormal	No	0	1	1
		Lymph node palpable	No	0	1	1
		Neurological examination abnormal	No	0	1	1
		Respiratory rate decreased	No	0	1	1
		Respiratory rate increased	No	0	1	1
		Weight decreased	No	0	8	8

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
	Protein and chemistry analyses NEC	C-reactive protein increased	No	0	13	13
		Inflammatory marker increased	No	0	2	2
		Protein total increased	No	0	1	1
	Renal and urinary tract investigations and urinalyses	Urine output decreased	No	0	1	1
		White blood cells urine positive	No	0	1	1
	Water, electrolyte and mineral investigations	Serum ferritin increased	No	0	1	1
Metabolism and nutrition disorders	Acid-base disorders	Acidosis	No	3	1	4
		Ketoacidosis	No	0	1	1
		Ketosis	No	0	1	1
		Lactic acidosis	No	1	0	1
		Metabolic acidosis	No	1	0	1
	Appetite and general nutritional disorders	Appetite disorder	No	0	1	1
		Decreased appetite	Yes	0	40	40
		Feeding disorder neonatal	No	0	1	1
		Hypophagia	Yes	0	3	3
		Increased appetite	No	0	1	1
		Weight gain poor	No	0	2	2
	Diabetic complications	Diabetic ketoacidosis	No	1	0	1
	Electrolyte and fluid balance conditions	Dehydration	No	0	6	6
		Fluid intake reduced	No	0	13	13
		Hypokalaemia	No	2	0	2
		Hyponatraemia	No	0	3	3
		Oligodipsia	No	0	18	18
		Polydipsia	No	0	3	3
	Food intolerance syndromes	Cow's milk intolerance	No	0	1	1
		Lactose intolerance	No	0	2	2
	Glucose metabolism disorders (incl diabetes mellitus)	Hyperglycaemia	No	0	1	1
		Type 1 diabetes mellitus	No	2	0	2
	Iron and trace metal metabolism disorders	Iodine deficiency	No	0	1	1
		Iron deficiency	No	0	1	1
	Metabolism disorders NEC	Metabolic disorder	No	0	1	1
	Protein and amino acid metabolism disorders NEC	Hypoalbuminaemia	No	0	2	2
	Vitamin related disorders	Vitamin B12 deficiency	No	0	1	1
Musculoskeletal and connective tissue disorders	Connective tissue disorders (excl congenital)	Myofascitis	No	0	1	1
	Joint disorders	Arthralgia	No	0	3	3

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
		Arthritis	Yes	0	3	3
		Joint hyperextension	No	0	4	4
		Joint range of motion decreased	No	0	1	1
		Joint stiffness	No	0	1	1
		Joint swelling	No	0	3	3
	Muscle disorders	Muscle disorder	No	0	2	2
		Muscle rigidity	No	0	8	8
		Muscle spasms	No	0	16	16
		Muscle tightness	No	0	1	1
		Muscle twitching	No	0	16	16
		Muscular weakness	Yes	0	6	6
		Myalgia	No	0	2	2
		Myosclerosis	No	0	1	1
		Myositis	No	0	2	2
		Nuchal rigidity	No	0	2	2
		Trismus	No	0	1	1
	Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)	Facial asymmetry	No	0	1	1
		Foot deformity	No	0	1	1
		Hip deformity	No	0	1	1
	Musculoskeletal and connective tissue disorders NEC	Mastication disorder	No	0	1	1
		Mobility decreased	No	0	5	5
		Muscle contracture	No	0	1	1
		Musculoskeletal stiffness	No	0	14	14
		Pain in extremity	No	0	20	20
		Posture abnormal	No	0	4	4
		Soft tissue necrosis	No	1	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Cutaneous neoplasms benign	Melanocytic naevus	No	1	0	1
	Haematopoietic neoplasms (excl leukaemias and lymphomas)	Histiocytosis haematophagic	No	1	0	1
	Leukaemias	B precursor type acute leukaemia	No	1	0	1
	Nervous system neoplasms malignant and unspecified NEC	Neuroblastoma	No	1	0	1
	Skin neoplasms malignant and unspecified	Neoplasm skin	No	1	0	1
Nervous system disorders	Central nervous system infections and inflammations	Central nervous system inflammation	No	0	1	1
		Encephalitis	Yes	4	0	4

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
		Myelitis transverse	No	1	0	1
	Central nervous system vascular disorders	Cerebral haemorrhage	No	1	0	1
		Cerebral ischaemia	No	2	0	2
		Cerebrovascular disorder	No	1	0	1
		Thalamus haemorrhage	No	1	0	1
	Cranial nerve disorders (excl neoplasms)	Facial paresis	Yes	3	0	3
		Tongue paralysis	Yes	1	0	1
		VIIth nerve paralysis	Yes	2	0	2
		VIth nerve paralysis	Yes	3	0	3
	Demyelinating disorders	Demyelination	No	2	0	2
	Encephalopathies	Encephalopathy	Yes	3	0	3
		Periventricular leukomalacia	No	1	0	1
	Headaches	Headache	No	0	2	2
	Increased intracranial pressure and hydrocephalus	Hydrocephalus	No	1	0	1
	Mental impairment disorders	Autism	No	2	0	2
		Cognitive disorder	No	0	1	1
		Disturbance in attention	No	0	2	2
		Mental impairment	No	0	4	4
		Mental retardation	No	0	1	1
	Movement disorders (incl parkinsonism)	Bradykinesia	No	0	1	1
		Choreoathetosis	No	0	1	1
		Dyskinesia	No	0	20	20
		Dystonia	No	0	1	1
		Extrapyramidal disorder	No	1	0	1
		Head titubation	No	0	1	1
		Hemiparesis	Yes	2	0	2
		Hypokinesia	No	0	7	7
		Masked facies	No	0	2	2
		Monoparesis	Yes	3	0	3
		Monoplegia	Yes	1	0	1
		Motor developmental delay	No	0	2	2
		Movement disorder	No	0	3	3
		Opisthotonus	No	0	9	9
		Paresis	Yes	2	0	2
		Postictal paralysis	Yes	1	0	1
		Psychomotor hyperactivity	No	0	4	4
		Spastic diplegia	No	1	0	1
		Tremor	No	0	22	22
	Neurological disorders NEC	Altered state of consciousness	No	6	0	6
		Aphasia	No	1	0	1
		Areflexia	No	0	4	4
		Ataxia	No	0	3	3
		Balance disorder	No	0	9	9
		Cerebellar ataxia	No	0	2	2

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
		Cerebral disorder	No	0	1	1
		Clonus	No	0	8	8
		Crying	Yes	0	264	264
		Depressed level of consciousness	No	56	0	56
		Dizziness	No	0	2	2
		Drooling	No	0	5	5
		Dysstasia	No	0	2	2
		Fontanelle bulging	No	0	2	2
		Hyperaesthesia	No	0	10	10
		Hyperreflexia	No	0	1	1
		Hypoaesthesia	Yes	0	1	1
		Hyporeflexia	No	0	2	2
		Hyporesponsive to stimuli	No	0	1	1
		Lethargy	No	0	7	7
		Loss of consciousness	No	69	0	69
		Meningism	No	0	1	1
		Motor dysfunction	No	0	6	6
		Myoclonus	No	0	13	13
		Nervous system disorder	No	0	2	2
		Neurological symptom	No	0	1	1
		Nystagmus	No	0	3	3
		Poor sucking reflex	No	0	1	1
		Postictal state	No	0	3	3
		Presyncope	No	6	1	7
		Psychomotor skills impaired	No	0	3	3
		Sensory loss	No	0	1	1
		Slow response to stimuli	No	24	0	24
		Somnolence	Yes	0	72	72
		Speech disorder	No	0	1	1
		Speech disorder developmental	No	0	3	3
		Stupor	Yes	0	2	2
		Subdural effusion	No	0	2	2
		Syncope	No	9	0	9
		Unresponsive to stimuli	No	21	1	22
	Neuromuscular disorders	Autonomic nervous system imbalance	No	0	1	1
		Cholinergic syndrome	No	0	2	2
		Hypertonia	No	0	27	27
		Hypotonia	No	0	165	165
		Hypotonic-hyporesponsive episode	Yes	2	100	102
		Muscle contractions involuntary	No	0	2	2
		Muscle spasticity	No	0	1	1
		Sensorimotor disorder	No	0	1	1
	Peripheral neuropathies	Demyelinating polyneuropathy	No	1	0	1
		Guillain-Barre syndrome	Yes	2	0	2

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
		Neuropathy peripheral	Yes	0	2	2
	Seizures (incl subtypes)	Atonic seizures	Yes	1	0	1
		Clonic convulsion	Yes	5	0	5
		Complex partial seizures	Yes	1	0	1
		Convulsion	Yes	107	0	107
		Convulsions local	Yes	1	0	1
		Epilepsy	Yes	20	0	20
		Febrile convulsion	Yes	98	0	98
		Grand mal convulsion	Yes	33	0	33
		Infantile spasms	Yes	8	1	9
		Lennox-Gastaut syndrome	No	1	0	1
		Partial seizures	Yes	7	0	7
		Petit mal epilepsy	Yes	5	0	5
		Seizure like phenomena	No	3	0	3
		Status epilepticus	No	6	0	6
		Tonic clonic movements	Yes	0	1	1
		Tonic convulsion	Yes	4	0	4
	Sleep disturbances (incl subtypes)	Cataplexy	No	1	0	1
		Circadian rhythm sleep disorder	No	0	2	2
		Hypersomnia	No	0	5	5
		Poor quality sleep	No	0	2	2
	Spinal cord and nerve root disorders	Spinal cord compression	No	0	1	1
	Structural brain disorders	Cerebral atrophy	No	2	0	2
		Cerebral ventricle dilatation	No	1	0	1
		Subdural hygroma	No	0	1	1
Pregnancy, puerperium and perinatal conditions	Neonatal and perinatal conditions	Poor weight gain neonatal	No	0	1	1
	Pregnancy, labour, delivery and postpartum conditions	Live birth	No	0	1	1
Psychiatric disorders	Anxiety disorders and symptoms	Agitation	No	0	19	19
		Anxiety	No	0	6	6
		Anxiety disorder due to a general medical condition	No	0	1	1
		Fear	No	0	1	1
		Nervousness	Yes	0	1	1
		Tension	No	0	1	1
	Changes in physical activity	Bruxism	No	0	1	1
		Decreased activity	No	0	6	6
		Restlessness	Yes	0	78	78
		Stereotypy	No	0	1	1
	Communication disorders and disturbances	Mutism	No	0	1	1
		Phonological disorder	No	0	1	1

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
		Screaming	No	0	31	31
	Deliria (incl confusion)	Disorientation	No	0	2	2
	Depressed mood disorders and disturbances	Psychomotor retardation	No	0	1	1
		Tearfulness	Yes	0	2	2
	Dissociative disorders	Dissociation	No	0	1	1
	Disturbances in thinking and perception	Delusion	No	0	1	1
	Eating disorders and disturbances	Eating disorder	No	0	2	2
		Food aversion	Yes	0	5	5
	Mood disorders and disturbances NEC	Apathy	No	0	19	19
		Emotional distress	No	0	1	1
		Listless	No	0	3	3
		Moaning	No	0	4	4
	Personality disorders and disturbances in behaviour	Indifference	No	0	2	2
		Personality change	No	0	3	3
	Psychiatric and behavioural symptoms NEC	Abnormal behaviour	No	0	10	10
		Breath holding	No	0	2	2
		Decreased eye contact	No	0	3	3
		Staring	No	0	42	42
	Schizophrenia and other psychotic disorders	Psychotic disorder	No	1	0	1
	Sleep disorders and disturbances	Insomnia	No	0	19	19
		Middle insomnia	No	0	3	3
		Sleep disorder	No	0	12	12
Renal and urinary disorders	Renal disorders (excl nephropathies)	Oliguria	No	0	1	1
		Pyelocaliectasis	No	0	1	1
		Renal impairment	No	0	2	2
	Ureteric disorders	Ureteric stenosis	No	0	1	1
	Urinary tract signs and symptoms	Enuresis	No	0	1	1
		Polyuria	No	0	2	2
Reproductive system and breast disorders	Reproductive tract disorders NEC	Oedema genital	No	0	1	1
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Asthma	No	2	0	2
		Bronchial hyperreactivity	No	1	0	1
		Bronchitis chronic	Yes	0	1	1
		Bronchospasm	No	0	3	3
		Obstructive airways disorder	No	1	0	1
	Lower respiratory tract	Atelectasis	No	1	0	1

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
	disorders (excl obstruction and infection)					
		Emphysema	No	0	1	1
		Interstitial lung disease	No	1	0	1
		Pneumonia aspiration	No	2	0	2
	Neonatal respiratory disorders	Apparent life threatening event	No	10	0	10
		Infantile apnoeic attack	No	1	0	1
	Respiratory disorders NEC	Acute respiratory failure	No	1	0	1
		Apnoea	Yes	47	0	47
		Apnoeic attack	Yes	0	6	6
		Asphyxia	No	1	1	2
		Aspiration	No	0	2	2
		Choking	No	3	0	3
		Choking sensation	No	0	1	1
		Cough	Yes	0	37	37
		Cyanosis central	No	1	0	1
		Dry throat	No	0	1	1
		Dysphonia	No	0	2	2
		Dyspnoea	No	0	30	30
		Hiccups	No	0	1	1
		Hypopnoea	Yes	0	1	1
		Hypoventilation	Yes	2	0	2
		Hypoxia	No	1	0	1
		Increased upper airway secretion	No	0	3	3
		Lung disorder	No	0	1	1
		Oropharyngeal pain	No	0	1	1
		Productive cough	Yes	0	2	2
		Rales	No	0	1	1
		Respiration abnormal	No	0	18	18
		Respiratory arrest	Yes	10	0	10
		Respiratory depression	Yes	1	0	1
		Respiratory disorder	No	0	12	12
		Respiratory failure	No	1	0	1
		Respiratory tract congestion	No	0	1	1
		Respiratory tract inflammation	No	0	1	1
		Rhinorrhoea	No	0	4	4
		Sleep apnoea syndrome	No	0	2	2
		Sneezing	No	0	2	2
		Snoring	No	0	1	1
		Tachypnoea	No	0	4	4
		Upper respiratory tract congestion	No	0	1	1
		Upper respiratory tract inflammation	No	0	2	2
		Yawning	No	0	1	1
	Upper respiratory tract disorders (excl infections)	Epistaxis	No	0	2	2

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
		Nasal congestion	No	0	1	1
		Pharyngeal erythema	No	0	13	13
		Rhinitis allergic	No	0	1	1
		Stridor	No	3	0	3
		Tonsillar disorder	No	0	1	1
		Tonsillar hypertrophy	No	0	1	1
Skin and subcutaneous tissue disorders	Angioedema and urticaria	Angioedema	Yes	12	0	12
		Urticaria	Yes	0	52	52
		Urticaria papular	No	0	3	3
		Urticaria thermal	No	0	2	2
	Cornification and dystrophic skin disorders	Keloid scar	No	0	1	1
		Skin hypertrophy	No	0	1	1
	Cutaneous neoplasms benign	Dermal cyst	No	0	1	1
	Epidermal and dermal conditions	Blister	No	0	9	9
		Decubitus ulcer	No	0	1	1
		Dermatitis	Yes	0	2	2
		Dermatitis allergic	Yes	0	4	4
		Dermatitis atopic	Yes	0	8	8
		Dermatitis diaper	Yes	0	2	2
		Dry skin	No	0	2	2
		Eczema	Yes	0	16	16
		Erythema	Yes	0	104	104
		Erythema multiforme	Yes	3	0	3
		Erythrosis	No	0	1	1
		Generalised erythema	Yes	0	4	4
		Granuloma skin	No	0	1	1
		Lichen striatus	No	0	1	1
		Macule	Yes	0	1	1
		Neurodermatitis	Yes	0	4	4
		Palmar erythema	Yes	0	1	1
		Papule	Yes	0	5	5
		Pemphigoid	No	1	0	1
		Prurigo	Yes	0	2	2
		Pruritus	Yes	0	13	13
		Rash	Yes	0	83	83
		Rash erythematous	Yes	0	14	14
		Rash generalised	Yes	0	13	13
		Rash macular	Yes	0	19	19
		Rash maculo-papular	Yes	0	15	15
		Rash morbilliform	Yes	0	7	7
		Rash papular	Yes	0	4	4
		Rash pruritic	Yes	0	1	1
		Rash vesicular	Yes	0	3	3
		Scab	No	0	3	3

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
		Scar	No	0	5	5
		Seborrhoeic dermatitis	Yes	0	1	1
		Skin chapped	No	0	1	1
		Skin discolouration	No	0	30	30
		Skin disorder	No	0	1	1
		Skin exfoliation	Yes	0	4	4
		Skin induration	No	0	1	1
		Skin lesion	No	0	4	4
		Skin reaction	No	0	2	2
		Skin tightness	No	0	1	1
		Skin warm	No	0	16	16
		Stevens-Johnson syndrome	Yes	1	0	1
		Swelling face	Yes	0	6	6
		Toxic skin eruption	Yes	0	1	1
		Yellow skin	No	2	0	2
	Pigmentation disorders	Schamberg's disease	No	0	1	1
		Skin depigmentation	No	0	4	4
	Skin and subcutaneous tissue disorders NEC	Erythema nodosum	No	0	2	2
		Lipoatrophy	No	1	0	1
		Skin erosion	No	0	1	1
		Skin ulcer	No	0	2	2
		Subcutaneous nodule	No	0	2	2
	Skin appendage conditions	Acne	Yes	0	1	1
		Cold sweat	No	0	4	4
		Hair growth abnormal	No	0	1	1
		Hyperhidrosis	No	0	14	14
		Hypertrichosis	No	0	2	2
	Skin vascular abnormalities	Acute haemorrhagic oedema of infancy	No	1	0	1
		Ecchymosis	No	0	5	5
		Henoch-Schonlein purpura	No	2	0	2
		Increased tendency to bruise	No	0	1	1
		Livedo reticularis	No	0	3	3
		Lividity	No	0	7	7
		Petechiae	No	0	49	49
		Purpura	No	0	8	8
		Skin oedema	No	0	1	1
		Spider naevus	No	0	1	1
Social circumstances	Lifestyle issues	Disability	No	1	0	1
		Immobile	No	0	3	3
Surgical and medical procedures	Gastrointestinal therapeutic procedures	Colectomy	No	0	1	1
		Ileostomy	No	0	1	1
		Small intestinal resection	No	0	1	1
	Haematological and lymphoid tissue therapeutic	Haemostasis	No	0	1	1

System Organ Class (SOC)	HLGT	Event (PT)	Listed	Serious	Non-Serious	Total Cases for BR period
	procedures					
	Nervous system, skull and spine therapeutic procedures	Neurosurgery	No	0	1	1
	Respiratory tract therapeutic procedures	Endotracheal intubation	No	0	1	1
		Mechanical ventilation	No	0	1	1
	Skin and subcutaneous tissue therapeutic procedures	Skin lesion excision	No	0	1	1
	Soft tissue therapeutic procedures	Tenotomy	No	0	1	1
	Therapeutic procedures and supportive care NEC	Abscess drainage	No	0	2	2
		Debridement	No	0	1	1
		Enteral nutrition	No	0	1	1
		Macrophage activation	No	0	1	1
		Off label use	No	0	22	22
		Resuscitation	No	0	3	3
		Surgery	No	0	1	1
Vascular disorders	Arteriosclerosis, stenosis, vascular insufficiency and necrosis	Peripheral coldness	Yes	0	5	5
	Decreased and nonspecific blood pressure disorders and shock	Circulatory collapse	Yes	8	0	8
		Hypotension	Yes	0	1	1
		Shock	Yes	5	0	5
	Embolism and thrombosis	Jugular vein thrombosis	No	1	0	1
		Thrombosis	No	1	0	1
	Vascular disorders NEC	Capillary disorder	No	0	1	1
		Flushing	No	0	4	4
		Hyperaemia	No	0	11	11
		Pallor	No	0	158	158
		Vasodilatation	No	0	2	2
	Vascular haemorrhagic disorders	Haematoma	No	0	16	16
		Haemorrhage	No	2	0	2
	Vascular hypertensive disorders	Hypertension	No	0	2	2
	Vascular inflammations	Kawasaki's disease	No	0	7	7
		Vasculitis	Yes	1	0	1

APPENDIX 2 : SUMMARY of CASES OF GAZE PALSY SINCE LAUNCH

Summary of cases of Gaze palsy since launch

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0559034A	12-Feb-09	Improved	12 Weeks	Male	Infanrix hexa		7 Hours	Febrile convulsion, Gaze palsy, Musculoskeletal stiffness	Poland	
B0564167A	06-Mar-09	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		3 Minutes	Loss of consciousness, Crying, Pyrexia, Inflammation, Pain, Diarrhoea, Pallor, Gaze palsy, Hypotonia	Netherlands	
B0566112A	20-Mar-09	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		3 Minutes	Convulsion, Loss of consciousness, Gaze palsy, Depressed level of consciousness, Respiration abnormal, Injection site swelling, Pyrexia, Crying, Decreased appetite, Oligodipsia	Netherlands	Apnoea
B0580036A	19-Jun-09	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Convulsion, Loss of consciousness, Depressed level of consciousness, Gaze palsy, Oligodipsia, Hypotonia, Pallor, Pyrexia	Netherlands	
B0581097A	26-Jun-09	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Depressed level of consciousness, Gaze palsy, Sense of oppression, Pallor, Hypotonia, Vomiting, Pyrexia	Netherlands	Nasopharyngitis

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0599801A	26-Oct-09	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		3 Seconds	Depressed level of consciousness, Crying, Hyperhidrosis, Vasodilatation, Gaze palsy, Pyrexia, Inflammation	Netherlands	
B0613669A	09-Dec-09	Resolved	2 Months	Male	Infanrix-polio-HIB, Infanrix hexa		2 Days	Infantile spasms, Gaze palsy, Muscle spasms, Sleep disorder, Condition aggravated, Motor dysfunction, Hypertonia	France	
B0614538A	08-Dec-09	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		5 Hours	Respiration abnormal, Gaze palsy, Loss of consciousness, Pallor, Cyanosis, Hypotonia	Netherlands	
B0642185A	19-Mar-10	Unknown	15 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		5 Days	Altered state of consciousness, Gaze palsy, Tonic convulsion, Convulsion, Epilepsy, Gastroenteritis, Febrile convulsion, Hypertonia, Ear infection, Gastritis, Nasopharyngitis, Hypotonia, Body temperature increased, Vomiting, Diarrhoea, Pyrexia	Czech Republic	Psychomotor retardation, Psychomotor skills impaired
B0646907A	09-Apr-10	Resolved	11 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		2 Hours	Convulsion, Pallor, Gaze palsy, Loss of consciousness, Hypotonia, Pyrexia, Pain, Fatigue	Netherlands	
B0647634A	13-Apr-10	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Gaze palsy, Pyrexia, Mental impairment, Crying	Netherlands	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0651462A	03-May-10	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		6 Hours	Loss of consciousness, Gaze palsy, Pallor, Cyanosis, Hypotonia, Vomiting	Netherlands	
B0652090A	07-May-10	Resolved	12 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Convulsion, Gaze palsy, Loss of consciousness, Pyrexia, Otitis media, Pallor	Netherlands	Nasopharyngitis
B0656946A	21-May-10	Resolved	1 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		8 Hours	Febrile convulsion, Loss of consciousness, Gaze palsy, Pain, Skin warm, Respiration abnormal, Pyrexia, Crying	Netherlands	
B0660020A	10-Jun-10	Resolved	11 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		2 Hours	Pneumonia, Loss of consciousness, Gaze palsy, Convulsion, Nasopharyngitis, Drooling, Pallor, Pyrexia	Netherlands	
B0662920A	03-Jun-10	Resolved	2 Years	Female	Infanrix hexa		5 Hours	Hypotonic-hyporesponsive episode, Depressed level of consciousness, Gaze palsy, Respiration abnormal, Injection site inflammation, Vomiting, Cold sweat, Injection site pain, Pallor, Pyrexia	Netherlands	
B0668856A	05-Aug-10	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		4 Hours	Gaze palsy, Crying, Pyrexia, Myoclonus	Netherlands	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0669299A	10-Aug-10	Unknown	6 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Epilepsy, Grand mal convulsion, Loss of consciousness, Gaze palsy, Cyanosis, Pyrexia, Salivary hypersecretion, Somnolence, Hyperaemia, Escherichia urinary tract infection, Electroencephalogram abnormal, Drooling, Tremor, Muscle spasms, Partial seizures, I	Italy	Haemangioma, Mental impairment
B0669438A	11-Aug-10	Resolved	16 Months	Male	Infanrix hexa		1 Days	Febrile convulsion, Gaze palsy, Unresponsive to stimuli, Pyrexia	Poland	
B0675842A	22-Sep-10	Unknown	12 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Cetirizine hydrochloride, Infanrix hexa, Pneumococcal vaccines (Non-GSK)	4 Hours	Convulsion, Leukocytosis, Shock, Gaze palsy, Loss of consciousness, Pyrexia	Italy	Urticaria
B0681967A	28-Oct-10	Resolved	2 Months	Female	Infanrix hexa, Meningococcal polysaccharide vaccine group C (Non-GSK), Pneumococcal vaccines (Non-GSK)		2 Hours	Gaze palsy, Hypotonia, Pallor	Spain	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0682745A	03-Nov-10	Unresolved	6 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Hours	Convulsion, Loss of consciousness, Gaze palsy, Pallor, Pyrexia, Crying	Netherlands	
B0683261A	05-Nov-10	Resolved	3 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Magaldrate, Ranitidine hydrochloride	10 Days	Gaze palsy, Hypotonia	Italy	
B0687865A	07-Dec-10	Resolved	11 Months	Male	Infanrix hexa	Priorix	2 Days	Loss of consciousness, Gaze palsy, Pallor, Hypotonia	Italy	
B0690071A	17-Dec-10	Unknown	3 Months	Male	Infanrix hexa, Synflorix		8 Hours	Hypotonic-hyporesponsive episode, Gaze palsy, Opisthotonus, Pallor, Apathy, Fear, Agitation, Hypotonia, Crying	Czech Republic	Dermatitis atopic
B0712712A	05-Apr-11	Resolved	13 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Hours	Loss of consciousness, Depressed level of consciousness, Convulsion, Gaze palsy, Respiration abnormal, Pallor, Hypotonia, Drooling, Cyanosis, Pyrexia, Vomiting	Netherlands	
B0717794A	06-May-11	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		36 Hours	Loss of consciousness, Apnoea, Depressed level of consciousness, Gaze palsy, Pallor, Cyanosis, Hypotonia, Peripheral coldness, Pyrexia	Netherlands	
B0722407A	24-May-11	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		14 Hours	Gaze palsy, Hypertonia, Pyrexia, Dyskinesia, Somnolence, Feeling hot	Netherlands	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0739945A	11-Aug-11	Unknown	5 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Convulsion, Gaze palsy, Clonus, Pyrexia	Italy	
D0042391A	04-Nov-03	Unresolved	2 Months	Female	Infanrix hexa		Same day	Cytomegalovirus infection, Pyrexia, Pallor, Hypotension, Tachypnoea, General physical health deterioration, Gaze palsy, Tachycardia, Hypotonia, Anuria, Transaminases increased, Disseminated intravascular coagulation, Haemolysis, Haematochezia, Hyperkalaem	Germany	Tobacco user, Alcohol use
D0042827A	07-Jan-04	Resolved	15 Weeks	Female	Infanrix hexa	Infanrix hexa	4 Hours	Hypotonic-hyporesponsive episode, Crying, Hypotonia, Vomiting, Pallor, Altered state of consciousness, Gaze palsy	Germany	
D0044170A	08-Jul-04	Resolved	3 Months	Female	Infanrix hexa		95 Minutes	Tonic convulsion, Opisthotonus, Pallor, Gaze palsy, Muscle twitching, Salivary hypersecretion, Crying	Germany	
D0047035A	07-Jul-05	Unknown	4 Months	Female	Infanrix hexa	Infanrix hexa	9 Days	Nervous system disorder, Developmental delay, Abnormal behaviour, Social avoidant behaviour, Gaze palsy, Syncope, Pallor, Apathy, Extrapyramidal disorder	Germany	Dermatitis atopic

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0049384A	12-Apr-06	Resolved	2 Months	Male	Infanrix hexa		10 Minutes	Hypotonic-hyporesponsive episode, Pallor, Hypotonia, Depressed level of consciousness, Gaze palsy, Immobile, Heart rate increased, Areflexia	Germany	Hyperbilirubinaemia, Strabismus, Jaundice
D0049670A	09-May-06	Unknown	5 Months	Female	Infanrix hexa		12 Hours	Epilepsy, Convulsion, Breath sounds abnormal, Gaze palsy, Staring, Depressed level of consciousness, Muscle twitching, Salivary hypersecretion, Crying, General physical health deterioration, Diarrhoea, Gastroenteritis, Haematochezia, Bronchitis, Nausea, V	Germany	
D0054763A	08-Oct-07	Resolved	3 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Hypotonic-hyporesponsive episode, Febrile convulsion, Pyrexia, Urinary tract infection, Leukocyturia, Haematuria, Hypotonia, Movement disorder, Gaze palsy, Pallor, Vaccination complication	Germany	Familial risk factor
D0056301A	27-Feb-08	Resolved	3 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		10 Hours	Hypotonic-hyporesponsive episode, Hypotonia, Retching, Vomiting, Pallor, Gaze palsy, Depressed level of consciousness, Vaccination complication, Gastroenteritis, Abnormal faeces, Diarrhoea	Germany	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0056982A	21-Apr-08	Unresolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Partial seizures, Developmental delay, Hypotonia, Plagiocephaly, Gaze palsy, Salivary hypersecretion, Daydreaming, Fatigue, Oxygen saturation decreased, Pyrexia	Germany	Vacuum extractor delivery, Foetal monitoring abnormal, Feeding disorder neonatal, Weight decrease neonatal
D0057056A	23-Apr-08	Unknown	4 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Zymafluor D, Paracetamol	4 Days	Cerebral haemorrhage, Convulsion, Partial seizures, Status epilepticus, Rhinitis, Somnolence, Oligodipsia, Gaze palsy, Unresponsive to stimuli, Oxygen saturation decreased, Hypothermia, Apnoea, Pallor, Oedema, Pneumonia, Brain oedema, Pyrexia, Pyelonephri	Germany	Premature baby, Respiratory distress, Sleep apnoea syndrome, Bradycardia, Sepsis, Retinopathy congenital, Familial risk factor
D0058126A	21-Jul-08	Unknown	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Epilepsy, Myoclonic epilepsy, Grand mal convulsion, Status epilepticus, Pyrexia, Screaming, Hyperhidrosis, Apathy, Respiration abnormal, Use of accessory respiratory muscles, Gaze palsy, Sleep disorder, Respiratory rate increased, Musculoskeletal stiffnes	Germany	Microcephaly, Foetal growth restriction, Hyperbilirubinaemia, Urinary tract obstruction

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0058650A	08-Sep-08	Unresolved	5 Months	Male	Infanrix hexa, DTPa-HepB-IPV-HIB (Non-GSK)		2 Months	Infantile spasms, Grand mal convulsion, Developmental delay, Gaze palsy, Salivary hypersecretion, Fatigue, Skin discolouration, Unresponsive to stimuli, Febrile infection, Otitis media, Hypotonia, Illusion, Neurodermatitis, Atopy	Germany	Delivery, Jaundice neonatal
D0058976A	09-Oct-08	Unknown	3 Months	Male	Infanrix hexa		0 Days	Depressed level of consciousness, Gaze palsy, Somnolence, Vomiting projectile, Pyrexia, Asthenia, Pallor	Germany	
D0059733A	03-Dec-08	Unknown	4 Months	Unknown	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		15 Days	Vaccination complication, Injury, Fluid intake reduced, Fatigue, Listless, Body temperature increased, Vomiting, General physical health deterioration, Insomnia, Crying, Gaze palsy, Dizziness, Haemoglobin decreased, Haemorrhagic anaemia, Thrombosis, Retin	Germany	Premature delivery
D0060368A	03-Feb-09	Resolved with Sequelae	4 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK), Dimethicone	9 Days	Epilepsy, Crying, Gaze palsy, Asthenia, Dyskinesia, Body temperature increased, Gastroenteritis adenovirus, Gastroenteritis norovirus, Dermatitis diaper, Motor developmental delay	Germany	Flatulence, Delivery
D0060421A	06-Feb-09	Resolved	3 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Gaze palsy, Chills, Pyrexia, Vomiting	Germany	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0060869A	13-Mar-09	Resolved	14 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	0 Days	Febrile convulsion, Pyrexia, Opisthotonus, Gaze palsy, Tremor, Unresponsive to stimuli, Fatigue, Agitation, Crying	Germany	
D0060889A	16-Mar-09	Unresolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Rotavirus vaccine, Paracetamol, Ergocalciferol, Ferrous glycine sulphate	14 Days	Seizure like phenomena, Gaze palsy, Crying, Opisthotonus, Benign familial neonatal convulsions, Epilepsy, Hypertonia, Unresponsive to stimuli, Dyskinesia, Lividity, Psychomotor hyperactivity, Excessive masturbation	Germany	Impetigo, Iron deficiency anaemia, Coordination abnormal, Physiotherapy
D0061561A	07-May-09	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Convulsion, Cyanosis, Apnoea, Musculoskeletal stiffness, Gaze palsy	Germany	
D0061751A	19-May-09	Resolved	9 Weeks	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		36 Hours	Convulsion, Gaze palsy, Staring, Unresponsive to stimuli, Opisthotonus, Hypotonia, Abnormal faeces	Germany	Plagiocephaly
D0061756A	27-May-09	Unknown	2 Years	Male	Infanrix hexa		1 Days	Febrile convulsion, Pyrexia, Convulsion, Loss of consciousness, Depressed level of consciousness, Musculoskeletal stiffness, Gaze palsy, Cyanosis, Disorientation, Viral infection, Injection site erythema, Injection site swelling	Germany	Fall, Haematoma

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0062153A	02-Jul-09	Resolved	2 Months	Female	Rotavirus vaccine, Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Febrile convulsion, Pyrexia, Gaze palsy, Muscle twitching	Germany	
D0064655B	02-Dec-09	Unknown	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Rotavirus vaccine	0 Days	Apparent life threatening event, Cyanosis, Hypotonia, Gaze palsy, Fatigue, Somnolence, Sleep apnoea syndrome, Gastroenteritis rotavirus, Apnoea, Apathy	Germany	
D0066414A	08-Feb-10	Unresolved	5 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK), Ergocalciferol	0 Days	Convulsion, Febrile convulsion, Atonic seizures, Grand mal convulsion, Pyrexia, Diarrhoea, Gaze palsy, Cyanosis, Disturbance in attention, Staring, Pharyngeal erythema, Rhinitis, Leukocytosis, Gastroenteritis, Gastroenteritis norovirus	Germany	
D0066491A	15-Feb-10	Resolved	2 Months	Female	Synflorix, Infanrix hexa	Ferrous glycine sulphate, Vitamin D	6 Hours	Convulsion, Gaze palsy, Muscle spasms, Tremor	Germany	Premature baby
D0067186A	09-Apr-10	Resolved	14 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Febrile convulsion, Loss of consciousness, Cataplexy, Gaze palsy, Pyrexia, Vaccination complication	Germany	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0067732A	25-May-10	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Convulsion, Gaze palsy, Musculoskeletal stiffness, Cyanosis	Germany	
D0067882A	08-Jun-10	Resolved	5 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Hypotonic-hyporesponsive episode, Gaze palsy, Hypotonia, Mental impairment, Feeling abnormal, Neutropenia	Germany	Abnormal weight gain, Rhinitis, Productive cough, Vomiting, Gastrooesophageal reflux disease, Testicular retraction
D0068260A	09-Jul-10	Resolved	23 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Febrile convulsion, Pyrexia, Diarrhoea, Gaze palsy, Grand mal convulsion, Pallor, Vomiting, Gastroenteritis	Germany	Febrile infection, Gastroenteritis, Vomiting
D0068398A	23-Jul-10	Resolved	8 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Febrile convulsion, Gaze palsy, Respiratory arrest, Respiratory tract infection, Pharyngeal erythema, Feeling of relaxation, Skin discolouration, Vaccination complication	Germany	
D0068812A	09-Sep-10	Unknown	13 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Weeks	Convulsion, Gaze palsy, Depressed level of consciousness, Pyrexia, Musculoskeletal stiffness, Fall, Concussion, Contusion, Hypotonia	Germany	Cyanosis

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0068914A	21-Sep-10	Resolved	14 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	0 Days	Febrile convulsion, Pyrexia, Fatigue, Gaze palsy, Loss of consciousness, Grand mal convulsion, Oxygen saturation decreased, Disorientation, Somnolence, Tachycardia, Pharyngeal erythema	Germany	Therapy regimen changed
D0069309A	03-Nov-10	Unknown	4 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Febrile convulsion, Pyrexia, Musculoskeletal stiffness, Gaze palsy, Somnolence, Transaminases increased, Pharyngeal erythema, Tympanic membrane hyperaemia	Germany	Cardiac murmur
D0071075A	18-Apr-11	Unknown	3 Months	Male	Rotavirus vaccine, Infanrix hexa, Synflorix		1 Days	Thalamus haemorrhage, Convulsion, Facial paresis, Hemiparesis, Hypophagia, Restlessness, Pyrexia, Screaming, Somnolence, Pallor, Hyperaesthesia, Eyelid oedema, Abdominal distension, Hypotonia, Apnoea, Gaze palsy	Germany	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0071143A	26-Apr-11	Unknown	6 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK), Intubation, Mechanical ventilation	0 Days	Apnoea, Cyanosis, Febrile convulsion, Gaze palsy, Altered state of consciousness, Convulsion, Body temperature increased, Breath holding, Moaning, Erythema, Swelling, Hypokinesia, Pain, Pyrexia, Dyspnoea, Infection	Germany	Premature baby, Neonatal respiratory distress syndrome, Neonatal respiratory failure, Infantile apnoeic attack, Bradycardia neonatal, Hyperbilirubinaemia neonatal, Regurgitation
D0071366A	13-May-11	Unknown	12 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Convulsion, Depressed level of consciousness, Gaze palsy, Hypochromic anaemia, Pyrexia, Injection site erythema, Musculoskeletal stiffness, Iron deficiency	Germany	
D0071548A	27-May-11	Unknown	8 Months	Female	Infanrix hexa, Synflorix		1 Days	Convulsion, Gaze palsy, Cyanosis, Vaccination complication, Restlessness, Feeling hot, Staring, Muscle twitching, Dyspnoea, Hypotonia, Somnolence, General physical health deterioration, Body temperature increased	Germany	
D0071728A	15-Jun-11	Resolved	3 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	0 Days	Hypotonic-hyporesponsive episode, Eye movement disorder, Convulsion, Gaze palsy, Opisthotonus, Crying	Germany	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0072315A	08-Aug-11	Resolved	4 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Salbutamol sulphate	1 Days	Febrile convulsion, Muscle rigidity, Opisthotonus, Gaze palsy, Pyrexia	Germany	Bronchitis
D0072318A	08-Aug-11	Resolved	15 Months	Female	Infanrix hexa		0 Days	Febrile convulsion, Pyrexia, Chills, Gaze palsy, Eye movement disorder, Cyanosis, Unresponsive to stimuli, Tremor, Grand mal convulsion, Upper respiratory tract infection	Germany	Familial risk factor, Febrile convulsion, Hospitalisation, Cardiac murmur, Underweight
D0073004A	11-Oct-11	Unknown	16 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		48 Hours	Convulsion, Pallor, Gaze palsy, Depressed level of consciousness, Joint hyperextension	Germany	

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APPENDIX 3 : PSUR - 23 OCTOBER 2010 to 22 OCTOBER 2011

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16th PERIODIC SAFETY UPDATE REPORT

FOR

Infanrix™ hexa

Date	15 December 2011
Department	Biological Clinical Safety and Pharmacovigilance, GlaxoSmithKline Research and Development Site de Wavre Nord, Avenue Fleming 20, B- 1300 Wavre, Belgium
Drug Name/ Generic	Infanrix™ hexa (Combined diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliomyelitis and *Haemophilus influenzae* type b vaccine)
Review Period	23 October 2010 to 22 October 2011
International Birth Date	23 October 2000 (EU)

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15 December 2011
Date

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15.12.2011
Date

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EXECUTIVE SUMMARY

- This is the 16th Periodic Safety Update Report (PSUR) of GSK Biologicals' combined diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliomyelitis and *Haemophilus influenzae* type b vaccine (Infanrix™ hexa, hereafter referred to as 'Infanrix hexa') which covers the reporting period between 23 October 2010 to 22 October 2011.
- Infanrix hexa is currently registered in 92 countries.During the period under review, no regulatory actions have been taken for safety reasons.
- There have been no amendments to the Reference Safety Information (RSI) in the current reporting period.
- Post-marketing exposure to Infanrix hexa during the period is estimated to be between 3 075 423 and 12 301 693 subjects. The number of subjects exposed since launch until the Data Lock Point (DLP) of this report is estimated as being between 18 232 834 and 72 931 338.
- The data received during the reporting period referred to a total of 1742 reports of which 1172 cases fulfilled the ICH E2C criteria for inclusion in the main line listings and summary tabulations of this report.
- No further amendment to the RSI is considered necessary at this time.
- No new safety signals were identified and/or evaluated during the reporting period.
- The benefit/risk profile of Infanrix hexa for active immunization of infants against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and *Haemophilus influenza* type b continues to be favourable.
- The Company will continue to monitor cases of anaemia haemolytic autoimmune, thrombocytopenia, thrombocytopenic purpura, autoimmune thrombocytopenia, idiopathic thrombocytopenic purpura, haemolytic anemia, cyanosis, injection site nodule, abcess and injection site abscess, Kawasaki's disease, important neurological events (including encephalitis and encephalopathy), Henoch-Schonlein purpura, petechiae, purpura, haematochezia, allergic reactions (including anaphylactic and anaphylactoid reactions), cases of lack of effectiveness as well as fatal cases.

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1. INTRODUCTION

This is the 16th Periodic Safety Update Report (PSUR) of GSK Biologicals' combined diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliomyelitis and *Haemophilus influenzae* type b vaccine (Infanrix™ hexa, hereafter referred to as 'Infanrix hexa') which covers the reporting period 23 October 2010 to 22 October 2011.

This PSUR covers all formulations and indications for the *combination* product Infanrix hexa and is prepared according to all applicable regulations [ICH, 1996; ICH, 2003; Volume 9A, 2008; CHMP/PhVWP, 2007; EMEA/CHMP, 2006].

1.1. Pharmacology and Indications

Infanrix hexa contains the following antigens adsorbed onto aluminium salts: diphtheria toxoid, tetanus toxoid, three purified pertussis antigens (pertussis toxoid [PT], filamentous haemagglutinin [FHA] and pertactin [PRN; 69 kiloDalton outer membrane protein], the purified major surface antigen (HBsAg) of the hepatitis B virus (HBV) and purified polyribosyl-ribitol-phosphate capsular polysaccharide (PRP) of *Haemophilus influenzae* type b (Hib), covalently bound to tetanus toxoid. It also contains three types of inactivated polio viruses (type 1: Mahoney strain; type 2: MEF-1 strain; type 3: Saukett strain).

Infanrix hexa is indicated for primary and booster immunisation against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and *Haemophilus influenzae* type b in infants from the age of 6 weeks and may be given to infants who received a first dose of hepatitis B vaccine at birth.

The primary vaccination schedule (such as 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months; 3, 5 and 11 or 12 months; 6, 10, 14 weeks) consists of three doses of 0.5 ml. An interval of at least one month should be respected between doses. If it is intended to administer Infanrix hexa according to the EPI schedule (Expanded Program on Immunisation; 6, 10, 14 weeks of age), then the vaccinee must receive a dose of hepatitis B vaccine at birth.

After a vaccination with 2 doses (e.g. 3, 5 months) of Infanrix hexa a booster dose must be given at least 6 months after the last priming dose, preferably between 11 and 13 months of age. After vaccination with 3 doses (e.g. 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months) of Infanrix hexa a booster dose may be given at least 6 months after the last priming dose and preferably before 18 months of age.

1.2. Presentations

A 0.5 ml dose of the vaccine contains not less than 30 IU of adsorbed diphtheria toxoid, not less than 40 IU of adsorbed tetanus toxoid, 25 µg of adsorbed PT, 25 µg of adsorbed FHA, 8 µg of adsorbed pertactin, 10 µg of adsorbed recombinant HBsAg protein, 40 D-antigen units of type 1 (Mahoney), 8 D-antigen units of type 2 (MEF-1) and 32 D-antigen units of type 3 (Saukett) of the polio virus. It also contains 10 µg of adsorbed purified capsular polysaccharide of Hib (PRP) covalently bound to 20-40 µg tetanus toxoid (T).

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2. WORLDWIDE MARKET AUTHORISATION STATUS

Infanrix hexa was first approved in the European Union on 23 October 2000 (centralized procedure) and is currently licensed in 92 countries. Details of all countries where Infanrix hexa is currently approved are presented in APPENDIX 1. During the period, there was no marketing authorisation withdrawal.

3. UPDATE OF REGULATORY AUTHORITY OR MARKETING AUTHORISATION HOLDER ACTIONS TAKEN FOR SAFETY REASONS

During the period under review, no actions have been taken for safety reasons concerning withdrawal, revocation, rejection, suspension or failure to obtain a renewal of a Marketing Authorisation; neither have there been any dosage modifications, changes in target population, formulation changes, restriction on distribution, or clinical trial suspension.

4. CHANGES TO REFERENCE SAFETY INFORMATION

Changes to the Reference Safety Information (RSI), including rationale, are communicated to Regulatory Agencies on an ongoing basis.

The RSI in effect at the beginning of the reporting period is presented in APPENDIX 2.

The RSI is the Global Prescriber Information (GPI) of the Global Datasheet (GDS) version 10 dated 21 October 2010; the RSI is highlighted in this document by gray shading.

There were no changes to the RSI during the time period of this report.

5. PATIENT EXPOSURE

5.1. Market Experience

Information on the actual number of people exposed to Infanrix hexa in the different countries is not available to the MAH. Therefore, the total subject exposure is approximated by the number of doses distributed which is the most reliable data available with regard to exposure for a vaccine in a post-marketing setting.

It is important to note that the sales database from which data are retrieved is an in-house 'living' database and is subject to updates and corrections depending on information provided by GSK local country subsidiaries (e.g. vaccine doses may be returned by subsidiaries to the central warehouse). These constant updates may result in discrepancies between consecutive queries of the database.

For this PSUR, the database was queried at time of PSUR preparation.

During the period covered by this report 12 301 693 doses of Infanrix hexa have been distributed. Since launch until the data lock point (DLP) of this PSUR, 72 931 338 doses

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have been distributed. As vaccination with Infanrix hexa can vary between 1 and 4 doses per subject in accordance with local recommendations and compliance with the vaccination schedule, post-marketing exposure to Infanrix hexa during the PSUR reporting period is estimated to be between 3 075 423 and 12 301 693 subjects. The number of subjects exposed since launch until the data lock point of this report is estimated to be between 18 232 834 and 72 931 338.

Refer to Section 9.4 for pregnancy exposure figures.

6. INDIVIDUAL CASE HISTORIES

6.1. Definitions

LISTEDNESS

Listedness is automatically assigned by GSK at the Medical Dictionary for Regulatory Activities (MedDRA) Preferred Term (PT) level.

Listed Event: An event is only considered listed if it is included in the RSI under all circumstances. Events that are only listed in specific situations (e.g. in overdose, for a specific indication, as part of a hypersensitivity reaction or post-treatment) are assessed as 'unlisted'. Lack of efficacy is assessed as listed. This is supported by CIOMS V which acknowledges that no vaccine can be expected to be effective in all patients.

Listed Case: A case is considered listed if all Adverse Events (AEs) are covered by the RSI when it is entered onto the safety database. This may be different from the RSI used for this PSUR. Note: For clinical trials and Post-Marketing Surveillance (PMS) cases, only serious, attributable events must be in the RSI for the case to appear as listed.

Unlisted Case: A case where at least one AE was not covered by the RSI at the time of case entry.

SERIOUSNESS

Serious Case: A case involving an untoward medical occurrence that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in disability/incapacity or is a congenital anomaly/birth defect.

Medical or scientific judgement is exercised in deciding whether other reports should also be considered serious, such as those involving important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the subject or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These events are also considered serious. Examples of such events are invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias, convulsions that do not result in hospitalisation, or development of drug dependency or drug abuse. In GSK, such medically important events are termed GSK 'medically serious AEs' (see below).

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GSK Medically Serious AE: As proposed by CIOMS V, GSK maintains a list of all events considered to be 'medically serious' that is regularly reviewed and updated by the company Safety Physicians. This list of MedDRA Lower Level Terms (LLTs) is automatically applied to all spontaneous, post-marketing and literature cases as they are entered onto the safety database. Inclusion of 'medically serious' events makes the case serious at case level.

OTHER DEFINITIONS

Attributability: A clinical trial case is classified as 'attributable' if the investigator or the company consider there is a reasonable possibility that a serious AE was caused by the study medication. These cases may also contain individual non-serious AEs. A clinical trial case is also considered 'attributable' if the investigator does not specify causality for any serious AE.

Primary Adverse Event: The main AE described by the reporter. If a diagnosis and associated signs/symptoms have been provided, GSK will consider the diagnosis the primary AE. Where the main AE is not clear, GSK assigns the most serious medical condition the reporter thought was associated with the drug as the primary AE.

6.2. Cases Presented as Line Listings

The following type of cases received by GSK from worldwide sources during the reporting period and referenced below are considered to fulfil ICH E2C criteria for inclusion in the main line listings and/or summary tabulations of this report:

- all serious adverse reactions and non-serious unlisted adverse reactions from spontaneous notifications (including published reports);
- all non-serious listed adverse reactions from spontaneous reporting;
- all serious adverse reactions (attributable to the vaccine by either investigator or sponsor) available from studies or named-patient/compassionate use;
- all serious adverse reactions from regulatory authorities.

In addition, the type of cases mentioned below is included as a line listing as well:

- all serious and non-serious (listed and unlisted) adverse reactions reported by patients/consumers and other non-healthcare professionals (non-medically verified cases).

The type of cases making up the PSUR line listings within Appendices 3 is summarized below and in Table 1.

APPENDIX 3A contains:

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- all serious cases from spontaneous notifications (including published reports and regulatory reports but excluding non-medically verified reports);
- all unblinded serious cases arising from clinical trials considered related by sponsor or investigator;
- all non-serious unlisted cases from spontaneous notifications (including published reports but excluding non-medically verified reports and reports received solely from regulatory authorities).

APPENDIX 3B contains all serious attributable clinical trial cases unblinded during the reporting period which were not included in a previous report because they were still blinded.

It is company policy that only those clinical trial reports which are expedited to regulatory authorities are unblinded on the safety database during study conduct. Clinical trial reports that are not expedited will be unblinded on study completion. Any clinical trial reports meeting ICH E2C criteria but not included in a previous PSUR, are included as follow-up information in APPENDIX 3B.

In order to ensure no cases are missed, GSK uses a broad search strategy to retrieve clinical trial cases unblinded during the reporting period. Therefore, APPENDIX 3B may include some cases which have already been included in a previous PSUR (e.g. non-blinded clinical trial cases).

Note that no such case was received during the period.

APPENDIX 3C contains all non-serious listed cases from spontaneous notifications including published reports but excluding all non-medically verified reports and all reports received solely from regulatory authorities.

APPENDIX 3D contains all non-medically verified cases, whether serious or non-serious, listed or unlisted.

Table 1 Appended Line Listings

Format	Appendix	Case Type
Line Listing	3A	All serious spontaneous cases (excluding consumer reports), all serious attributable clinical trial cases and all non-serious unlisted cases (excluding consumer and regulatory reports)
	3B	All serious attributable clinical trial cases which were received prior to the period of this PSUR but unblinded during the reporting period *No such case was received during the period*
	3C	All non-serious listed cases (excluding consumer and regulatory authority reports)
	3D	All non-medically verified cases
	3E	Cases from a previous period not included in previous PSUR

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Explanation of line listings content

- Within the line listings a case is considered serious if it fulfils the ICH definition of serious (see Section 6.1). Serious cases are identified by a "#" beside the case ID.
- An unlisted case contains at least one AE that is not covered by the RSI which was in place at the time of data entry.
- The AEs within a case are presented at MedDRA PT level. System Organ Class (SOC) is assigned automatically according to the Primary AE.
- Literature citations for all published cases are noted in the 'Comments' column of the line listing.

6.3. Cases Presented as Summary Tabulations

An aggregate summary for each of the line-listings is presented in Appendices 4 as summarised below and in Table 2. All AEs are presented at MedDRA PT level within summary tabulations.

APPENDIX 4A contains all reported AEs for cases included in APPENDIX 3A, meaning AEs from all serious spontaneous cases (excluding consumer reports), all serious attributable clinical trial cases and all non-serious unlisted cases (excluding consumer and regulatory reports).

APPENDIX 4B contains all reported AEs for cases included in APPENDIX 3C, meaning AEs from all non-serious listed cases (excluding consumer and regulatory authority reports).

APPENDIX 4C contains all reported AEs from non-medically verified serious cases + non-medically verified non-serious unlisted cases.

APPENDIX 4D contains all reported AEs from non-medically verified non-serious listed cases.

APPENDIX 4E is a cumulative tabulation of all unlisted events from serious unlisted spontaneous reports (including non-medically verified reports) and all serious unlisted reactions from clinical trial cases reported since launch.

Of note, differences may appear between numbers in the previous PSUR cumulative counts of unlisted events for the following reasons:

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- changes in the listedness of some AEs due to an update in the RSI;
- increased consistency in the listedness assessment has been achieved following implementation of an automated listedness attribution applied to the case reports received;
- in "old" cases diagnostics could have been coded with signs and symptoms. These signs and symptoms are not included in the cumulative count anymore.
- in the previous tables all AEs, listed and unlisted were taken into account while in the new outputs, only the unlisted AEs are provided.

Table 2 Appended Summary Tabulations

Summary Tabulation	4A	All reported AEs for cases included in APPENDIX 3A
	4B	All reported AEs for cases included in APPENDIX 3C
	4C	All reported AEs from non-medically verified serious cases and non-serious unlisted cases
	4D	All reported AEs from non-medically verified non-serious listed cases
	4E	Cumulative tabulation of all unlisted events from serious unlisted spontaneous reports and all serious unlisted reactions from clinical trial cases reported since launch

Explanation of summary tabulations content

The following information is important when evaluating the summary tabulations.

Seriousness

AEs from spontaneous, post-marketing or literature cases are only classified as serious within the tabulations if they are on the list of GSK medically serious terms (see Section 6.1). Therefore, although an AE may reside in a case that fulfils the ICH criteria of serious, if the event is not on the list of GSK medically serious terms it will appear within the non-serious column in the summary tabulations.

GSK believes that applying the GSK medically seriousness criteria to AEs will provide a consistent and more meaningful presentation of data within the tabulations, and help with aggregation of terms for signal review activities. Counts of events are presented in the tabulations for the reporting period of the PSUR and cumulatively (APPENDIX 4E).

Note: In rare situations an event may appear in both the ***serious and non serious*** *columns within the summary tabulations, this may occur for the following reasons:*

- *GSK only applies its list of medically serious terms to events reported in spontaneous reports, literature cases and post-marketing surveillance studies. Serious criteria for events originating from clinical trial cases are determined by the reporter. Therefore, as events can originate from different report sources seriousness assessments may differ.*
- *The GSK medically serious list is compiled at the MedDRA LLT level. Summary tabulations present counts of events at the MedDRA PT level. A PT may therefore have both serious and non serious LLTs associated with it.*

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6.4. Overview

An overview of the 1742 reports received in the time period is presented in Table 3. Out of this grand total of 1742 cases, 1736 were reported spontaneously and six were clinical trial cases. Based on the exposure data presented in Section 5.1, a reporting rate of 14.16 cases per 100 000 doses distributed can be estimated (against 17.36 cases per 100 000 doses distributed during the previous one-year period). This corresponds to a 18.43% decrease in the overall reporting rate and was mainly driven by a decrease in the reporting rate of non-medicaly verified ('consumer') cases, which decreased by 81.74%.

Table 3 Reports received in Time Period of PSUR

	NUMBER OF CASES
REPORTS FULFILLING ICH E2C CRITERIA	
Serious Unlisted	503
Serious Listed	56
Non-serious Unlisted	545
TOTAL (Line listing)	**1104**
Non-Serious Listed	68
TOTAL (ICH E2C criteria)	**1172**
OTHER REPORTS	
Non-Medically Verified	54
Regulatory, non-serious	516
TOTAL (Other reports)	**570**
GRAND TOTAL (All reports)	**1742**

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The majority of reports were received from 41 countries (Table 4), mainly Italy with 595 cases (34.2%), Germany with 382 cases (21.9%) and France with 298 cases (17.1%).

Table 4 Distribution of cases by country

Country of Reporter	Number of Cases (%)
Italy	595 (34,2)
Germany	382 (21,9)
France	298 (17,1)
Netherlands	112 (6,4)
Poland	91 (5,2)
Australia	36 (2,1)
Spain	25 (1,4)
Czech Republic	24 (1,4)
Belgium	23 (1,3)
South Africa	22 (1,3)
Austria	20 (1,1)
Sweden	14 (0,8)
Ireland	11 (0,6)
Kenya	9 (0,5)
Switzerland	8 (0,5)
Canada	7 (0,4)
Greece	7 (0,4)
Latvia	7 (0,4)
Argentina	5 (0,3)
Romania	5 (0,3)
Viet Nam	5 (0,3)
Brazil	3 (0,2)
Ecuador	3 (0,2)
Peru	3 (0,2)
Singapore	3 (0,2)
Ukraine	3 (0,2)
Andorra	2 (0,1)
Colombia	2 (0,1)
Hong Kong	2 (0,1)
New Zealand	2 (0,1)
Slovakia	2 (0,1)
Thailand	2 (0,1)
Chile	1 (0,1)
Croatia	1 (0,1)
Mexico	1 (0,1)
Namibia	1 (0,1)
Philippines	1 (0,1)
Saudia Arabia	1 (0,1)
Serbia	1 (0,1)
Taiwan, ROC	1 (0,1)
United Arab Emirates	1 (0,1)
TOTAL	**1742 (100,0)**

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Based on the initial reporting source (Table 5), 1007 cases were received from regulatory authorities (57,8%), 667 from healthcare professionals (38.3%) and 68 cases from non-healthcare professionals (4%).

Table 5 Distribution of cases by source

Source	Number of Cases (%)
Regulatory Authority	1007 57,8)
Physician	513 (29,4)
Other Health Professional	85 (4,9)
Pharmacist	69 (4,0)
Consumer	63 (3,6)
Literature	3 (0,2)
Other	1 (0,1)
Representative	1 (0,1)
TOTAL	**1742 (100,0)**

Table 6 shows the numbers of cases by system organ class (SOC) for all AEs received during the period. Note that in this tabulation, seriousness and listedness are assigned at event level.

Table 6 Number of cases by SOC for all AEs received during the period

Event SOC	Number of Cases (%)
General disorders and administration site conditions	1056 30.9
Nervous system disorders	461 13.5
Skin and subcutaneous tissue disorders	358 10.5
Injury, poisoning and procedural complications	330 9.6
Infections and infestations	181 5.3
Psychiatric disorders	165 4.8
Gastrointestinal disorders	141 4.1
Vascular disorders	129 3.8
Respiratory, thoracic and mediastinal disorders	118 3.5
Investigations	82 2.4
Cardiac disorders	79 2.3
Musculoskeletal and connective tissue disorders	69 2.0
Eye disorders	60 1.8
Metabolism and nutrition disorders	59 1.7
Blood and lymphatic system disorders	46 1.3
Immune system disorders	34 1.0
Surgical and medical procedures	18 0.5
Ear and labyrinth disorders	9 0.3
Hepatobiliary disorders	6 0.2
Congenital, familial and genetic disorders	5 0.1
Renal and urinary disorders	5 0.1
Social circumstances	4 0.1
Endocrine disorders	2 0.1
Reproductive system and breast disorders	2 0.1
Neoplasms benign, malignant and unspecified (including cysts and polyps)	1 0.0
TOTAL	**3420 100.0**

* This number is greater than the Grand total of cases in Table 3 since each case may include AEs from multiple SOCs

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In addition to the grand total of 1742 cases, 10 cases where identified as received prior to the period of the present report, but not included in any previous PSUR (APPENDIX 3E). The reasons are as follows:

- For 9 cases (B0591710A, B0631888A, B0637096A, B0674885A, D0060830A, D0061162A, D0063259A, D0066216A, D0066224A) the suspect vaccine name was changed to Infanrix hexa after the data lack point of the previous PSUR.
- Case B0647987A was initially coded as Postmarketing surveillance (PMS) case. These cases types are not included in PSURs when they are non-serious (case B0647987A is non-serious). During the period, the case type was corrected to 'Spontaneous' and thus fulfilled the criteria for inclusion in the PSUR.

These cases are described and discussed among adverse events of interest as appropriate in Sections 6.5 and 9.3.

6.5. Manufacturer's Analysis of Individual Case Histories

As a company policy, all incoming AEs are reviewed on an ongoing basis to detect any new safety signal. Once identified, all available data relating to the AEs under review are routinely evaluated in a cumulative manner for a possible causal association with the suspect product.

The selection of the AEs of interest as described in this section is based on the following criteria: reporting frequency, medical significance, severity of the events, mechanisms of action, issues that are being monitored, or requests by regulatory authorities.

The events of interest are described for all cases (irrespective of source, seriousness and listedness) within the PSUR review period. The events from the non-serious reports received solely from regulatory authorities are not included in the Line Listings and Summary Tabulations as per guideline E2C(R1). Separate Line Listings and Summary Tabulations are provided for consumer reports as per guideline E2C(R1). Therefore some reports may be reviewed and described in this section but will not appear in the line listing and summary tabulations of the PSUR.

The events are presented by MedDRA SOCs. Reports with a fatal outcome are discussed separately, regardless of the SOC of the primary AE is classified by MedDRA.

Where relevant, a company comment is provided.

6.5.1. Cases with a Fatal Outcome

Thirteen (13) cases with a fatal outcome were received during the reporting period. Narratives are presented in APPENDIX 5A. Note that non-medically verified reports are included. The narratives are produced directly from the safety database using a standard search strategy. The search strategy retrieves all cases in which the patient died or which are coded with MedDRA PTs indicating that death occurred. Thus the case narratives may include reports where the AE outcome is not specified as fatal in the line listings as well as reports of intra-uterine death or stillbirth.

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Cases with a fatal outcome are reviewed on an ongoing basis, as described in Section 9.1.

1. **B0683335A (Netherlands): Meningitis viral, Convulsion, Yellow skin, Cyanosis, Dehydration, Diarrhoea, Somnolence, Crying, Vomiting**

   This case was reported by a regulatory authority (NL-College ter Beoordeling van Geneesmiddelen # NL-LRB-111158) and described the occurrence of meningitis in a 2-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenza type b vaccine (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevenar) for prophylaxis. The subject had no medical history and no concomitant medication. On 13 September 2010, the subject received 1st dose of Infanrix hexa (unknown route, unknown injection site), 1st dose of Prevenar (unknown route, unknown injection site). 3 minutes after vaccination, the subject experienced crying and sleepiness on the same day. On 18 September 2010, 5 days after vaccination, the subject was found in bed with eyes half-opened and a blue mouth. His skin was yellow/pale. He vomited pink, foaming milk. No fever was observed (37 degrees C). The boy was hospitalized, diarrhea aggravated and dehydration was diagnosed. Blood test and spinal tap were performed. The boy had several afebrile convulsions and a MRI showed severe damage of the brain. No further treatment was given. On 25 September 2010, 12 days after vaccination, the subject died from viral meningitis. The regulatory authority considered the events were unlikely to be related with vaccination with Infanrix hexa and Prevenar. Additional information has been requested but could not be obtained from regulatory authority (new regulatory number: NL-LRB-116469). It was unknown whether an autopsy was performed.

   Company comment: Case of death due to viral meningitis in a 2-month-old male subject 12 days after 1st combined vaccination with Infanrix hexa and Prevenar. There was severe brain damage on MRI. It is unknown whether an autopsy was performed.

2. **B0700040A (Sweden): Meningitis, Sepsis, Shock, Pneumococcal infection, Renal impairment, Hepatic function abnormal, Pyrexia, Diarrhea, Vomiting**

   This case was reported by a consumer and described the occurrence of meningitis in a 9-month-old female subject who was vaccinated with synflorix (GlaxoSmithKline) and combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) for prophylaxis. A physician or other health care professional has not verified this report. Previous and/or concurrent vaccination included Bacillus Calmette - Guerin vaccine (non-gsk) given on 28 October 2010; diphtheria and tetanus toxoids and acellular pertussis vaccine; GlaxoSmithKline given on 20 May 2010; hepatitis B vaccine recombinant; manufacturer unspecified given on 20 May 2010; synflorix; GlaxoSmithKline; given on 20 May 2010. Concurrent medications included Paracetamol for her growing teeth. On 17 August 2010, the subject received 2nd dose of Synflorix (administration site and route unknown, batch number not provided). On 26 November 2010, 101 days after vaccination with Synflorix, the subject experienced fever, vomiting and diarrhea. This continued the whole day between 11 am to 6 pm. She suddenly got better and she was not vomiting and her fever went down. She got fluid replacement and was able to urinate. On 27

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November 2010, at 7 am, the subject was not breathing any longer. At the hospital, they tried to save her during 40 minutes. The subject died on 27 November 2010 from meningitis and sepsis. An autopsy was performed and showed abnormal renal function, hepatic function abnormal and possible pneumococcal infection. The body was in shock.

Company comment: Death of a 9 month-old female subject due to meningitis and sepsis 191 days after combined vaccination with Infanrix Hexa and Synflorix.

3. **B0706503A (Thailand): Shock, Respiratory arrest, Cardiac arrest, Pyrexia, Somnolence, Hypotonia, Vomiting, Crying, Apnoea.**

This case was reported by a physician and described the occurrence of fatal shock in a 2-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. The subject was born by C-section. Apgar score was 10 at 0 and 5 min. Birth weight was 3.2 kg and experienced a normal growth and development. Medical condition included a possible genetic abnormality due to a family history of death after vaccination (subject's brother died 2 years ago after vaccination with DTwP). On 9 March 2011, the subject received unspecified dose of Infanrix hexa (.5 ml, unknown route of adminstration). The subject was normal before vaccination. On 10 March 2011, 24 hours after vaccination with Infanrix hexa, the subject experienced shock. She experienced low-grade fever, drowsiness and stopped breathing. The subject was floppy and had no heart rate. Cardiopulmonary resuscitation was performed during 3 hours but the subject did not respond to it. The physician considered the events were probably related to vaccination with Infanrix hexa. The subject died on 10 March 2011 from cardiorespiratory arrest. An autopsy was not performed. Follow-up received on 21 March 2011: The subject's brother was 2 month-old when he died (11 years ago), after received DTwP which was EPI vaccine (no record available). After vaccination (no specific time available), the subject experienced vomiting (single episode) and had colicky crying at home. On 10 March 2011, the subject was taken to the clinic due to fever and crying. After massive crying, the subject experienced apnea and no heart beat was detected after stimulation. Cardiopulmonary resuscitation was performed for 10 minutes and subject responded by crying. One hour later, the subject experienced apnea again and resuscitation was continued for 3 hours without any response. Neither lab results nor autopsy results were available. Shock was the final diagnosis.

Company comment: This case described a SUDI (Sudden Unexpected Death in Infancy) in a 2 month-old female subject 24 hours after vaccination with Infanrix hexa. Autopsy or lab results were not provided. There is a notion of post-vaccine death in a sibling.

4. **B0712016A (Italy): Hypotonia, Hyperhidrosis, Pyrexia.**

This case was reported by a regulatory authority (IT-Agenzia Italiana del Farmaco # 137473) and described the occurrence of hypotonia nos in a 11-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine.

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(Infanrix hexa, GlaxoSmithKline) and pneumococcal vaccines (non-gsk) (Prevenar 13) for prophylaxis. The subject was born after 41 weeks + 3 days, normal pregnancy and spontaneous delivery. Concurrent medical conditions included severe respiratory distress at birth. He was reanimated and resigned from the prenatal intensive care on 20 May 2010. He was not able to feed spontaneously (dysphagia) so a nasogastric tube was inserted with pump infusion. According to the doctor, the subject had contraindication to the vaccine. He was hospitalised from 22 May 2010 to 25 May 2010 due to respiratory distress. From 14 to 21 July 2010 due to seizures. On 18 August 2010, diagnostic results showed cerebral palsy, gastroesophageal reflux, hypoxic-ischemic encephalopathy of grade 3, microcephaly, psychomotor retardation and spastic quadriplegia (mainly the upper limbs). Concurrent medications included Paracetamol (Tachipirina), Vitamin, Vigabatrin, Topiramate, Antibiotics (Antibiotic), Bronchodilator and Steroid. On 25 March 2011, the subject received 3rd dose of Infanrix hexa (intramuscular, right thigh) and 3rd dose of Prevenar 13 (intramuscular, left thigh). On 26 March 2011, 1 day after vaccination with Infanrix hexa and Prevenar 13, the subject experienced fever (38 to 38.5 deg.C). On 27 March 2011, 2 days after vaccination with Infanrix hexa and Prevenar 13, the subject experienced hypotonia nos and crisis of sweating. The regulatory authority reported that the events were possibly related to vaccination with Infanrix hexa and Prevenar 13. The subject died on 28 March 2011, cause of death was not reported. It was unknown whether an autopsy was performed. Follow-up information received on 15 July 2011: As no additional information could be obtained, the case has been closed.

Company comment: This case described death of an 11-month old male subject 48 hours after third combined vaccination with Infanrix hexa and Prevenar. The subject died in the context of severe hypoxic-ischemic encephalopathy (cerebral palsy leading to quadriplegia and microcephaly).

5. B0727175A (France): Death.

This case was reported by the French regulatory authority (FR-Agence Françaiss de Sécurité Sanitaire des Produits de Santé # NT20110388) and described the occurrence of unexplained death in a 18-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. The subject had no known and relevant medical history. On 26 October 2010, the subject received an unspecified dose of Infanrix hexa (batch A21CA724A, intramuscular, injection site unknown). On 27 October 2010, 1 day after vaccination with Infanrix hexa, the subject was found dead after her nap. Autopsy did not identify any cause of death. Respiratory aspiration was assessed as not very probable. No other information was available. According to the French method of assessment, the AFSSaPS considered the causal relationship between vaccination with Infanrix hexa and unexplained death as dubious. Autopsy (2010): no identified cause of death.

Company comment: This case described a SIDS in an 18 month-old female subject 1 day after vaccination with Infanrix hexa. No cause was found after autopsy.

6. B0735723A (Australia): Death.

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This case was reported by a consumer and described the occurrence of death unspecified in a 6-week-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline), live attenuated human rotavirus vaccine (Rotarix) and pneumococcal vaccines (non-gsk) (Prevenar 13) for prophylaxis. A physician or other health care professional has not verified this report. On 20 July 2011, the subject received unspecified dose of Infanrix hexa (administration site and route unknown), an unspecified dose of Rotarix (route unknown) and an unspecified dose of Prevenar 13 (unknown). On 21 July 2011, 14 hours after vaccination with Infanrix hexa, Prevenar 13 and Rotarix, the subject died for unknown reasons. The subject died on 21 July 2011, cause of death was not reported. An autopsy was performed. Autopsy results are not yet available. Further information has been expected.

Company comment: This case reported a SUDI in a 6-week old male subject 14 hours after combined vaccination with Infanrix hexa, Prevenar and Rotarix. An autopsy was performed but results are not available.

7. D0071496A (Germany): Death

This case was reported by a health professional via a regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2011016343) and described death of a 3-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) and pneumococcal vaccines (non-gsk, Prevenar 13) for prophylaxis. Previous vaccinations with Infanrix hexa and Prevenar 13 (on 14 April 2011) have been well tolerated. On 16 May 2011 the subject received the second dose of Infanrix hexa (intramuscular, unknown thigh) together with the second dose of Prevenar 13 (intramuscular, unknown thigh). At this time the subject had suffered from a mild intestinal infection. In the morning of the following day, on 17 May 2011, the subject was found dead. An autopsy was performed and a preliminary autopsy report was provided. According to the autopsy protocol very early in the morning of 17 May 2011 the subject had been found "cold and lifeless" by her parents. On 05:02 an emergency physician had been called. Cardiopulmonary resuscitation by the parents and later by the emergency personal failed and death was testified. Policemen were involved at 06:20. Interrogation of the subject's parents revealed that the subject and her four siblings had always been healthy. Follow-up information was received from the institut of legal medicine Halle (Saale) on 04 August 2011: The final autopsy report was provided. The causes and mode of death could not be clarified. The infant had been suffering from an acute unilateral otitis media at the time of death (smear from the left middle ear: proof of Haemophilus influenzae; smear from the right middle ear: no proof of microorganisms). Within the scope of additional examinations no alcohol (alcohol concentration 0.00 %) or other pharmacologic could be detected. There was neither evidence of an allergic reaction. (total IgE 5.65 kU/l, reference <20kU/l) nor of a gastrointestinal infection. Nor was there any evidence of a postvaccinal disorder." According to the autopsy report, the onset date of the subject's otitis media was "very recent", but it could not be clarified whether it had been prior to or following the vaccination. Although no evidence of a relation of the event to the vaccination was found during the autopsy, the close

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temporal relation might be seen as an indication that the subject's death was possibly related to the vaccination with Infanrix hexa and Prevenar 13.

Company comment: This case described a SUDI in a 13 month-old female subject 1 day after 2nd combined vaccination with Infanrix hexa and Prevenar. A recent acute haemophilus influenzae otitis media was diagnosed on autopsy.

8. D0072663A (Germany): Death

This case was reported by a German regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2011029271) and described the occurrence of unexplained death in a 9-week-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenza type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Co-suspect vaccinations included 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer Pharma). Pregnancy and birth had been normal. The subject's medical history included neonatal jaundice. The subject was developing normal. Family history included no allergies. Concurrent medical conditions included suspicion of congenital hip dysplasia. Hip ultrasonography, performed on 09 August 2011, showed type IIa left and type I right. Follow-up hip ultrasonography, performed on 05 September 2011, showed type I both sides. At the time of vaccination, on 05 September 2011, the subject was well. The subject showed small white plaques in oral mucus (oropharyngeal plaques) left but most likely no oral candidiasis. Previous vaccination with Rotavirus vaccine (non-GSK) (RotaTeq; Sanofi Pasteur MSD), given orally at 2 ml on 09 August 2011, was well tolerated. Concurrent medications included colecalciferol + sodium fluoride (D-Fluoretten) and paracetamol (Ben-u-ron). On 05 September 2011 the subject received the first dose of Infanrix hexa (0.5 ml, intramuscular, unknown thigh lateral) and the first dose of Prevenar 13 (.5 ml, intramuscular, unknown thigh lateral). Approximately two days post vaccination with Infanrix hexa and Prevenar 13, on 07 September 2011, the subject died. The cause of death was unknown (death unexplained). The event had also been reported as life threatening. An autopsy was performed on 07 September 2011 at an institute for forensic pathology. At the time of reporting, on 08 September 2011, examinations had not been finished and no autopsy results have been reported. The German regulatory authority (DE-Paul-Ehrlich-Institut) has requested further information. Quality test result was received on 11 October 2011. A complete review of the batch records has been performed by Quality Assurance and Production. No deviation that could impact the quality of the product has been highlighted during the GlaxoSmithKline Biologicals investigation. At the moment no further information was available.

Company comment: This case described a SUDI in a 9 week-old male subject two days after combined vaccination with Infanrix hexa and Prevenar. An autopsy was performed but results are not yet available.
Since 12 September 2011, five cases linked to batch A21CB094A were reported to GSK (D0072663A, D0072852A, D0072638A, D0072908A, D0072920A). All five were serious reports and two had a fatal outcome. A complete review of the batch records was performed by Quality Assurance and Production. No deviation that could impact the quality of the product was highlighted by the GlaxoSmithKline Biologicals investigation. There is insufficient information provided in the individual

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case reports to make a thorough causality assessment. Autopsy reports of the fatalities.were pending. The three non-fatal cases were all different in nature (no cluster of any kind). These subjects all received Infanrix hexa with either Prevenar 13 or Synflorix. Allergic reactions, febrile convulsions, exanthema and fever are not unexpected to possibly occur after vaccination.

9. D0072852A (Germany): Circulatory collapse, Sepsis, Shock, Crying, Pallor

This case was reported by a regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2011030856) and described the occurrence of circulatory failure in a 5-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Co-suspect vaccination included 13-valent pneumococcal vaccine (non-GSK) (Prevenar 13, Pfizer). First vaccination with both vaccines on 23 August 2011 was well tolerated. Information about anamnesis was provided by a hospital report from intensive care treatment after birth. The mother had been pregnant for the first time. The mother had former surgery because of false lung vein opening and received permanent treatment with bisoprolol. The subject was delivered prematurely in 31+4 weeks of gestation, by section from breech presentation after pathologic CTG. There was no premature rupture of the amnion and amniotic fluid was clear. The subject had an APGAR of 6/10/10, a weight of 1490 g, length of 39 cm, head circumference of 32.6 cm, navel artery pH was 7.16. After birth the subject had neonatal respiratory distress syndrome grade I with continuous positive airway pressure for 24 hours. The subject developed possible meconium ileus due to microcolon, transient intestinal transportation disorder, cholestatic hepatosis after parenteral nutrition, with increased transaminases (alanine aminotransferase 131 U/l, aspartate aminotransferase 100 U/l, creatine kinase 342 U/l, total bilirubin 3 mg/dl, direct bilirubin 2.75 mg/dl). Additional diagnoses after birth included neonatal anemia and iron deficiency, asymmetry from lying, small hemangioma right gluteal and dystrophic growth and weight increase. On the sixth day of life, the subject's condition worsened and he was transferred to an intensive care unit for neonates. Intravenous antibiotics were given for seven days. The subject had abdominal distension since birth and not yet passed meconium. Acute abdomen was suspected on the seventh day of life. The subject was transferred to a pediatric chirurgic unit for further intervention, but after conservative treatment the symptoms resolved. Test results were normal for ions, blood gases, immune reactive trypsin (tested on 06 May and 06 June 2011), sonogram of head, abdomen and hip (Graf classification Ib) and hearing screening. Cytomegalovirus (CMV) and toxoplasmosis IgM and IgG antibodies were negative. Initially increased Thyroid stimulating hormone normalised on control. Bile acid was increased (74.6 mcmol/l), pancreatic kinase was decreased (68 mcg/g). Eye examination showed vascularisation limit zone III at both sides. The subject was discharged after 39 days in good condition and received rachitis prophylaxis and iron substitution. On 20 September 2011 the subject received 2nd dose of Infanrix hexa (unknown route and application site), 2nd dose of Prevenar (unknown route and application site). On 20 September 2011 in the evening, less than one day after vaccination with Infanrix hexa and Prevenar, the subject had been crying and turned grey while lying in bed. The vaccinating physician was consulted and admitted the

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infant to hospital, where the subject died on 21 September 2011, from circulatory depression or possible sepsis. Different lot numbers were reported on follow-up. Approximately 20 hours after vaccination with Infanrix hexa and Prevenar 13, the subject experienced shock with circulatory failure. An emergency physician was called and the subject was hospitalized on emergency to an intensive care unit. Approximately 10 hours after onset of symptoms the subject died despite intensive care. According to follow-up information received on 07 October 2011 via the German regulatory authority (PEI), the lot number A21CB094A was documented in vaccination certificate, while there was no documentation for the mentioned lot numbers A21CB105A and A21CB115A. Quality test result was received on 11 October 2011. A complete review of the batch records has been performed by Quality Assurance and Production. No deviation that could impact the quality of the product has been highlighted during the GlaxoSmithKline Biologicals investigation. An autopsy was performed. A duplicate case was reported by a physician, via a sales representative and no further details about the reported event were provided.

Company comment: Case D0072949A was identified as a duplicate of case D0072852A that was voided. A complete review of the batch records has been performed and no deviation was evidenced during investigation process. Due to lack of relevant information the causality remains uncertain: possible circulatory or sepsis shock of unknown origin several hours after 2nd vaccination with Infanrix hexa and Prevenar. An autopsy was performed, but the results were not available (see also Section 8.2).

Since 12 September 2011, five cases linked to batch A21CB094A were reported to GSK (D0072663A, D0072852A, D0072638A, D0072908A, D0072920A). All five were serious reports and two had a fatal outcome. A complete review of the batch records was performed by Quality Assurance and Production. No deviation that could impact the quality of the product was highlighted by the GlaxoSmithKline Biologicals investigation. There is insufficient information provided in the individual case reports to make a thorough causality assessment. Autopsy reports of the fatalities.were pending. The three non-fatal cases were all different in nature (no cluster of any kind). These subjects all received Infanrix hexa with either Prevenar 13 or Synflorix. Allergic reactions, febrile convulsions, exanthema and fever are not unexpected to possibly occur after vaccination.

10. B0688734A (France): Sudden infant death syndrome, Respiratory tract congestion, Cough, Nasal congestion

This case was reported by the French regulatory authority (AFSSaPS reference PS20101095) and described a sudden infant death in a 10-week-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) and pneumococcal vaccine (Prevenar, non-gsk) for prophylaxis. The subject had mixted diet. At birth she weighed 2.99 kg and her height was 49.5 cm. She had no neonatal disorder. Medical condition included jaundice with abnormal skin reflection on 01 October 2010. On 09 November 2010, the subject received primary course of Infanrix hexa (batch A21CA777A as data entry and 121CA777A as reported, intramuscular, injection site unknown) and a

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primary course of Prevenar (batch E74711, intramuscular, injection site unknown). On 10 November 2010, the subject presented with bronchial and nasal congestions, cough, and serous fluid in tympanum (with crying at night) which was diagnosed before the administration of vaccines (medical condition). At 19:00, the subject received her last bottle (250 ml). She went to bed at 19:15 and she was layed in her parent's bed, on a pillow. At 21:45, the father went to bed and found the subject unconscious. Mobile emergency medical unit was contacted which arrived at 22:00. At 22:23 pm, a pediatric mobile emergency medical unit arrived. Resuscitation procedure was started. The subject was intubated and received adrenaline. She was hospitalized and died at 00:00. Tracheal aspiration was positive for klebsiella pneumoniae. Causal relationship of vaccination with Infanrix hexa and Prevenar and sudden infant death was assessed as dubious, according to the French method of imputability.

Company comment: Suspected case of SUDI in a 10-week old female subject 1 day after combined vaccination with Infanrix hexa and Prevenar. The subject had an upper respiratory tract infection before vaccination. It is unknown whether an autopsy was performed.

11. B0705290A (France) Sudden death, Pyrexia, Lymphadenopathy, Emphysema, Product quality issue, Cardio-respiratory arrest, Asphyxia, Febrile convulsion

This case was reported by a physician and described the occurrence of death (cause unknown) in a 10-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenza type b vaccine (Infanrix Hexa, GlaxoSmithKline) for prophylaxis. The subject had no known pathology and took no concurrent medication. Vaccinal history included one dose of DTPa-IPV-Hib vaccine (Infanrixquinta, GlaxoSmithKline) administered on and one dose of tuberculosis vaccine (BCG), both administered on 31 August 2010 (information was corrected during AFFSaPS follow-up under reference TO20110471A). The vaccination schedule of the subject did not comply with French medical authority recommendations. The subject's medical history included bronchiolitis during last winter. On 07 March 2011, the subject received a second dose of Infanrix Hexa (batch A21CA598F, route and injection site unknown). During the following night, the subject experienced fever. Mobile emergency medical unit was contacted by the parents. On their arrival, the subject was dead. No diagnostic was made, sudden infant death was suspected. An autopsy was agreed by the parents (not a complete forensic). Results were not available at the time of reporting. According to the reporter, a causal relationship between the death and Infanrix Hexa was not established.

Clinical examination was normal before vaccination. Infanrix Hexa was administered intramuscularly at 11:00 on 07 March 2011. At 15:00, he presented with fever which resolved after paracetamol administration. The evening meal was taken without reportable incident. During the following night, fever recurred and the parents called the mobile emergency unit. On 08 March 2011, the subject was dead on mobile emergency medical unit arrival. He was found, by his father; laid on his stomach with face on his pillow. There were no signs of inhalation or vomiting. There was no sign of righting reflex, normally present at this age. Post mortem

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analyses were negative for C-reactive protein, blood culture and cerebrospinal fluid. Post-mortem virus tests were negative excepted positive for Respiratory Syncytial Virus in nose sample. Anatomical pathology evidenced major mesenteric adenopathy. Further information concerning autopsy report were pending. According to the French method of assessment, the AFSSaPS considered the causal relationship between vaccination with Infanrix Hexa and sudden death as dubious. Upon follow-up received from quality department on 31 March 2011: A product complaint has been recorded (Ref 2011-13789). QA analysis revealed the complaint to be unsubstantiated. A complete review of the batch records had been performed and no deviation that could have an impact on the product was highlighted. A search was also performed in the GSK safety database for the final bulk A21CA598 and it did not reveal a safety signal.

A standard follow-up anamnesis was received from a physician on 05 April 2011: no abnormal matters during pre and post-partum conditions. Upon follow-up received from AFSSaPS on 14 April 2011: Autopsy results were provided and evidenced major lymphoid hyperplasia of mesenteric lymph nodes, of intestinal lymphoid tissu and of appendix with cellular dystrophy suggestive of viral etiology possibly subclinical. No Cytomegalovirus, Epstein-Barr virus or Herpes virus infection was found. At lung level, bilateral pseudo-emphysemateous pulmonary lesions were noticed, suggestive of suffocation phenomenon as no resuscitation was attempted. No sign suggestive of massive inhalation, no sign suggestive of infectious pneumopathy and no visceral congenital anomaly were reported. According to the AFSSAPS, based on the French method of assessment, the events were unlikely related to vaccination with Infanrix hexa.

Follow-up was received on 21 April 2011 from the AFSSAPS: Psychomotor development was normal. The subject had one half-brother and one half-sister aged 6 and 5 years with medical history of convulsions. The half-brother was treated with Micropakine. On 07 March 2011, at 03:00PM, body temperature was at 39.6 Celsius degrees. On 08 March 2011, around midnight, the father still had not heard from him while he usually woke up at this time for his feed. When the father went to the bedroom, the subject was in ventral decubitus with the face on his pillow; he had cyanosis and was cold. The mobile emergency unit arrived and cardiorespiratory arrest was confirmed (the subject could not be resuscitated). His body temperature was at 35 Celsius degrees. Skull and skeleton ultrasounds were normal.

Company comment: Case of SUDI in a 10-month-old male subject 1 day after a dose of Infanrix hexa (non compliant 2nd vaccination schedule following Infanrix penta + BCG). An autopsy was performed and no clear explanation was found to the subject death. Hypothesis of respiratory asphyxia as cause of death was made, due to circumstances in which the subject was found as well as the aspect of his lungs. Another hypothesis was febrile convulsion. The AFSSAPS reported that the responsibility of respiratory syncytial virus in the inflammatory lesions was unlikely. The time between vaccination with Infanrix hexa and death, was deemed too recent to provide a clear explanation for causality.

12. **B0716780A (Italy): Cardiac arrest, Multi-organ failure, Pneumonia aspiration, Cerebral, ischemia, Sudden infant death syndrome, Unresponsive to stimuli, Peripheral coldness, Staring, Musculoskeletal stiffness, Pyrexia, Somnolence**

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This case was reported by a regulatory authority (IT-Agenzia Italiana del Farmaco # 139520) and described the occurrence of cardiac arrest in a 5-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevenar 13) for prophylaxis. On an unspecified date, the subject received 1st dose of Infanrix hexa (unknown route of administration, unknown site of injection, batch number not provided). At an unspecified time after vaccination with 1st dose of Infanrix Hexa, the subject experienced fever. This is the reason why the second dose was not administered in the last 4 weeks. On 14 April 2011, the subject received 2nd dose of Infanrix hexa (.5 ml, intramuscular, unknown route of administration), and 2nd dose of Prevenar 13 (.5 ml, intramuscular, unknown route of administration, batch number not provided). On 14 April 2011, less than one day after vaccination with 2nd doses of Infanrix hexa and Prevenar 13, the subject experienced fever (more than 39 Deg.C). On 15 April 2011, the fever was resolved. In the afternoon of 15 April 2011, the subject did not respond to stimuli. She was admitted at the first aid with cold extremities, fixed gaze, overtone, stiff neck and normotensive fontanel. Afterwards, the subject recovered completely. At the neurological visit, the subject was alert, reactive and the state of drowsiness has been related to vaccination. Electroencephalogram was without clear anomalies irritative. On 23 April 2011 (night), the subject had a cardiac arrest. After 20 minutes of reanimation the cardiac activity resumed but with irreversible neurological sequelae. The regulatory authority reported that fever, stiff neck, fixed gaze, cold extremities, unresponsive to stimuli and cardiac arrest were possibly related to vaccination with Infanrix hexa and Prevenar 13, but almost certainly for drowsiness. On 25 April 2011, the subject died, cause of death is not specified. It was unknown whether an autopsy was performed. Follow-up information received on 19 May 2011: The parents of the subject were young, both were born in 1992. No information regarding important diseases or neonatal problems were reported. Artificial sucking from the early days due to maternal hypogalactia, was reported. The subject's growth had always been regular, between 50 Deg and 75 Deg percentile. The first dose of the vaccines Infanrix Hexa and Prevenar 13 were administered on 10 February 2011. Within weeks of vaccination with 1st dose of Infanrix Hexa and Prevenar 13, the subject experienced fever. An autopsy was performed and there had been no element attributed to encephalitis. The histological evaluation was in course. Follow-up information received on 6 September 2011: An autopsy was performed and the results were reported on the basis of available information and histological investigations. The death occurred at 15:10 on 25 April 2011. The death was caused by multiple organ failure, ab-ingestis pneumonia, cerebral anoxia, following sudden cardiac arrest. Other significant causes were not found; therefore cardiac arrest might correspond to Sudden Infant Death Syndrome (SIDS). There was no available scientific evidence to show a causal relationship between vaccine administrations and cardiac arrest. Follow-up information received on 14 September 2011: No concomitant medication was reported. The subject was in good health before vaccination. Full report on resuscitation measures and full autopsy report were not available.

Company comment: Case of SIDS in a 5-month-old female subject 1 day after a 2nd dose of combined vaccination with Infanrix hexa and Prevenar. An autopsy was

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performed and no clear explanation was found. Therefore cardiac arrest and MOF were placed within a sudden infant death syndrome.

13. D0070324A (Germany): Sudden infant death syndrome, Death, Vomiting, Cardiomyopathy

This case was reported by a physician via another manufacturer and described the occurrence of possible sudden infant death syndrome (SIDS) in a 3-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Co-suspect vaccinations included 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer Pharma). Concurrent or previous medical conditions included hyperbilirubinemia. At the time of vaccination the subject was otherwise healthy. On 18 January 2011 the subject received the first dose of Infanrix hexa (0.5 ml, intramuscular, unknown) and the first dose of Prevenar 13 (0.5 ml, intramuscular, unknown), contralaterally. Less than one week post vaccination with Infanrix hexa and Prevenar 13, In January 2011, the subject experienced possible sudden infant death syndrome (SIDS). The subject died on an unknown date between 18 January 2011 (date of vaccination) and 24 January 2011 (date when police has informed the physician) from possible sudden infant death syndrome (SIDS). It was unknown whether an autopsy was performed. The reporting physician considered that the event was unlikely related to vaccination with Infanrix hexa and/or Prevenar 13. The case was received from Pfizer Pharma GmbH, Berlin, Germany. The other manufacturer has already reported this case under international number DE-PFIZER-INC-2011025551. The same case was reported on 18 February 2011 by the same physician via a sales representative. Approximately three days post vaccination with Infanrix hexa and Prevenar 13, on an unspecified date, the subject was found dead in prone position lying in vomit.

The subject was born by normal delivery at 38 weeks of pregnancy with a birth weight of 3130 g, a length of 49 cm and an Apgar score of 10/10. The subject has no underlying or concurrent medical conditions or other risk factors. On 18 January 2011 the subject received the first doses of Infanrix hexa (lot number: A21CA922C) and Prevenar 13. For the next three days following vaccination with Infanrix hexa and Prevenar 13 the subject was well. Then the subject died from at present unknown cause. The subject was found dead in prone position lying in vomit. An autopsy was performed. At the moment the result of autopsy was unknown. Follow-up information was received on 28 February 2011 from the reporting physician. The reported lot number for Prevenar 13 was E90728, not E40728. According to follow-up information the subject died five days post vaccination with Infanrix hexa and Prevenar 13, on 23 January 2011, and not three days post vaccination with Infanrix hexa and Prevenar 13 as reported initially. The subject has no underlying or concurrent medical conditions or other risk factors. Concurrent medications included colecalciferol + sodium fluoride (D-Fluoretten) for prophylaxis and simethicone (Espumisan) as needed for infantile colic. On 18 January 2011 the subject received the first dose of Infanrix hexa (0.5 ml, intramuscular, left thigh) and the first dose of Prevenar 13 (0.5 ml, intramuscular, right thigh), contralaterally. Approximately five days post vaccination with Infanrix hexa and Prevenar 13, on 23 January 2011, the subject died from at present unknown cause. The subject received no treatment. An

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autopsy was performed on an unknown date, but the autopsy report was not available at the moment. According to the reporting physician, in the meantime, there had been signs of possible cardiomyopathy. No further information was available.

Company comment: Case of SUDI in a 3-month-old male subject less than 1 week after 1st dose of combined vaccination with Infanrix hexa and Prevenar. According to the reporting physician, there had been concerns of cardiomyopathy but no further information was available to document this. Autopsy was performed but results not available.

6.5.2. Other adverse event of interest

6.5.2.1. Blood and lymphatic system disorders

6.5.2.1.1. Anaemia haemolytic autoimmune

One (1) case of Anaemia haemolytic autoimmune was reported during the period:

- **D0072751A (Germany): Anaemia haemolytic autoimmune, Autoantibody positive**

  This case was reported by a physician and described the occurrence of anemia in a 7-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. On an unknown date in 2011 the subject received the third dose of Infanrix hexa (0.5 ml, unknown). At an unspecified time post vaccination with Infanrix hexa, on an unknown date in 2011, the subject experienced anemia. This case was assessed as medically serious by GSK criteria. Follow-up was received from the physician on 26 September 2011, including a questionnaire. Co-suspect vaccinations included 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer). There was no concurrent medical condition or concurrent medication or any other risk factors. On 5 July 2011 the subject received 3rd dose of Infanrix hexa (.5 ml, intramuscular, unknown thigh), together with 3rd dose of Prevenar 13 (intramuscular, the other thigh). On 2 August 2011, 28 days after vaccination with Infanrix hexa and Prevenar 13, the subject experienced autoimmune hemolytic anemia ("Waerme auto antibodies", autoantibody positive). The subject was hospitalised. The subject was treated with blood (Blood transfusion) for several times. At the time of reporting the event was unresolved. The physician considered the event was unlikely to be related to vaccination with Infanrix hexa and and Prevenar 13.

  Company comment: A subject developed autoimmune haemolytic anemia within 28 days after vaccination with Infanrix Hexa.The subject was treated with several blood transfusions.

6.5.2.1.2. Autoimmune thrombocytopenia

No case of Autoimmune thrombocytopenia was reported during the period.

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6.5.2.1.3. Haemolytic anaemia

No case of Haemolytic anaemia was reported during the period.

6.5.2.1.4. Haemorrhagic diathesis

Two (2) cases of Haemorrhagic diathesis were reported during the period:

- **B0737478A (Poland): Haemorrhagic diathesis, Petechiae, Pyrexia**

  This case was reported by a regulatory authority (PL-Office of Medicinal Products # PL-URPL-OCR-20110318006) and described the occurrence of hemorrhagic diathesis in a 4-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-GSK) (Prevenar 13) for prophylaxis. On 18 February 2011, the subject received 2nd dose of Infanrix hexa (intramuscular, unknown injection site), 1st dose of Prevenar 13 (intramuscular, unknown injection site). On 18 February 2011, 8 hours after vaccination with Infanrix hexa and Prevenar 13, the subject experienced fever (38-38.6 deg. C), petechiae and manifestations of hemorrhagic diathesis: small-spot effusions all over the body. The subject was hospitalised. On 18 February 2011, lab test were performed and showed the following: C-reactive protein: 0.32; White blood cell count: 8.5; D dimer: 2184; Activated partial thromboplastin time: 33.1; Fibrynogen: 177; Thrombin time: 17.8; Prothrombin time: 130.06; Smear test from the nose: negative. The second day manifestations yielded. At the time of reporting the events were resolved. No further information can be obtained; this case has therefore been closed.

  Company comment: This episode relates to acute febrile petechial signs 8 hours after second dose of Infanrix hexa during combined vaccination with Prevenar. Manifestations yielded spontaneously after 24 hours.

- **D0070397A (Germany): Haemorrhagic diathesis, Ecchymosis, Petechiae, Upper respiratory tract infection**

  This case was reported by a physician via a sales representative and described the occurrence of possible hemorrhagic diathesis both lower legs in a 3-month-old male subject who was vaccinated with live attenuated human rotavirus vaccine (Rotarix, GlaxoSmithKline) and combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Co-suspect vaccinations included 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer Pharma). On 08 February 2011 the subject received the first dose of Rotarix (0.5 ml, oral), the first dose of Infanrix hexa (0.5 ml, unknown) and the first dose of Prevenar 13 (0.5 ml, unknown). Approximately one day post vaccination with Rotarix, Infanrix hexa and Prevenar 13, on 09 February 2011, the subject was diagnosed with possible hemorrhagic diathesis both lower legs. On the next day, on 10 February 2011, the subject was hospitalised for an unknown period of time. Laboratory parameters for blood coagulation were normal. Inflammation parameters were normal. The subject experienced no fever. At the time of reporting the outcome of the event was

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unspecified. On 08 February 2011 the subject received the first dose of Rotarix (0.5 ml, oral), the first dose of Infanrix hexa (0.5 ml, intramuscular, right thigh, reported lot was not distributed to Germany) and the first dose of Prevenar 13 (0.5 ml, unknown). The following day, on 09 February 2011, the subject was observed with subcutaneous bleedings at both his lower legs. The subject was hospitalised. The physician considered the event was possibly related to vaccination with Rotarix and Infanrix hexa. One day after the vaccination with Rotarix, Infanrix hexa and Prevenar 13, on 10 February 2011, the subject was hospitalized. Overall diagnoses were upper respiratory tract infection, hemorrhagic diathesis, status post vaccination and persistent foramen ovale. According to anamnesis the subject developed subcutaneous bleedings in the morning of the day of hospitalization, on 10 February 2011. There was no fever or restlessness. At the time of hospitalization the subject was noticed with multiple subcutaneous bleedings at both lower thighs and possible petechiae at the knees. The remaining body surface and mucosa was free of bleedings. Gingiva, throat and tonsils were free of bleedings. Mucosa was wet and free of bleedings. Tongue was wet and without coverings. There was no struma. Eyes, ears and nose were normal and free of bleedings. Eardrums were free. Respiration was normal with mixed and equal ventilation and free of aspiratory retractions. The subject's body temperature was 37.4 deg C. The subject was treated with inhalations of sodium chloride solution and Vitamin K. Coagulation tests resulted normally. Hemorrhagic diathesis following vaccination was suspected. The following day, on 11 February 2011, the subject was discharged from the hospital. In another examination within the following days the subject's skin bleedings were found fading and the subject was in a good general condition.

Company comment: This episode relates to acute febrile haemorragic signs (bleedings at both lower thighs and possible petechiae at the knees) one day after first dose of Infanrix hexa during combined vaccination with Prevenar and Rotarix in a 3-month-old male subject. There was a context of upper respiratory tract infection and manifestations yielded spontaneously after 24 hours.

6.5.2.1.5. Idiopathic thrombocytopenic purpura

Five (5) cases of Idiopathic thrombocytopenic purpura were reported during the period and are described below. Note that four cases of Thrombocytopenic purpura were also reported during the period (see Section 6.5.2.1.7 Thrombocytopenic purpura).

- **B0684234A (Italy): Idiopathic thrombocytopenic purpura, Thrombocytopenia, Rhinitis, Petechiae, Pyrexia**

  This case was reported by a physician via a regulatory authority (IT-Agenzia Italiana del Farmaco # 126680) and described the occurrence of idiopathic thrombocytopenic purpura in a 10-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevenar) for prophylaxis. On 7 April 2010, the subject received unspecified dose of Infanrix hexa (route and injection site unknown) and unspecified dose of Prevenar (route and injection site unknown). On 17 April 2010, 10 days after vaccination with Infanrix hexa and Prevenar, the subject

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experienced thrombocytopenia. 48 hours before the admission to the hospital, he presented some petechiae on the face and then all over the body. The subject was hospitalised on 19 April 2010. During the hospitalization, the subject was treated with normal immunoglobulin (Immunoglobulin). On 25 April 2010, 18 days after vaccination with Infanrix hexa and Prevenar, the subject developed fever and serious rhinitis. The diagnosis of idiopthic thrombocytopenic purpura was made. On 7 May 2010, relevant test was performed: bone marrow aspirate showed normal results. On June 201, the subject was treated with corticosteroid due to persistent thrombocytopenia. On 16 July 2010 and on 17 September 2010, plateled counts were respectively 111.000/mm^3 and 194.000/mm^3. At the time of reporting, the outcome of the events was unspecified. The regulatory authority reported that the thrombocytopenia was possibly related to vaccination with Infanrix hexa and Prevenar.

Company comment: A case of ITP in a 10 month-old subject, 10 days after vaccination with Infanrix Hexa and Prevenar. Autoimmune thrombocytopenia has not been confirmed by positive antiplatelet antibodies. At the time of reporting, the outcome of the events was unknown.

- **B0686840A (Czech Republic): Idiopathic thrombocytopenic purpura, Febrile convulsion, clonic convulsion, Tremor, Dyskinesia, Petechiae, Platelet count decreased, Pyrexia.**

  This case was reported by a physician via a regulatory authority (CZ-State Institute for Drug Control # CZ-CZSUKL-10001869) and described the occurrence of idiopathic thrombocytopenic purpura in a 5-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) for prophylaxis. On 7 May 2009, the subject received 2nd dose of Infanrix hexa (intramuscular, injection site unknown, batch number not provided). On 7 May 2009, 3-4 hours after vaccination with Infanrix hexa, the subject experienced fever (38° C). The subject was treated with antipyretics. On 8 May 2010, 1 day after vaccination with Infanrix hexa, the fever raised to 40 deg.C accompanied by shaking of hands and facial jerkings during sleep. After awaking by mother, there were no clonic convulsions yet. The subject also developed multiple petechias on skin of lower extremities and trunk. The subject was hospitalised and the regulatory authority reported that the events were clinically significant (or requiring intervention). Relevant tests were performed and showed platelet count which decreased to 7000 10^6/l. The subject was treated with prednisone (Prednison) and paracetamol (Paralen). The petechias intermittently regressed and erupted during 1 month. The diagnosis was stated as febrile convulsions and idiopathic thrombocytopenic purpura. At the time of reporting, the idiopathic thrombocytopenic purpura, fever and febrile convulsions were resolved. Follow-up information received on 7 January 2011: The subject had a normal growth without serious family and personal anamnesis, but family history of cardiovascular disorder. The subject's mother anamnesis included st. post myocardial infarction. Medical condition included CMV infection which was showed by positive CMV infection test on May 2009. During hospitalization from 13 May 2009 to 15 May 2009, relevant tests were performed: electroencephalogram examination was normal, bone marrow tap did not

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proved hemoblastosis. O2 saturation was 91.92%. Platelet count was performed several times: 10 10^9/l, 10 10exp9/l, 47 10^9/l and finally 210 10^9/l. Blood pH was increased (7.447). Blood count and blood gases were also performed but no results were provided. Follow-up information received on 11 January 2011: The subject was hospitalised on 13 May 2009 for 2 days. The subject's medical condition included CMV infection which was proved by following positive CMV infection test on May 2009: serology showed CMV IgG 3,1; CMV IgM 36; HSV Ig 4,3; EBV VCA IgG 0; EBV VCA IgM 0; EBV EBNA IgG 7, EBV EA IgG 0. Other relevant tests have been performed: Blood test on 13 May 2009 showed thrombocytopenia 10. Other results were in normal range. Biochemistry showed normal results. Neurological examination and psychomotorical development were also normal. At the hospital, the subject was treated with corticosteroids: methylprednisolone sodium succinate (Solumedrol), calcium carbonate (Vitacalcin) and vigantol. On 15 May 2009, the subject was discharged in good condition. On 19 May 2009, a check up showed thrombocytes which increased to 428. Petechias recovered in 1 month, fever, shaking, jerkings or convulsions were not reapeted. Then, at the time of reporting the events were resolved. Observation on neurology outpatient clinic was recommended.

Company comment: A case of ITP in a 5 month-old male subject 1 day after vaccination with Infanrix Hexa in the context of concurrent CMV infection. On the basis of the information provided, the time to onset appears short to consider autoimmune thrombocytopenia (no antiplatelet antibodies test performed).

- **B0705987A (Ireland): Idiopathic thrombocytopenic purpura, Haemorrhage, Platelet count decreased, Petechiae, Fall, Increased tendency to bruise, Upper respiratory tract infection**

  This case was reported by a pharmacist and described the occurrence of idiopathic thrombocytopenic purpura in a 8-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. In December 2009, the subject completed full course of Infanrix hexa (unknown route, unknown lot number). In January 2010, 1 month after vaccination with Infanrix hexa, the subject experienced idiopathic thrombocytopenic purpura, hemorrhage, platelet count decreased, petechiae, and frequent falls and bruised easily. In 2010, the subject also experienced upper respiratory tract infection treated with rituximab in June 2010. This case was assessed as medically serious by GSK. Relevant test results included: platelet count was 15 then went down to 1. A scan for leukaemia was clear. At the time of reporting, the subject was 22 months old and the outcome of the events was unspecified. The physician was not sure of what caused it. No further information was available at the time of reporting.

  Company comment: A case of ITP in a 8-month-old male subject 1 month after vaccination with Infanrix Hexa. A reported recent upper respiratory tract infection may have been a trigger. The outcome of the events is unknown.

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- **B0740099A (Netherlands): Idiopathic thrombocytopenic purpura, Petechiae, Diarrhoea, Inflammation, Pyrexia.**

  This case was reported by a regulatory authority (NL-College ter Beoordeling van Geneesmiddelen # NL-LRB-119820) and described the occurrence of idiopathic thrombocytopenic purpura in a 4-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-GSK) (Prevenar) for prophylaxis. The subject had no concomitant medication and no medical history. On 6 April 2009, the subject received 2nd dose of Infanrix hexa (unknown route, unknown injection site), 2nd dose of Prevenar (unknown route, unknown injection site). On 6 April 2009, within hours of vaccination with Infanrix hexa and Prevenar, the subject experienced fever (39deg C) for one day. In April 2009, 2 weeks after vaccination, the subject developed petechiae all over the body diagnosed as idiopathic thrombocytopenic purpura. The subject also experienced, at unspecified time after vaccination, diarrhea and inflammation localized. The subject was referred to a pediatrician. This case was assessed as medically serious by GSK. Relevant test results included: in April 2009, thrombocytes: 32. Further investigations showed no abnormalities. After 3 months, thrombocytes elevated to 130. At the time of reporting the events were resolved. The regulatory authority reported that the events were possibly related to vaccination with Infanrix hexa and Prevenar.

  Company comment: A case of ITP in a 4-month-old female subject 2 weeks after combined vaccination with Infanrix Hexa and Prevenar. At unspecified time after vaccination, the subject experienced an infectious episode which may have been a trigger. The event resolved spontaneously.

- **D0071950A (Germany): Idiopathic thrombocytopenic purpura, Mouth haemorrhage, Haematoma**

  This case was reported by a hospital physician and described the occurrence of idiopathic thrombocytopenic purpura (ITP) in a 12-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. On 30 June 2011 the subject received an unspecified dose of Infanrix hexa (0.5 ml, unknown). Approximately three days post vaccination with Infanrix hexa, on 03 July 2011, the subject was hospitalised for idiopathic thrombocytopenic purpura (ITP). Co-suspect vaccinations included 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer Pharma). The subject has no underlying or concurrent medical conditions or other risk factors. The subject received no concomitant medication Previous vaccinations with previous doses of combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) and 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer Pharma), given on unknown dates, have been well tolerated. On 30 June 2011 the subject received a booster with the fourth dose of Infanrix hexa (0.5 ml, intramuscular, unknown thigh) and a booster with the fourth dose of Prevenar 13 (0.5 ml, intramuscular, unknown thigh). Approximately two days post

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vaccination with Infanrix hexa and Prevenar 13, on 02 July 2011, the subject experienced idiopathic thrombocytopenic purpura (ITP). The subject was hospitalised for an unknown period of time. The subject was treated with normal immunoglobulin (Immunoglobulins) and prednisolone (Prednisolon). At the time of reporting, on 14 July 2011, the events were unresolved. The reporting physician considered that the event was probably related to vaccination with Infanrix hexa and Prevenar 13. The reporter provided the answers to a GSK targeted questionnaire for the occurrence of thrombocytopenic purpura: Thrombocytopenic purpura was diagnosed. The symptoms started about two days post vaccination with Infanrix hexa and Prevenar 13. The outcome of the symptoms was unknown. Symptoms included petechiae, ecchymoses / hematoma and hemorrhage specified as hematoma of while trunk of the size of about 1 Euro, oral mucosa ecchymosis and mouth bleeding. Symptoms did not include join hematoma or joint hemorrhage. Platelet count was 6, 17 and 11 (units not specified) on 03 July 2011, 07 July 2011 and 11 July 2011, respectively (normal range was 150 - 400). Treatment included gamma globulins (Sandoglobulin 4 g; Privigen 4 g) and corticosteroids (Prednisolon 20 mg once daily from 03 July 2011 - 11 July 2011). No relevant medical history has been reported. No further information will be available.

Company comment: A case of ITP in a 12 month-old male subject 2 days after combined vaccination with the 4th dose of Infanrix Hexa (all previous doses were well tolerated) and Prevenar. Treatment included gamma globulins and corticosteroids.

6.5.2.1.6. Thrombocytopenia

Nine (9) cases of Thrombocytopenia were reported during the period:

- **B0684234A (Italy): Idiopathic thrombocytopenic purpura, Thrombocytopenia, Rhinitis, Petechiae, Pyrexia**

  See Section 6.5.2.1.5 Idiopathic thrombocytopenic purpura.

- **B0693767A (France): Thrombocytopenic purpura, Petechiae, Haematoma, Epistaxis, Splenomegaly, Thrombocytopenia, Gingival bleeding**

  See Section 6.5.2.1.7 Thrombocytopenic purpura.

- **B0694143A (Italy): Thrombocytopenia, Petechiae, Pyrexia**

  This case was reported by a regulatory authority (IT-Agenzia Italiana del Farmaco # 132290) and described the occurrence of thrombocytopenia in a 2-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevenar) for prophylaxis. On 4 February 2010, the subject received 1st dose of Infanrix hexa (intramuscular, unknown injection site), 1st dose of Prevenar (intramuscular, unknown injection site). On 5 February 2010, 1 day after vaccination with Infanrix hexa and Prevenar, the subject experienced thrombocytopenia and diffuse petechiae. The subject was hospitalised. Relevant test results included: platelets count: 9000

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/mm^3. The subject was treated with normal immunoglobulin (Immunoglobulin G) and cortisone. On 12 February 2010, the events were resolved. The regulatory authority reported that the events were possibly related to vaccination with Infanrix hexa and Prevenar. Follow up information received on 01 April 2011: The subject also experienced fever. The subject was hospitalised from 9 to 12 February 2010. Relevant test results included: On 9 February 2010: AST:73 IU/L; Fibrin D-dimer: 2941 ng/ml; On 10 February 2010: Platelet count: 32000 /mm3; Fibrin D-dimer: 2280 ng/ml; On 12 February 2010: Platelet count: 244000 /mm3; Fibrin D-dimer: 1400 ng/ml; AST:63 IU/L; ALT: 41IU/L; LDH: 624IU/L; Urine analysis: negative The subject was treated with normal immunoglobulin (Immunoglobulin G), cortisone, paracetamol and cefixime. After discharge, the subject was given beclomethasone dipropionate (Clenil) and salbutamol sulphate (Salbutamol) for therapy at home.

Company comment: Thrombocytopenia in a 2-month-old female subject 1 day after vaccination with Infanrix hexa and Prevenar. Pyrexia and elevated inflammatory parameters suggest an infectious cause. Autoimmune thrombocytopenia has not been confirmed (no antiplatelet antibodies test performed).

- **B0695084A (France): Thrombocytopenia, Anaemia, Haematoma, Pyrexia, Gingival bleeding, Fall, Epistaxis, Blood lactate dehydrogenase increased, Incorrect route of drug administration**

  This case was reported by the French regulatory authority (AFSSaPS reference PS20110053) and described the occurrence of thrombocytopenia in a 2-year-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) and combined measles, mumps and rubella vaccine, live and attenuated (new strain) (Priorix, GlaxoSmithKline) for prophylaxis. The subject had no relevant medical history. On 14 September 2010, the subject received unspecified doses of Infanrix hexa (intramuscular, batch and injection site unknown) and of Priorix (batch and injection site unknown). It was reported that Priorix was administered intramuscularly instead of subcutaneously (wrong route of administration). On the same day, the subject presented with a febrile episode which resolved spontaneously. On 15 September 2010, the subject experienced gingivorrhagia which resolved. On 25 September 2010, a consultation at emergency unit was made due to a fall with secondary frontal hematoma. Neurological examination was normal. The subject was not hospitalized. On the same day, she accidentally fell again. On 26 September, for the third time, she fell headlong. On 27 September 2010, she consulted at emergency unit for epistaxis. Physical examination showed a voluminous frontal and periorbital hematoma. Neurological and ENT examinations were normal. Cerebral CT-scan was normal without fracture. The subject was not hospitalized. On 28 September 2010, epistaxis recurred with worsening of frontal hematoma without new fall. Laboratory tests evidenced hemoglobin at 6.2 g/dl (anemia), reticulocytes at 71000, platelet count at 2000 /l (thrombocytopenia), neutrophils at 11000 /l, prothrombine level at 85 percent, lactate dehydrogenase at 591 (normal<480), ALAT and ASAT normal. The subject received 2 packed red blood cell transfusions and one platelet concentrate resulting in an increased of hemoglobin to 11.4 g/dl, with reticulocytes at 80000.

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Platelets remained at 2000 /l. In the evening of 28 September 2010 and on 29 September morning, she received a new platelet concentrate. Hemoglobine was at 10.5 g/dl with platelets at 13160 /l. Blood electrolytes were normal. Fever recurred. Gentamicin sulphate (Gentalline), piperacilline + tazobactam (Tazocilline) and paracetamol (Perfalgan) were started. On 29 September 2010, the subject was transfered in another hospital. Ophtalmological examination (including dilated fundus examination) was normal. Cerebral CT-scan and myelogram (no tumorous cells and good cellularity of bone marrow) were normal. Dexamethasone was started (10 mg/m2). On 01 October 2010, platelets were lower than 10000 /l, hemoglobin was at 9.7 g/dl. Lumbar puncture was sterile. Normal immunoglobulin (Tegeline) was initiated (1g / kg on two days). On 03 October 2010, platelets were at 67000 /l, hemoglobin at 10.3 g/dl. Dexamethasone was discontinued and replaced by prednisone. Antibiotics were discontinued as the subject was apyretic. On 04 October 2010, the subject was discharged from hospital. At the time of reporting, anemia, thrombocytopenia, hematoma and fever were resolved.

Company comment: A case of thrombocytopenia and anaemia in a context of recurring fever of unknown cause starting 1 day after combined vaccination with Infanrix Hexa and Priorix in a 2 year-old female subject. Hematomata due to repetitive falling. The event was resolved with antibiotics, packed red blood cell transfusions, platelet concentrate and steroids.

- **B0699373A (Sweden): Thrombocytopenia, Contusion**

  This case was reported by a regulatory authority (SE-Medical Products Agency # 110404) and described the occurrence of thrombocytopenia in a 12-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) and pneumococcal vaccines (non-gsk) (Prevenar) for prophylaxis. The subject's medical history included contusions after previous vaccinations. On 8 November 2010, the subject received an unspecified dose of Infanrix hexa (intramuscular, administration site unknown) and an unspecified dose of Prevenar (intramuscular, unknown). On 16 November 2010, 8 days after vaccination with Infanrix hexa and Prevenar, the subject experienced thrombocytopenia and contusions. 6 months earlier, she had normal platelets. The subject was hospitalised for observation and the platelets rose spontaneously. Lab results: On 15 November 2010: hemoglobin: 118 g/l, platelets: 6 10E9/l, white blood cells: 17.1 10E9/l. On 15 December 2010: hemoglobin: 122 g/l, platelets: 61 10E9/l, white blood cells: 8.4 10E9/l. On 28 December 2010: hemoglobin: 126 g/l, platelets: 159 10E9/l, white blood cells: 11.4 10E9/l. At the time of reporting, the events were resolved. The regulatory authority reported that the events were possibly related to vaccination with Infanrix hexa and Prevenar. As no additional information could be obtained, the case has been closed.

  Company comment: A 12-month-old female subject experienced thrombocytopenia and contusions 8 days after vaccination with Infanrix hexa. No clear cause of this event was reported and the symptoms resolved spontaneously.

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- **B0724575A (France): Thrombocytopenic purpura, Thrombocytopenia, Petechiae, Injection site haematoma**

  See Section 6.5.2.1.7 Thrombocytopenic purpura.

- **D0070216A (Germany): Henoch-Schonlein purpura, Thrombocytopenia, Petechiae, Pyrexia, Upper respiratory tract infection, Anaemia**

  See Section 6.5.2.11.3 Henoch-Schonlein purpura.

- **D0071125A (Germany): Thrombocytopenia, Gastroenteritis rotavirus, Leukopenia, Petechiae, Haematoma, Ureteric stenosis, Pyelocaliectasis**

  This case was reported by a regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2011012061), by a Health care Professional, and described the occurrence of thrombocytopenia in a 3-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Co-suspect vaccinations included 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer). Previous vaccination with Infanrix hexa and Prevenar 13 on 16 February 2011 was well tolerated. On 16 March 2011 the subject received 2nd dose of Infanrix hexa (unknown route and application site), together with 2nd dose of Prevenar 13 (unknown route and application site). On 28 March 2011, 12 days after vaccination with Infanrix hexa and Prevenar 13, the subject experienced thrombocytopenia (Platelet count was 4000 /ul). At the same time, the subject experienced rotavirus gastroenteritis. The subject was hospitalised. Repeated blood examinations were performed. "Initially, the subject additionally experienced mild leukopenia". Hemoglobin was normal, HLA antibodies, thrombocytic allo- or auto-antibodies were negative. Follow-up was received from the regulatory authority (German Regulatory Authority (vaccines, biologicals) on 6 May 2011, including 2 hospital reports and 4 physicians' reports. According to the 1st hospital report, provided on 11 April 2011, the subject was hospitalised due to rotavirus gastroenteritis from 28 March 2011 to 4 April 2011. A distinct thrombocytopenia was diagnosed (Platelet count was 4000 /ul). The subject was treated with platelet concentrate once. Platelet count increased to 39000. One day later platelet count decreased to 12000 again. The subject was treated with normal immunoglobulin (Immunoglobins) and platelet count increased to 60000 on 4 April 2011 and the subject was discharged from the hospital. On an ambulatory control on 7 April 2011, platelet count was 15000. On 8 April 2011 the subject was hospitalised again with a platelet count of 13000. The subject again was treated with normal immunoglobulin (Immunoglobins) with a dosage of 1 g/kg body weight. On 10 April 2011 platelet count increased to 21000. On 11 April 2011 platelet count decreased to 10000 again. Clinically the subject was in good general condition, there was no indication for infection. On 11 April 2011 the subject was transferred to another hospital. During previous hospitalization from 28 March 2011 to 4 April 2011, a stool test for Rotavirus was positive. At that time, the subject experienced petechiae and a small hematoma on the left side. Physical examination on admission on 11 April 2011 was without pathologic findings, especially there were no mucosal bleeding and no hematoma. Thrombopenia was diagnosed. Ureteric stenosis (renal pelvis dilatation) was suspected. There were no

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known allergies. Concurrent medications included D-fluoretten. Test for thrombocyt autoantibodies in eluat and for thrombocyt antibodies in plasma on 14 April 2011: In the plasma monospecific thrombocyt autoantibodies were found, which could be indication for existing autoantibodies, despite missing indication from the eluat. In case of previous thrombocyte transfusion these maybe possible thrombocyt alloantibodies. Or they may be cross-reactive antibodies within other underlying diseases like autoimmune disease, infection, CLL, monoclonal gammopathy). Another report, approximately from 18 April 2011, reported there was no splenomegaly, hepatomegaly and no lymph node enlargement. According to a pathological histological expertise from 21 April 2011, a bone marrow punch biopsy was performed. "There were sufficient megacaryocytes of all maturation stages without significant dysplastic maturation disturbances." A bone marrow smear showed "megacaryocytes with the above described morphology." Diagnosis: The bone marrow punch biopsy showed "tangential hit poor subcortical medullary spaces with little granulopoietic hypoplasia, little left-shift of erythropoesis, interstitial lymphocytosis and hemophagocytosis." The bone marrow smear showed "lymphocytosis, blast cells at limit and abnormal hemophagocytosis. Left-shift of granulopoiesis with poor indication of segmented neutrophils." Clinically thrombopenia and neutropenia were diagnosed. "The morphological changes were not characteristic for myelodysplastic syndrome. The findings point to an immunologic genesis of thrombopenia and neutropenia. Were there indications for a chronic inflammatory underlying disease, maybe Systemic Lupus erythematodes?" Immunohistochemic examinations were planned for exclusion of a blast cell excess. According to a report from 21 April 2011, from the same physician, "immunohistochemic examination showed that CD34-positive precursor cells took approximately 5 to at most 10 %. CD117-positive blast cells were not increased. CD68-positive macrophages were clearly increased, occasional with signs of hemaphagocytosis. There also was increase of CD68-positive monocytes. Only according to these histologic findings it was difficult to decide whether there was a monocytoid propagation of blast cells. The bone marrow smear showed a number of blast cells at limit and a propagation of lymphoid cells (like haematogones). An additional immunohistochemic examination in case of the CD34-positive haematogones was planned. No further information will be available.

Company comment: This 3-month year old female subject experienced thrombocytopenia and neutropenia 12 days after vaccination with Infanrix hexa and Prevenar. There was a concomitant Rotavirus gastroenteritis. The thrombopenia dissolved with immunoglobins. Test for thrombocyt autoantibodies was inconclusive. After reoccurrence of the thrombocytopenia additional investigations were performed (immunohistochemistry and bone marrow smear) to exclude underlying chronic inflammatory disease.

- **D0072425A (Germany): Thrombocytopenia, Petechiae, Haematoma.**

  This case was reported by a hospital physician and described the occurrence of thrombocytopenia in 24-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) and combined measles, mumps and rubella vaccine, live, attenuated (new strain) (Priorix,

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GlaxoSmithKline) for prophylaxis. On an unspecified date the subject received an unspecified dose of Infanrix hexa (0.5 ml, unknown). At an unspecified time post vaccination with Infanrix hexa, on an unspecified date, the subject experienced thrombocytopenia. This case was assessed as medically serious by GSK criteria. At the time of reporting the outcome of the event was unspecified. Follow-up information was received on 14 October 2011 form the reporting hospital physician. In follow-up information the reporting hospital physician reported Infanrix hexa as Infanrix and for the first time vaccination with Priorix. The lot number had not been known. The subject has no risk factors. The subject received no permanent concomitant medication. On 18 July 2011 the subject received an unspecified dose of Priorix (0.5 ml, intramuscular, unknown). On 04 August 2011 the subject received unspecified dose of Infanrix hexa (0.5 ml, intramuscular, unknown). Approximately 24 days post vaccination with Priorix and approximately seven days after vaccination with Infanrix hexa, on 11 August 2011, the subject experienced thrombocytopenia. The subject was hospitalised for an unknown period of time. Platelet count was as low as 1 G/l. Over time platelet count was 17, 67,101, 148, 140 and 102 G/l. The exact dates of platelet count determination had not been reported. The subject was treated with normal immunoglobulin (Immunoglobulin) and prednisolone (Prednisolon). After about eight days, on 18 August 2011, the event was resolved. The reporting hospital physician considered that the event was possibly related to vaccination with Priorix and Infanrix hexa. Follow-up information was received on 24 October 2011 form the reporting hospital physician. Symptoms of thrombocytopenia included petechiae and hematoma. Platelet count was 1, 17, 67,101, 148, 140 and 102 G/l on 12 August 2011, 13 August 2011, 14 August 2011, 15 August 2011, 16 August 2011, 18 August 2011 and 20 August 2011, respectively. Follow-up information has been requested.

Company comment: Thrombocytopenia in a 24 month-old subject 7 days post-vaccination with Infanrix Hexa.The event resolved after 8 days of treatment with immunoglobulin and steroids.

6.5.2.1.7. Thrombocytopenic purpura

Four (4) cases of Thrombocytopenic purpura were reported during the period (see Section 6.5.2.1.5 for Idiopathic thrombocytopenic purpura cases):

- **B0693767A (France): Thrombocytopenic purpura, Petechiae, Haematoma, Epistaxis, Splenomegaly, Thrombocytopenia, Gingival bleeding**

  This case was reported by the French regulatory authority (AFSSaPS reference PV20100367) and described the occurrence of thrombocytopenic purpura in a 25-week-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, inactivated poliomyelitis and Haemophilus influenzae type b with or without hepatitis B vaccine (unknown manufacturer) and pneumococcal vaccines (Prevenar, non-gsk) for prophylaxis. The subject was born at 39 weeks and 6 days of amenorrhea with a birth weight of 3.5 kg. The subject weighed 6.9 kg and measured 68 cm on admission. Her head circumference was 48 cm. Subject's parents had blood relations. Her mother suffered from migraine. On 21 September 2010, the subject received unspecified doses of unspecified Infanrix (reported batch number G4046,

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which was not a GSK batch number) (coded DTPa-HBV-IPV-HIB from unknown manufacturer) and Prevenar (batch E45165). Both vaccines were administered intramuscularly in unknown sites of infjection. On 09 October 2010, 18 days after vaccination, the subject presented with palate and tongue petechiae associated with epistaxis which stopped spontaneously. On 10 October 2010, dermatologic examination showed petechiae all over the body and arch of the foot hematoma. Clinical examination showed normal ganglionic area, splenomegaly and no hepatomegaly. Other part of this examination was unremarkable. Laboratory tests evidenced thrombopenia with platelets at 1000 /mcl. Hemoglobine was at 10.3 g/dl, white blood cells were at 9400 /mcl and C-reactive protein at 1 mg/ml. The subject received a first course of normal immunoglobulin (Tegeline) at 1 mg/kg. Platelets rose to 22000 /mcl. As petechiae persisted associated with a mild gingival bleeding which stopped spontaneously, a second course of Tegeline was administered on 12 October 2010. On 14 October 2010, platelets were at 163000 /mcl, hemoglobine at 9.4 g/dl and white blood cells at 8900 /mcl. Physicians concluded to a thrombocytopenic purpura suggestive of an idiopathic thrombocytopenic purpura. On discharge from hospital the subject weighed 6.78 kg. The subject was hospitalised. At the time of reporting, petechiae and hematoma were improved.

Company comment: Acase of thrombocytopenic purpura suggestive of ITP in a 25 week-old female subject 18 days after vaccination with combined diphtheria, tetanus-acellular pertussis, inactivated poliomyelitis and Haemophilus influenzae type b with or without hepatitis B vaccine (unknown manufacturer) and Prevenar. The event resolved after treatment with immunoglobulin.

- **B0693944A (Czech Republic): Thrombocytopenic purpura, Petechiae, Haematoma**

  This case was reported by a physician via a regulatory authority (CZ-State Institute for Drug Control # CZ-CZSUKL-10002001) and described the occurrence of thrombocytopenic purpura in a 4-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevenar 13) for prophylaxis. The subject had no relevant medical history and no concomitant medication. On 10 December 2010, the subject received 2nd dose of Infanrix hexa (intramuscular, injection site unknown, batch number not provided) and 2nd dose of Prevenar 13 (intramuscular, injection site unknown, batch number not provided). On 11 December 2010, 1 day after vaccination with Infanrix hexa and Prevenar 13, the subject developed petechiae and small hematoma without any symptoms. On 13 December 2010, the subject was hospitalised for 3 days. The subject was diagnosed as having idiopathic thrombocytopenic purpura. Relevant test were performed on 13 December 2010 and showed platelets count of 4.5, APPT (activated partial prothrombine time) of 40.2, and INR (international normalized ratio) of 0.98. The subject was treated with infusion of normal immunoglobulin (Immunoglobulin). On 14 December 2010, the subject's status remained unchanged. On 16 December 2010, the subject was discharged from the hospital, recovering and with improved laboratory data. On 4 January 2011, the subject underwent follow-up examination. Blood count was normal, platelets count was 204 (normal value). At the time of

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reporting, the events were resolved. The physician reported that the events were more likely related to vaccination with Infanrix hexa. He recommended any vaccination shouldn't be administrated to the subject in next months. Despite attempts to obtain follow-up details, no additional information could be obtained and the case has been closed.

Company comment: A case of thrombocytopenic purpura suggestive of ITP in a 4 month-old male subject one day after second combined vaccination with Infanrix Hexa and Prevenar. The haematologic status recovered after intravenous immunoglobulin.

- **B0695999A (Taiwan): Thrombocytopenic purpura.**

  This case described the occurrence of thrombocytopenic purpura in a 3-month-old subject of unspecified gender who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (DTPa-HBV-IPV-HIB, manufacturer unspecified) for prophylaxis. On 10 December 2007 the subject received 2nd dose of DTPa-HBV-IPV-HIB (unknown, lot number not provided). On 15 December 2007, 5 days after vaccination with DTPa-HBV-IPV-HIB, the subject experienced thrombocytopenic purpura. The subject was hospitalised. Relevant test results included platelet count: 2x103/mm3 and hemoglobin: 8 g/dl. The subject was treated with normal immunoglobulin (Immunoglobulin). The event was resolved within 6 days. The author considered the event was possibly related to vaccination with DTPa-HBV-IPV-HIB. The event did not reoccur.

  Company comment: A case of thrombocytic purpura 5 days after 2nd dose of Infanrix hexa in a 3-month-old subject. No autoimmune cause of this event was confirmed. No clear triggers or further episodes were reported.

- **B0724575A (France): Thrombocytopenic purpura, Thrombocytopenia, Petechiae, Injection site haematoma**

  This case was reported by the French regulatory authority (FR-Agence Francais de Securite Sanitaire des Produits de Sante # PO20110384) and described the occurrence of thrombocytopenic purpura in a 19-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), mmr vaccine () (M-M-RvaxPro, non-gsk) for prophylaxis. Medical history included bronchiolitis and upper respiratory tract infection (NOS). On 01 March 2011, the subject received an unspecified dose of M-M-RVaxPro (intramuscular, batch and injection site unknown). On 26 April 2011, the subject received an unspecified dose of Infanrix hexa (intramuscular, batch and injection site unknown). After this vaccination, the subject presented a severe hematoma at injection site (that could be suggestive of a decrease of platelet count at this time). On 16 May 2011, the subject was hospitalized with diffuse cutaneomucous petechial purpura. He had no fever. Lab test evidenced a severe thrombocytopenia with decrease of platelet at 3 G/l (normal 150-400). The subject was treated with normal immunoglobulin (Tegeline). In 48 hours, platelet count increased to 64 G/l. Subject's discharge was planned for 18 May 2011. At the time of reporting, thrombocytopenia

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was improved. Outcomes of hematoma at injection site and purpura, and petechiae were unspecified. According to the French method of assessment, the AFSSaPS considered the causal relationship between vaccination with Infanrix hexa and M-M-RvaxPro and the events as dubious.

Company comment: A case of thrombocytopenic purpura in a 19-month-old male subject 20 days after 2nd dose of Infanrix-hexa. No autoimmune cause of this event was confirmed. No clear triggers orfurther episodes were reported.

6.5.2.1.8. Thrombocytosis

Two (2) cases of Thrombocytosis were reported during the period:

- **B0729166A (Spain): Pemphigoid, Leukocytosis, Thrombocytosis, Blister, Scab, Skin lesion, Pruritus, Eosinophilia, Urticaria**

  This case was reported in a literature article and described the occurrence of bullous pemphigoid in a 3-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (DTPa-HBV-IPV-HIB, manufacturer unspecified), meningococcal polysaccharide vaccine group C and unspecified Pneumococcal vaccine for prophylaxis. On an unspecified date, the subject received an unspecified dose of DTPa-HBV-IPV-HIB (administration site and route unknown, batch number not provided), an unspecified dose of Meningococcal polysaccharide vaccine group C (administration site and route unknown, batch number not provided) and an unspecified dose of Pneumococcal vaccine (administration site and route unknown, batch number not provided). 3 weeks after vaccination with DTPa-HBV-IPV-HIB, Meningococcal polysaccharide vaccine group C and Pneumococcal vaccine, the subject experienced bullous pemphigoid with blistering eruption on her palms and soles and back of the fingers, scabs and denuded areas and urticaria plaque on trunk and face. Subsequently, they were appearing lesions on the trunk, arms and andretroauricular region dominated by erythematous plaques of annular morphology. No mucosal involvement. The lesions were itchy and woke up the girl during the night. This case was assessed as medically serious by GSK. A skin biopsy was performed which showed a subepidermal blister with eosinophils and a few polymorphonuclears. In the superficial dermis, it was identified perivascular eosinophilic infiltrate. The direct immunofluorescence showed linear deposits of IgG and C3 in the epidermal basal membrane, with negativity for the markers IgA, IgM and C1q. Laboratory tests revealed leukocytosis with eosinophilia and thrombocytosis. Antibasement membrane antibodies and the rest of the profile of autoimmunity were negative. The subject was treated with antibiotics and steroid (Topical steroid) with a very good evolution and control of the lesions. After vaccination at 4 months-old, 3 to 4 days after vaccination, she presented a sudden worsening of the lesions, with involvement of palms, soles, trunk, arms and face in a generalized way. The subject was treated with deflazacort. 15 days after the start of the treatment, the lesions had completely disappeared in all locations. At the 6 months-old vaccination, in hours after vaccination, she experienced a slight outbreak, keeping the dose of corticosteroids orally. Later, there was a progressive decrease until its suppression at 3 months, no

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relapse during 12 months of follow-up. After vaccination at 15 months-old, no AEs occurred. At the time of reporting, the events were resolved. The author considered the events were related to vaccination with DTPa-HBV-IPV-HIB, Meningococcal polysaccharide vaccine group C and Pneumococcal vaccine.

Company comment: A case of bullous pemphigoid 3 weeks after vaccination in a 3-month-old subject in childhood. Although there is a temporal relationship with repeat vaccinations at 4 and 6 months, it is difficult to determine a causal relationship.

- **D0072024A (Germany): Meningitis pneumococcal, Gastroenteritis rotavirus, Respiratory syncytial virus infection, Pneumococcal sepsis, Pharyngitis, Somnolence, Pyrexia, Fluid intake reduced, Respiration abnormal, Crying, Diarrhoea, Cardiovascular insufficiency, Pallor, Tachypnoea, Anaemia, Thrombocytosis**

  See Section 6.5.2.7.11 Sepsis.

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6.5.2.2. Cardiac disorders

6.5.2.2.1. Bradycardia

Eleven (11) cases including the event Bradycardia were identified during the period:

Table 7 Summary of cases of Bradycardia identified during the reporting period

Case ID	Initial Date Received By Dept	Age	Gender	Case Outcome	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
A0901400A	23-Dec-10	67 Days	Female	Improved	Infanrix hexa	Tri-Vi-Sol, Ferrous sulfate	Hours	Apnoea, Bradycardia, Oxygen saturation decreased, Wrong technique in drug usage process	Canada	Anaemia neonatal, Bronchopulmonary dysplasia, Premature baby, Apnoea, Bradycardia, Oxygen saturation decreased
B0691130A	28-Dec-10	2 Months	Male	Resolved	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Dopram	5 Hours	Apnoea, Bradycardia, Oxygen saturation decreased, Blood pressure decreased, Apparent life threatening event, Urine output decreased, Cholinergic syndrome, Eye movement disorder, Gastrooesophageal reflux disease, Aspiration	France	Premature baby, Infantile apnoeic attack, Inguinal hernia

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Case ID	Initial Date Received By Dept	Age	Gender	Case Outcome	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0694497A	19-Jan-11	8 Weeks	Female	Resolved	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Paracetamol	16 Hours	Cyanosis, Acidosis, Apnoea, Inflammation, Oxygen saturation decreased, Bradycardia, Injection site pain, Injection site swelling, Injection site erythema, Bacterial infection	Netherlands	Premature baby, Nasopharyngitis, Small for dates baby
B0698663A	08-Feb-11	4 Months	Male	Resolved	Infanrix hexa	Respiratory syncytial virus vaccine, Palivizumab, Frusemide, Iron polymaltose, Multivitamins, Nutritional supplement, Emollient, Ibuprofen, Indomethacin, Cortisone	0 Days	Anaphylactic reaction, Circulatory collapse, Slow response to stimuli, Cyanosis, Hypotonia, Hypothermia, Pallor, Bradycardia, Oxygen saturation decreased, Pyrexia	Italy	Premature baby, Mechanical ventilation, Patent ductus arteriosus, Bronchopulmonary dysplasia
B0705098A	08-Mar-11	2 Months	Female	Resolved	Infanrix hexa		Immediate	Presyncope, Bradycardia, Hypotonia, Injection site pain, Loss of consciousness, Cyanosis	France	
B0711289A	28-Mar-11	6 Weeks	Unknown	Unknown	Synflorix, Infanrix hexa	Rotavirus vaccine, Infanrix hexa	8 Hours	Cardiopulmonary failure, Pyrexia, Bradycardia	South Africa	Premature baby

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Case ID	Initial Date Received By Dept	Age	Gender	Case Outcome	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0714363A	19-Apr-11	2 Months	Male	Resolved	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Ranitidine hydrochloride, Domperidone	8 Hours	Hypotonic-hyporesponsive episode, Anaemia, Hypotonia, Pallor, Dyspnoea, Bradycardia, Hypopnoea, Staring	Netherlands	Gastrooesophageal reflux disease, Bradycardia, Vomiting, Dyspnoea
B0754941A	07-Oct-11	2 Months	Female	Resolved	Infanrix hexa, Rotavirus vaccine, Pneumococcal vaccines (Non-GSK)		Minutes	Apnoea, Bradycardia, Pallor, Foaming at mouth	Belgium	
B0755056A	13-Oct-11	2 Months	Female	Resolved	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Poractant alfa, Betamethasone sodium phosphate, Whole human blood, Epoetin beta	Same day	Apnoea, Hypoxia, Bradycardia, Malaise, Inflammation, Respiratory disorder	France	Premature baby, Neonatal respiratory distress syndrome, Lung infection, Bronchopulmonary dysplasia, Anaemia neonatal, Gastrooesophageal reflux disease

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Case ID	Initial Date Received By Dept	Age	Gender	Case Outcome	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0069341A	05-Nov-10	3 Months	Male	Resolved	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Hours	Circulatory collapse, Apnoea, Loss of consciousness, Pallor, Bradycardia, Salivary hypersecretion, Cyanosis, Epilepsy, Partial seizures, Foaming at mouth, Hypotonia, Cardiac arrest, Vomiting, Dyskinesia, Eye movement disorder, Productive cough, Depressed level of consciousness, Hypokinesia, Bronchitis	Germany	Atrial septal defect
D0071220A	02-May-11	12 Weeks	Male	Unresolved	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Apnoea, Bradycardia	Germany	Premature baby, Neonatal respiratory distress syndrome, Bronchopulmonary dysplasia, Retinopathy

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6.5.2.2.2. Cardiac arrest

Three (3) cases including the PT Cardiac arrest were reported during the period. Cases B0706503A and B0716780A are described in Section 6.5.1 Cases with a fatal outcome. The third case is described below:

- **D0069341A (Germany):Circulatory collapse, Apnoea, Loss of consciousness, Pallor, Bradycardia, Salivary hypersecretion, Cyanosis, Epilepsy, Partial seizures, Foaming at mouth, Hypotonia, Cardiac arrest, Vomiting, Dyskinesia, Eye movement disorder, Productive cough, Depressed level of consciousness, Hypokinesia, Bronchitis**

  This case was reported by a physician and described the occurrence of collapse unspecified in a 3-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. On 5 November 2010 the subject received 2nd dose of Infanrix hexa (unknown route and application site). Approximately less than one hour after vaccination with Infanrix hexa, while being in the office yet, the subject experienced unspecified collapse. This case was assessed as medically serious by GSK. Follow-up was received by the physician on 10 December 2010, including a questionnaire. Co-suspect vaccinations included 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer) Previous vaccination with Infanrix hexa and Prevenar 13 was well tolerated. On 5 November 2010 the subject received 2nd dose of Infanrix hexa (intramuscular, left thigh), together with unspecified dose of Prevenar 13 (intramuscular, right thigh). At an unspecified time after vaccination with Infanrix hexa and Prevenar 13, the subject experienced "abrupt pallor and hypopnoea/apnea for 3-4 minutes, short-time bradycardia for over 1 minute, salivation and loss of consciousness for 2-3 minutes". The subject was treated with oxygen. The subject was hospitalised for 2-4 days. At the time of reporting, on 9 November 2010, all events were resolved. The physician considered pallor, hypopnoea/apnea, short-time bradycardia, salivation and loss of consciousness were probably related to vaccination with Infanrix hexa and Prevenar 13. Follow-up was received from the reporting physician on 20 April 2011, including a questionnaire and 4 reports from other physicians. According to the questionnaire, there was no concurrent medical condition or any other risk factors. On an unspecified date the subject experienced cyanosis, apnea and bradycardia. These events were resolved after 3 minutes. The subject was treated with oxygen. At the time of reporting, all events were resolved. After the next vaccination with Infanrix hexa the events did not recur. The physician considered cyanosis, apnea and bradycardia were unrelated to vaccination with Infanrix hexa. "According to the physicians' reports, the suspicion of adverse events was not confirmed". According to the 1st physician's report from 17 December 2010, "suspected beginning generalized idiopathic epilepsy with unspecific epileptic seizures (atonic seizures with myoclonia) (possible epilepsy) was diagnosed. Secondary generalized epilepsy of focal origin (focal secondary epileptic convulsions) was considered by differential diagnosis. "Six weeks ago, after a vaccination, the subject experienced collapse with pallor, blue lips (cyanosis), foaming at mouth, unresponsive episode, atonia and loss of consciousness. These

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events were resolved after 3 minutes. The subject was hospitalised and 48 hours observed. On discharge from hospital the subject was in normal condition. Electroencephalogram one week later showed normal findings. The events were interpreted as cardio-vascular phenomenon. Ultrasonic findings of heart showed small foramen ovale." It was reported that the subject experienced asystole lasting for 3 seconds. On 17 December 2010 the subject was vomiting. There was no fever. When the subject was laid down, the subject experienced pallor and blue lips. He experienced occasional jerking in head-shoulder area, salivation with forming of vesicles, loss of consciousness, unresponsiveness and eyes rolling. These events were resolved after approximately 5 minutes. Afterwards, the subject gradually came to himself, started crying and fell asleep. At the moment, the subject suffered from cough with mucus and was teething. The patient's family history included suspected benign infantile myoclonic epilepsy (the subject's brother). "Pregnancy anamnesis of subject's mother was without findings. After 40+2 weeks of pregnancy the subject was born, weighing 3750 g, with a size of 52 cm and an Apgar score of 9 / 10 / 10. The subject was healthy. Infant development was normal. There were no operations, no internal diseases, no special accidents. The subject was vaccinated only once, with the reported seizure. Despite that, there were no unusual findings." Electroencephalogram was performed and showed "sleep electroencephalogram according to age with well pronounced sleep architecture up to sleep phase C." "The subject now experienced his 2nd afebrile convulsive seizure with rather atypic progress. This time atonic with sprinkled myoclonia or cloni, trunk and head stressed, respectively. No relationship to a triggering situation or fever could be found, although the subject was suffering from phlegm and so suspicion of an infection associated seizure could not be ruled out completely." According to the 2nd physician's report from 3 January 2011, since the event on December 2010 there were no further events. Electroencephalogram was performed on 3 January 2011 and showed awake electroencephalogram according to age. Cerebral magnetic resonance tomography showed normal findings. "Immediately after electroencephalogram, the subject was atonic at trunk and extremities for 3-4 minutes, was pale and unusually calm. There was no fixed stare, but looking straight on, no indication for a focal event, no cloni. This was the 3rd event. It could possibly have been a seizure, too. Afterwards, there was no tiredness like after the former events." According to the 3rd physician's report from 11 April 2011, the subject visited the surgery on 17 February 2011. Sleep electroencephalogram was performed and showed normal findings. Concerning the Cerebral magnetic resonance tomography performed on 17 December 2010, "in the T2 assessed picture discrete signal increase in the area of white brain substance were conspicuous, which spread from the posterior horn rather diffuse". A second magnetic resonance tomography was recommended. It was reported that the subject's mother reported about mild motor retardation. According to the 4th physician's report, when the subject was 7 months old, there was no indication for structural abnormality of the heart, no indication of clinically relevant formation of a vascular ring. Affect spasm was considered by differential diagnosis. There were repeated incidents of loss of consciousness, at the 1st time at the age of 3 months after vaccination. A 2nd time after vomiting and 2 further times when expectorating mucus during bronchitis. There never was stridor. Electrocardiogram and echocardiography showed normal findings. Foramen ovale was functionally closed. "There was no indication of structural abnormality of the heart or anomaly in

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the area of the great vessels. Especially there was no indication for pulmonal sling or arterial vascular ring, which could have been causal for such syncopal symptoms."

Company comment: Unspecified collapse in a 3 month-old female subject less than 1 hour after 2nd vaccination with Infanrix hexa, combined with Prevenar. Spontaneous recovery after 3 minutes with oxygen therapy. The event occurred 2 times more, unrelated to vaccinations. Suspicion of epileptic origin without conclusive results on EEG or MRI.

6.5.2.2.3. Cardio-respiratory arrest

One (1) case including the PT Cardio-respiratory arrest was received during the period (B0705290A) and is described in Section 6.5.1 Cases with a fatal outcome.

6.5.2.2.4. Cardiogenic shock

One (1) case including the PT Cardiogenic shock was reported during the period:

- **D0070772A (Germany): Cardiogenic shock, Cardiac failure, Congestive cardiomyopathy, Atrial tachycardia, Supraventricular tachycardia, Acidosis, Pyrexia, Gastrointestinal pain, Hypokalaemia, Fluid intake reduced, Hypertension, H1N1 influenza, Cholecystitis, Psychotic disorder, Crying**

  This case was reported via a regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2011007870) and described the occurrence of cardiogenic shock in a 3-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa), live attenuated human rotavirus vaccine (Rotarix) and pneumococcal vaccines (non-gsk, Prevenar) for prophylaxis. Previous vaccinations were well tolerated. On 01 March 2011 the subject received a dose of Rotarix, a dose of Prevenar (right thigh) and a dose of Infanrix hexa (left thigh). According to the report Infanrix was administered, based on the provided lot number however it was evident that Infanrix hexa was administered. Twelve days after vaccination, on 13 March 2011, the subject developed atrial tachycardia and dilated cardiomyopathy. The following day, on 14 March 2011, cardiogenic shock occurred. The subject was hospitalised. Diagnosis was confirmed by means of laboratory examinations, ultra sound scan and electrocardiography (Results not specified). Meningitis was excluded. The reporter considered the events were life threatening. At the time of reporting the events were unresolved. Follow-up information was received on 26 April 2010 via the regulatory authority by means of structured information and a hospital report. On 01 March 2011 the subject received a dose of Infanrix hexa (left thigh) together with a dose of Prevenar (right thigh) and a dose of Rotarix. Twelve days after vaccination, on 13 March 2011, the subject presented at a hospital and suffered from reduced fluid intake, stomach pain and a mild increase in temperature (38.4 deg C). Cholecystitis was suspected and the subject was treated with claforan and ampicillin trihydrate. The subject's symptoms worsened continuously, tachycardia occurred (heart rate: 220-240 bpm) and the subject was in need of oxygen. The following day, on 14 March 2011 myocarditis was suspected and the subject was transferred to another hospital by helicopter. The subject was diagnosed with cardiogenic shock (with associated acidosis and arterial hypertension), received

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artificial ventilation as well as an insertion of arterial and central venous catheters. In echocardiogram atrial enlargement and spherical ventricular dilation (left) were observed. Supraventricular tachycardia with alternating heart rates (occasionally above 220 bpm) was observed in electrocardiogram. For clarification of the origin of the subject's cardiac insufficiency, myocarditis was excluded by means of serologic findings. The subject was negative for cardiotropic infections. Cardiac muscular enzymes were borderline but normal. Antiarrythmic therapy was started with propafenone hydrochloride (Rytmonorm), sotalol hydrochloride (Sotalex) and digoxin. Anticongestive therapy was started with enoximone (Perfan), frusemide (Furosemid), captopril and spironolactone (Aldactone). Additionally he was treated with teicoplanin (Targocid). Subsequently the subject's cardiac function improved and in echocardiogram ventricular dilation was found regressing. As myocarditis could be excluded, the subject was suspected with pre-existing focal atrial tachycardia and resulting heart insufficiency and current cardiogenic shock. Daily dose of antiarrythmic medication was increased continuously. Heart rate was reduced significantly but continuous sine rhythm could not be established. Phases with extrasystoles were declining. At the hospital the subject was also observed with recurrent crying attacks and received treatment with sedatives (promethazine hydrochloride (Atosil) and phenobarbitone (Phenobarbital)). As there were no signs of pain or hunger, the subject's crying attacks were considered symptoms of transitory psychotic syndrome. On 18 March 2011 artificial ventilation was removed and the subject was observed with sufficient spontaneous respiration. The subject's general condition improved significantly and the subject could be switched to oral nutrition with supportive volume replacement. On 19 March 2011 pharyngeal swab was positive for H1N1 virus and treated with oseltamivir phosphate (Tamiflu) and meropenem (Meronem). In serologic examinations the subject was negative for Influenza A antibodies and positive for Influenza B IgG. The subject was also diagnosed with hypokalemia and received treatment with sodium fluoride (Zymafluor). After nine days the subject was discharged from the hospital. The regulatory authority reported that the subject was recovering.

Company comment: Cardiogenic shock in a 3 month-old male subject, 12 days after vaccination with Infanrix hexa, combined with Rotarix and Prevenar. Diagnosis of pre-existing focal atrial tachycardia and heart insufficiency recovered with anti-arritmica.

6.5.2.2.5. Cyanosis

Fifty eight (58) cases including the event cyanosis were identified during the period of this report. Most cases were reported in association with a concurrent disease likely to have caused cyanosis, as shown in Table 8. Only one concurrent disease is shown per case, however more than one relevant concurrent disease may have been reported for a given case. This table also includes one case received prior to the period of this report but never included in a previous PSUR (B0591710A). This case's ID is marked by a '*' in Table 8.

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Table 8 Concurrent diseases reported among cyanosis cases identified during the period

Concomitant diseases (Number of Cyanosis cases received with given concomitant disease)	**Case IDs**
Seizures (n=15)	B0683335A, B0690279A, B0692681A, B0712712A, B0715581A, B0716294A, B0716693A, B0722809A, B0741792A, B0747746A, D0069341A, D0069889A, D0071143A, D0071548A, D0072318A
Circulatory collapse (n=4)	B0698663A, B0713106A, D0069341A, D0070901A
(Pre)Syncope (n=2)	B0705098A, D0072433A
Hypotonia (n=18)	B0683004A, B0692681A, B0698663A, B0705098A, B0706016A, B0711564A, B0712712A, B0715332A, B0716345A, B0716693A, B0717794A, B0726312A, B0734041A, D0069341A, D0070901A, D0071548A, D0072433A, B0591710A*
Hypertonia (n=6)	B0706228A, B0715581A, B0716294A, B0716693A, B0719722A, D0069889A
Apnoea (n=9)	B0694497A, B0706228A, B0713567A, B0715332A, B0717794A, D0069341A, D0071143A, D0071156A, D0072273A
Dyspnoea (n=5)	B0712985A, B0719722A, B0729115A, D0071143A, D0071548A
Apparent life threatening event (n=0)	Not Applicable
Sudden Infant death Syndrome, Sudden death (n=0)	Not Applicable

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6.5.2.3. Eye disorders

6.5.2.3.1. Gaze palsy

Eighteen (18) cases including the event Gaze palsy were identified during the period of this report. In 12/18 cases the event was associated to a reported convulsion (febrile in 4 cases). The event lasted between 2 hours and 10 days by mean. The outcomes had been documented in half of cases and were favourable (resolved). Cases are summarized in the table below.

Table 9 Summary of cases of Gaze palsy identified during the period

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0681967A	28-Oct-10	Resolved	2 Months	Female	Infanrix hexa, Meningococcal polysaccharide vaccine group C (Non-GSK), Pneumococcal vaccines (Non-GSK)		2 Hours	Gaze palsy, Hypotonia, Pallor	Spain	
B0682745A	03-Nov-10	Unresolved	6 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Hours	Convulsion, Loss of consciousness, Gaze palsy, Pallor, Pyrexia, Crying	Netherlands	
B0683261A	05-Nov-10	Resolved	3 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Magaldrate, Ranitidine hydrochloride	10 Days	Gaze palsy, Hypotonia	Italy	
B0687865A	07-Dec-10	Resolved	11 Months	Male	Infanrix hexa	Priorix	2 Days	Loss of consciousness, Gaze palsy, Pallor, Hypotonia	Italy	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0690071A	17-Dec-10	Unknown	3 Months	Male	Infanrix hexa, Synflorix		8 Hours	Hypotonic-hyporesponsive episode, Gaze palsy, Opisthotonus, Pallor, Apathy, Fear, Agitation, Hypotonia, Crying	Czech Republic	Dermatitis atopic
B0712712A	05-Apr-11	Resolved	13 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Hours	Loss of consciousness, Depressed level of consciousness, Convulsion, Gaze palsy, Respiration abnormal, Pallor, Hypotonia, Drooling, Cyanosis, Pyrexia, Vomiting	Netherlands	
B0717794A	06-May-11	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		36 Hours	Loss of consciousness, Apnoea, Depressed level of consciousness, Gaze palsy, Pallor, Cyanosis, Hypotonia, Peripheral coldness, Pyrexia	Netherlands	
B0722407A	24-May-11	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		14 Hours	Gaze palsy, Hypertonia, Pyrexia, Dyskinesia, Somnolence, Feeling hot	Netherlands	
B0739945A	11-Aug-11	Unknown	5 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Convulsion, Gaze palsy, Clonus, Pyrexia	Italy	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0069309A	03-Nov-10	Unknown	4 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Febrile convulsion, Pyrexia, Musculoskeletal stiffness, Gaze palsy, Somnolence, Transaminases increased, Pharyngeal erythema, Tympanic membrane hyperaemia	Germany	Cardiac murmur
D0071075A	18-Apr-11	Unknown	3 Months	Male	Rotavirus vaccine, Infanrix hexa, Synflorix		1 Days	Thalamus haemorrhage, Convulsion, Facial paresis, Hemiparesis, Hypophagia, Restlessness, Pyrexia, Screaming, Somnolence, Pallor, Hyperaesthesia, Eyelid oedema, Abdominal distension, Hypotonia, Apnoea, Gaze palsy	Germany	
D0071143A	26-Apr-11	Unknown	6 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK), Intubation, Mechanical ventilation	0 Days	Apnoea, Cyanosis, Febrile convulsion, Gaze palsy, Altered state of consciousness, Convulsion, Body temperature increased, Breath holding, Moaning, Erythema, Swelling, Hypokinesia, Pain, Pyrexia, Dyspnoea, Infection	Germany	Premature baby, Neonatal respiratory distress syndrome, Neonatal respiratory failure, Infantile apnoeic attack, Bradycardia neonatal, Hyperbilirubinaemia neonatal, Regurgitation

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0071366A	13-May-11	Unknown	12 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Convulsion, Depressed level of consciousness, Gaze palsy, Hypochromic anaemia, Pyrexia, Injection site erythema, Musculoskeletal stiffness, Iron deficiency	Germany	
D0071548A	27-May-11	Unknown	8 Months	Female	Infanrix hexa, Synflorix		1 Days	Convulsion, Gaze palsy, Cyanosis, Vaccination complication, Restlessness, Feeling hot, Staring, Muscle twitching, Dyspnoea, Hypotonia, Somnolence, General physical health deterioration, Body temperature increased	Germany	
D0071728A	15-Jun-11	Resolved	3 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	0 Days	Hypotonic-hyporesponsive episode, Eye movement disorder, Convulsion, Gaze palsy, Opisthotonus, Crying	Germany	
D0072315A	08-Aug-11	Resolved	4 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Salbutamol sulphate	1 Days	Febrile convulsion, Muscle rigidity, Opisthotonus, Gaze palsy, Pyrexia	Germany	Bronchitis

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0072318A	08-Aug-11	Resolved	15 Months	Female	Infanrix hexa		0 Days	Febrile convulsion, Pyrexia, Chills, Gaze palsy, Eye movement disorder, Cyanosis, Unresponsive to stimuli, Tremor, Grand mal convulsion, Upper respiratory tract infection	Germany	Familial risk factor, Febrile convulsion, Hospitalisation, Cardiac murmur, Underweight
D0073004A	11-Oct-11	Unknown	16 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		48 Hours	Convulsion, Pallor, Gaze palsy, Depressed level of consciousness, Joint hyperextension	Germany	

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6.5.2.4. Gastrointestinal disorders

6.5.2.4.1. Diarrhoea haemorrhagic

Two (2) cases of Diarrhoea haemorrhagic were reported during the period:

- **B0747304A (Poland): Diarrhoea haemorrhagic, Pyrexia, Crying, Restlessness, Abnormal behaviour**

  This case was reported by a physician via regulatory authority (PL-Office of Medicinal Products # -PL-URPL-OCR-20110905014) and described the occurrence of hemorrhagic diarrhea in a 4-month-old subject of unspecified gender who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), live attenuated human rotavirus vaccine (Rotarix) for prophylaxis. On 12 August 2011 the subject received unspecified dose of Infanrix hexa (intramuscular, unknown injection site), unspecified dose of Rotarix (oral). On 14 August 2011, 2 days after vaccination with Infanrix hexa and Rotarix, the subject experienced hemorrhagic diarrhea, fever (38 deg C) lasting for 2 days, crying, restlessness and change in behavior. Diarrhea withdrew after 11 hours. The subject was hospitalized from 14 to 18 August2011. Relevant test results included: Rotavirus test: negative; Adenovirus test: negative; Salmonella test: negative; At the time of reporting the events were resolved. No further information is expected.

  Company comment: The symptoms and test results confirming the diagnosis of digestive Haemorrhage (during 48 hours) after Infanrix hexa and Rotarix vaccination were not reported. Fever was associated to the episode but infectious cause could not be evidenced.

- **B0754698A (Poland): Diarrhoea haemorrhagic, Pyrexia, Vomiting, Faeces discoloured, Dermatitis diaper, Erythema, Dyspepsia**

  This case was reported by a physician via a regulatory authority (PL-Office of Medicinal Products # PL-URPL-OCR-20110923001) and described the occurrence of bloody diarrhea in a 2-month-old subject of unspecified gender who was vaccinated with live attenuated human rotavirus vaccine (Rotarix, GlaxoSmithKline), combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa) and pneumococcal vaccines (non-GSK) (Prevenar 13) for prophylaxis. Since the 29 July 2009, the subject experienced restlessness. On 02 August 2011, during a medical visit, the subject had abdominal pain and inflated abdomen, which was decompressed with catheter. On 04 August 2011, during another medical visit, inflated abdomen decreased and it was also decompressed with catheter. On 10 August 2011, the baby was in good general condition, ultrasonography of the abdomen and urine cultures were without abnormalities. The subject had a soft belly. On 18 August 2011, the subject received unspecified dose of Rotarix (oral), unspecified dose of Infanrix hexa (intramuscular, unknown injection site), unspecified dose of Prevenar 13 (intramuscular, unknown injection site). On 19 August 2011, 1 day after vaccination with Infanrix hexa, Prevenar 13 and Rotarix, the subject experienced bloody diarrhea, fever (37.8 deg. C) and vomiting. The

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subject was hospitalised. On 23 August 2011, at a medical control, the subject experienced dyspepsia, and still has stools with blood since a few days. On 24 August 2011, at the next medical control, the subject experienced diaper dermatitis, the stools became normal but severe reddening of skin on buttocks appeared. On 13 September 2011, the subject was hospitalised at Gastroenterological Clinic. At the time of reporting the outcome of the events was unspecified. No further information is expected, the regulatory Authority has provided GSK with all the available information for the time being, if they ever get any further information they will send it to GSK. Follow-up information received by the RAN: Hospitalisation dates were unclear so no clarification was possible. On 19 August 2011, the subject experienced green stools. On 24 August 2011, bloody diarrhea and green stools were resolved. The outcome of the rest of the events was unspecified.

Company comment: Episodes of haemorragic diarrhea in a 2-month-old subject starting 1 day after combined vaccination with Infanrix hexa, Priorix and Prevenar. The subject was hospitalized but diagnostic test results are not available. The event has been resolved.

6.5.2.4.2. Haematochezia

Three (3) cases of Haematochezia were reported over the period:

- **B0714317A (Czech Republic): Haematochezia, Gastrointestinal inflammation, Restlessness, Flatulence, Frequent bowel movements**

  This case was reported by a physician and described the occurrence of blood streaks in stools in a 2-month-old female subject who was vaccinated with live attenuated human rotavirus vaccine (Rotarix, GlaxoSmithKline), combined diphtheria, tetanus-acellular pertussis, hepatitis B and inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa) for prophylaxis. The subject was healthy full term baby. On 23 March 2011, the subject received 1st dose of Rotarix (oral) and unspecified dose of Infanrix hexa (route and injection site unknown, batch number not provided). On 30 March 2011, 7 days after vaccination with Infanrix hexa and Rotarix, the subject experienced impurity of blood in stools, restlessness, flatulent belly and frequent stools. The physician considered the events were clinically significant (or requiring intervention). In April 2011, relevant test results included normal stool culture and normal sonography of abdomen which excluded intussusception. The subject was treated with symptomatic therapy. At the time of reporting, the events were unresolved. The physician considered the events were probably related to vaccination with Rotarix and the relationship between the events and Infanrix hexa was unspecified. Follow-up information received on 28 April 2011: The final diagnosis provided was unspecified gastrointestinal inflammation. The subject's condition was improved, but not resolved. Streaks of blood in stools appeared occasionally. Despite attempts to obtain follow-up details, no additional information could be obtained and the case has been closed.

  Company comment: Intermittent haematochezia in a 2-month-old female subject starting 7 days after vaccination with Infanrix hexa and Rotarix. Final diagnosis of unspecified gastrointestinal inflammation after exclusion of infection and intussusception.

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- **B0754377A (South Africa): Intussusception, Diarrhoea, Haematochezia**

  This case was reported by a healthcare professional (nurse) and described the occurrence of intussusception in a 4-month-old female subject who was vaccinated with live attenuated human rotavirus vaccine (Rotarix, GlaxoSmithKline), combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa) and Synflorix for prophylaxis. The child was breastfeeding and was on formula. On 29 September 2011, the subject received unspecified dose of Rotarix (oral), unspecified dose of Infanrix hexa (unknown route of administration), unspecified dose of Synflorix (unknown route of administration). On 4 October 2011, 5 days after vaccination with Infanrix hexa, Rotarix and Synflorix, the subject experienced intussusception, diarrhea and blood in stools. The subject was seen by a paediatrician. This case was assessed as medically serious by GSK. On 5 October 2011, the subject was operated due to intussusception. At the time of reporting the outcome of the events was unspecified. The healthcare professional considered the events were possibly related to vaccination with Rotarix, Infanrix hexa and Synflorix.

  Company comment: A bowel intussusception needing surgery in a 4-month-old female subject 5 days after combined vaccination with Infanrix hexa, Synflorix and Rotarix.

- **D0073097A (Germany): Haematochezia, Gastrointestinal pain**

  This case was reported by a physician via a German regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2011033460) and described the occurrence of blood in stools in a 13-week-old male subject who was vaccinated with live attenuated human rotavirus vaccine (Rotarix, GlaxoSmithKline) and combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Co-suspect vaccinations included 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer Pharma). The subject's past medical history was not provided. The subject has received no previous vaccination. On 29 September 2011 the subject received the first dose of Rotarix (0.5 ml, oral) as well as the first dose of Infanrix hexa (0.5 ml, intramuscular, left thigh) and the first dose of Prevenar 13 (0.5 ml, intramuscular, right thigh), contralaterally. Approximately two days post vaccination with Rotarix, Infanrix hexa and Prevenar 13, on 01 October 2011, the subject experienced blood in stools and gastrointestinal pain. The subject was hospitalised for an unknown period of time. Bacteria stool tests for Salmonella, Shigella, Yersinia and Campylobacter were negative. After about two days, on 02 October 2011, blood in stools was resolved. After about seven days, on 07 October 2011, gastrointestinal pain was resolved. The vaccination courses with Rotarix, Infanrix hexa and Prevenar 13 were discontinued. The German regulatory authority (DE-Paul-Ehrlich-Institut) has requested further information. At the moment no further information was available.

  Company comment: Haematochezia 2 days after combined vaccination with Infanrix hexa, Rotarix and Rotarix in a 13-week-old male subject Infectious causes were

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excluded and the event resolved spontaneously. Vaccination courses were discontinued.

6.5.2.4.3. Intussusception

One (1) case of Intussusception was reported during the period (B0754377A) and is described in Section 6.5.2.4.2 Haematochezia.

6.5.2.4.4. Rectal haemorrhage

One (1) case of Rectal haemorrhage was received during the period:

- **B0749250A (France): Rectal haemorrhage.**

  This case was reported by a regulatory authority (Afssaps case ID # RS20110348) and described the occurrence of rectorrhagia in a 2-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) and pneumococcal vaccines (Prevenar 13, non-gsk) for prophylaxis. Concurrent medical conditions included cow milk protein allergy with the following symptoms vomiting and bloating. The subject was fed with Neocate (hypoallergenic, amino-acid based, nutritionally complete infant formula). On 20 March 2011 the subject received a 1st dose of Infanrix hexa (intramuscular, batch and injection site unknown) and a 1st dose of Prevenar 13 (intramuscular, batch and injection site unknown). On 21 March 2011, 12 to 24 hours after vaccination with Infanrix hexa and Prevenar 13, the subject experienced rectorrhagia which persisted for 24 to 48 hours. One month later, rectorrhagia recurred. The regulatory authority reported that the event was clinically significant (or requiring intervention). At the time of reporting, rectorrhagia was resolved. According to the French method of assessment, the AFSSaPS considered unlikely the causal relationship between vaccination with Infanrix hexa and Prevenar 13 and rectorrhagia.

  Company comment: 24 to 48 hours of rectorrhagia in a 2-month-old male subject1 day after vaccination with Infanrix hexa and Prevenar. No details on symptoms, physical examination, investigations and treatment were reported. Recurrence after administration of another DTP-IPV-Hib (Pentavac, non GSK) 1 month later.

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6.5.2.5. General disorders and administration site conditions

6.5.2.5.1. Abscess sterile, Injection site abscess sterile

Seven (7) cases of Abscess sterile/Injection site abscess sterile were received during the period and are summarized in Table 10. Note that case **D0069239A (Germany): Soft tissue necrosis, Debridement, Incorrect route of drug administration** described a sterile abscess complication indicated for surgery and is reported in Section 6.5.2.8.2 Soft tissue necrosis.

Table 10 Summary of cases of Abscess sterile/Injection site abscess sterile identified during the period

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0068815B	09-Sep-10	Unresolved	19 Months	Male	Infanrix hexa	Infanrix hexa	0 Years	Abscess sterile, Injection site swelling, Injection site induration, Scar, Abscess drainage, Purulence, Cyst	Germany	Nephroplasty
D0070025A	19-Jan-11	Unknown	6 Years	Male	Infanrix hexa	Pneumococcal vaccines (Non-GSK)	64 Days	Abscess sterile, Neoplasm skin, Induration, Injection site swelling, Injection site discolouration, Granuloma skin, Scar, Surgery, Vaccination complication	Germany	
D0070846A	30-Mar-11	Unresolved	10 Months	Male	Infanrix hexa	Pneumococcal vaccines (Non-GSK), Sodium Fluoride	27 Days	Aspartate aminotransferase increased, Alanine aminotransferase increased, Injection site nodule, Injection site induration, Injection site erythema, Febrile convulsion, Soft tissue infection, Abscess sterile, Respiratory tract infection	Germany	Milk allergy
D0071850A	27-Jun-11	Unknown	8 Years	Female	Infanrix hexa	Pneumococcal vaccines (Non-GSK)	Unknown	Abscess sterile	Germany	

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0071850B	27-Jun-11	Unknown	8 Years	Female	Infanrix hexa	Pneumococcal vaccines (Non-GSK)	Unknown	Abscess sterile	Germany	
D0072316A	08-Aug-11	Resolved	9 Months	Female	Infanrix hexa		0 Months	Injection site abscess sterile, Injection site nodule, Injection site erythema, Injection site swelling	Germany	Hypoplastic left heart syndrome, Aortic valve atresia, Coarctation of the aorta, Atrial septal defect, Patent ductus arteriosus
D0072409A	13-Aug-11	Resolved	7 Months	Male	Infanrix hexa		2 Days	Abscess sterile, Foreign body reaction, Allergy to metals, Lymphadenopathy, Local swelling, Induration	Germany	

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6.5.2.5.2. Extensive swelling of vaccinated limb

Twenty-eight (28) cases of Extensive swelling of vaccinated limb were reported, out of which 5 serious. The reported outcome was resolved in 13 cases, improved in 3, unresolved in 8 and unknown in 4 cases. Concerning serious cases, the outcome was resolved in 4 out of 5 cases and improved in one case. These cases are summarised in Table 11.

Table 11 Summary of cases of Extensive swelling of vaccinated limb identified during the period

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0681184A	22-Oct-10	Resolved	18 Months	Male	Infanrix hexa		1 Days	Extensive swelling of vaccinated limb, Injection site inflammation	France	
B0685430A	18-Nov-10	Unresolved	18 Months	Unknown	Infanrix hexa		0 Weeks	Extensive swelling of vaccinated limb, Injection site erythema, Injection site warmth, Injection site vesicles	France	
B0685437A	18-Nov-10	Resolved	18 Months	Male	Infanrix hexa		0 Hours	Extensive swelling of vaccinated limb, Injection site warmth, Injection site pain, Pyrexia, Injection site oedema, Skin discolouration	France	Asthma
B0692009A	04-Jan-11	Resolved	26 Months	Unknown	Infanrix hexa		1 Days	Injection site oedema, Injection site erythema, Injection site pain, Body temperature increased, Extensive swelling of vaccinated limb	Poland	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0700208A	16-Feb-11	Resolved	4 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Oedema, Extensive swelling of vaccinated limb, Skin warm, Pyrexia, Vomiting	France	
B0702458A	22-Feb-11	Unknown	11 Months	Male	Infanrix hexa	Pneumococcal vaccines (Non-GSK)	1 Days	Extensive swelling of vaccinated limb	Italy	
B0702525A	25-Feb-11	Unresolved	16 Months	Male	Infanrix hexa		1 Days	Extensive swelling of vaccinated limb, Injection site erythema, Injection site warmth, Injection site induration, Injection site infection, Ill-defined disorder	France	
B0703201A	22-Feb-11	Resolved	20 Months	Male	Infanrix hexa	MMR vaccine, strain not specified	24 Hours	Extensive swelling of vaccinated limb, Injection site erythema, Injection site reaction, Injection site warmth, Pyrexia	Switzerland	
B0703591A	03-Mar-11	Resolved	20 Months	Male	Infanrix-polio-HIB, Infanrix hexa	Infanrix hexa	2 Days	Extensive swelling of vaccinated limb, Injection site erythema, Injection site warmth, Injection site oedema, Pyrexia, Wrong drug administered	France	
B0705104A	09-Mar-11	Unresolved	22 Months	Male	Infanrix hexa	Pneumococcal vaccines (Non-GSK)	24 Hours	Extensive swelling of vaccinated limb, Injection site induration, Product quality issue	France	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0705108A	09-Mar-11	Unresolved	22 Months	Male	Infanrix hexa	Pneumococcal vaccines (Non-GSK)	24 Hours	Extensive swelling of vaccinated limb, Injection site induration, Product quality issue	France	
B0711364A	06-Apr-11	Improved	2 Years	Female	Infanrix hexa		2 Days	Extensive swelling of vaccinated limb, Injection site warmth, Injection site inflammation, Injection site erythema, Incorrect route of drug administration	France	
B0713123A	14-Apr-11	Resolved	17 Months	Male	Infanrix hexa		0 Days	Extensive swelling of vaccinated limb, Injection site warmth, Injection site erythema, Injection site pruritus	France	Coeliac disease
B0715647A	26-Apr-11	Resolved	17 Months	Male	Infanrix hexa		1 Days	Extensive swelling of vaccinated limb, Pyrexia, Injection site oedema, Injection site erythema, Injection site warmth, Gait disturbance	France	
B0729084A	28-Jun-11	Improved	2 Years	Female	Infanrix hexa		Same day	Injection site induration, Disability, Oedema, Extensive swelling of vaccinated limb	France	
B0729737A	13-Jun-11	Resolved	5 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Extensive swelling of vaccinated limb, Injection site erythema	Italy	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0730870A	20-Jun-11	Resolved	18 Months	Unknown	Infanrix hexa		Hours	Injection site oedema, Injection site erythema, Injection site pain, Pyrexia, Extensive swelling of vaccinated limb	Poland	
B0731114A	20-Jun-11	Resolved	8 Months	Unknown	Infanrix hexa		1 Days	Injection site oedema, Injection site erythema, Extensive swelling of vaccinated limb	Poland	
B0734758A	18-Jul-11	Unresolved	10 Months	Male	Infanrix hexa		Unknown	Injection site erythema, Extensive swelling of vaccinated limb, Injection site induration	Italy	
B0735472A	27-Jul-11	Unresolved	Infant	Female	Infanrix hexa, Infanrix-polio-HIB	DTPa-Polio-HIB (Non-GSK), Pneumococcal vaccines (Non-GSK)	0 Days	Extensive swelling of vaccinated limb, Injection site reaction, Injection site nodule, Injection site erythema, Injection site warmth, Injection site induration, Injection site pruritus, Hypersensitivity	France	
B0736271A	01-Aug-11	Unresolved	3 Months	Female	Infanrix hexa	Synflorix	0 Days	Injection site inflammation, Extensive swelling of vaccinated limb, Injection site erythema, Injection site warmth, Injection site discolouration	Netherlands	
B0741001A	18-Aug-11	Unknown	16 Months	Unknown	Infanrix hexa		1 Days	Extensive swelling of vaccinated limb, Injection site erythema, Injection site warmth, Injection site induration	France	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0741418A	19-Aug-11	Resolved	19 Months	Unknown	Infanrix hexa		1 Days	Injection site warmth, Injection site erythema, Injection site oedema, Extensive swelling of vaccinated limb	Poland	
B0747623A	14-Sep-11	Unknown	6 Months	Male	Infanrix hexa		Unknown	Injection site cellulitis, Extensive swelling of vaccinated limb, Injection site oedema	Belgium	Multiple allergies
B0750035A	20-Sep-11	Resolved	17 Months	Unknown	Infanrix hexa		1 Days	Extensive swelling of vaccinated limb, Injection site swelling, Injection site erythema, Injection site pain	Poland	
B0750091A	20-Sep-11	Resolved	11 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		2 Hours	Injection site inflammation, Crying, Pyrexia, Hypertonia, Extensive swelling of vaccinated limb, Erythema	Netherlands	
B0751834A	22-Sep-11	Unresolved	25 Months	Male	Infanrix hexa, Varicella virus vaccine, Meningococcal polysaccharide vaccine group C (Non-GSK)		1 Days	Injection site reaction, Extensive swelling of vaccinated limb, Decreased appetite, Pyrexia, Crying, Malaise, Diarrhoea, Ear pain, Injection site warmth, Injection site erythema	Australia	
B0751948A	22-Sep-11	Unknown	17 Months		Infanrix hexa		1 Days	Injection site warmth, Injection site oedema, Injection site erythema, Body temperature increased, Extensive swelling of vaccinated limb	Poland	

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6.5.2.5.3. Gait disturbance

During the period, 19 cases of Gait disturbance were received, out of which 8 serious. In almost all cases (18/19) the event described was associated with at least one other adverse event. The outcome was resolved for 14/19 of these cases and for 6/8 of the serious cases. In the other cases the outcome was unknown. These cases are summarised in Table 12.

Table 12 Summary of cases of Gait disturbance identified during the period

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0686828A	30-Nov-10	Resolved	17 Months	Male	Infanrix hexa, Priorix		Immediate	Hypotonia, Cerebellar ataxia, Gait disturbance, Pain, Hyperthermia, C-reactive protein increased	France	
B0690264A	20-Dec-10	Resolved	13 Months	Male	Infanrix hexa		0 Days	Muscular weakness, Gait disturbance, Tremor, Pyrexia	Italy	
B0691863A	29-Dec-10	Resolved	15 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		2 Days	Guillain-Barre syndrome, Neuropathy peripheral, Pyrexia, General physical health deterioration, Restlessness, Asthma, Decreased appetite, Gait disturbance, Dysstasia, Nuchal rigidity, Hyperaemia, Dysphonia, Hyporeflexia, Hypotonia, Asthenia	Italy	
B0692411A	05-Jan-11	Resolved	12 Months	Male	Infanrix hexa	Pneumococcal vaccines (Non-GSK)	7 Days	Gait disturbance	Italy	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0696325A	27-Jan-11	Resolved	11 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Gait disturbance, Pyrexia	Italy	Pharyngeal erythema
B0715647A	26-Apr-11	Resolved	17 Months	Male	Infanrix hexa		1 Days	Extensive swelling of vaccinated limb, Pyrexia, Injection site oedema, Injection site erythema, Injection site warmth, Gait disturbance	France	
B0716859A	18-Apr-11	Resolved	5 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Gait disturbance, Stupor, Somnolence	Italy	
B0720639A	10-May-11	Resolved	1 Years	Female	Infanrix hexa, Meningococcal polysaccharide vaccine group C (Non-GSK)		0 Days	Gait disturbance, Pyrexia	Italy	
B0720709A	19-May-11	Unknown	23 Months	Female	Infanrix hexa		6 Hours	Insomnia, Gait disturbance, Hypotonic-hyporesponsive episode	Poland	Dermatitis atopic
B0722375A	26-May-11	Resolved	22 Months	Unknown	Infanrix hexa, Synflorix		Hours	Hypotonic-hyporesponsive episode, Pain in extremity, Gait disturbance, Body temperature increased, Somnolence	Poland	
B0728126A	31-May-11	Resolved	13 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Pyrexia, Gait disturbance, Muscular weakness	Italy	

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0733393A	12-Jul-11	Unresolved	3 Years	Female	Infanrix hexa		0 Days	Gait disturbance, Injection site swelling, Pyrexia	Viet Nam	
B0737089A	04-Aug-11	Resolved	18 Months	Female	Infanrix hexa		1 Days	Tremor, Gait disturbance, Oropharyngeal pain, Injection site reaction, Tonsillar disorder, White blood cells urine positive, Bacterial test positive, Anxiety, Upper respiratory tract congestion, Crying, Restlessness	Poland	
B0754191A	04-Oct-11	Unknown	26 Months		Infanrix hexa, Pneumococcal vaccines (Non-GSK)		2 Days	Joint swelling, Gait disturbance, Body temperature increased, Arthritis	Poland	
B0755866A	04-Oct-11	Unknown	11 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)			Infection, Injection site reaction, Gait disturbance	Italy	
D0069517A	22-Nov-10	Resolved	13 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		2 Days	Balance disorder, Vestibular neuronitis, Gait disturbance, Fall	Germany	
D0069888A	07-Jan-11	Resolved		Female	Infanrix hexa		1 Days	Labyrinthitis, Gait disturbance, Balance disorder	Germany	
D0070015A	19-Jan-11	Resolved	16 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	0 Days	Ataxia, Balance disorder, Encephalitis, Gait disturbance, Pyrexia, Upper respiratory tract infection, Otitis media acute, Cerebellar ataxia	Germany	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0072372A	12-Aug-11	Unknown		Female	Infanrix hexa		0 Days	Pain in extremity, Gait disturbance, Crying	Germany	

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6.5.2.5.4. Injection site nodule

Twenty three (23) cases of Injection site nodule were received during the period, out of which 4 serious. The outcome was known as resolved or improved in 10/23 cases. These cases are summarised in Table 13. This table also includes one case received prior to the period of this report but never included in a previous PSUR (B0637096A). This case's ID is marked by a '*' in Table 13.

Table 13 Summary of cases of Injection site nodule identified during the period

Case ID	Initial Date Received By Dept	Age	Gender	Case Outcome	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0682340A	20-Oct-10	12 Months	Male	Improved	Infanrix hexa		0 Days	Injection site nodule	Italy	
B0684107A	09-Nov-10	Infant	Female	Unresolved	Infanrix hexa		Unknown	Injection site nodule, Injection site pruritus	France	
B0686040A	24-Nov-10	14 Months	Male	Improved	Infanrix hexa		11 Days	Injection site nodule	Italy	
B0690263A	20-Dec-10	1 Years	Male	Resolved	Infanrix hexa		0 Days	Injection site nodule, Pyrexia	Italy	
B0691683A	29-Dec-10	Infant	Female	Unresolved	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Unknown	Injection site nodule, Injection site discolouration	France	
B0697403A	01-Feb-11	2 Months	Male	Unresolved	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Injection site nodule	France	
B0698664A	02-Feb-11	5 Months	Female	Improved	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Injection site nodule	Italy	

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Case ID	Initial Date Received By Dept	Age	Gender	Case Outcome	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0708070A	23-Mar-11	18 Months	Female	Unresolved	Infanrix hexa		Same day	Injection site oedema, Injection site nodule, Injection site induration	France	
B0709808A	30-Mar-11	2 Years	Female	Unknown	Infanrix hexa		3 Weeks	Injection site nodule, Injection site pruritus	France	Nodule
B0716281A	26-Apr-11	3 Years	Male	Unresolved	Infanrix-polio-HIB, Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Unknown	Injection site nodule, Injection site pruritus	France	Underweight
B0718957A	12-May-11	2 Months	Male	Resolved	Infanrix hexa		Unknown	Injection site abscess, Injection site nodule, Injection site erythema	France	
B0729606A	10-Jun-11	19 Months	Male	Improved	Infanrix hexa		0 Days	Injection site warmth, Tenderness, Injection site nodule, Injection site induration, Injection site swelling, Injection site erythema, Injection site pain	South Africa	
B0733037A	06-Jul-11	10 Months	Female	Resolved	Infanrix hexa		0 Days	Injection site nodule	Italy	
B0734171A	20-Jul-11	Infant	Female	Unresolved	Infanrix hexa, Hepatitis B vaccine, Vaccine		Unknown	Injection site reaction, Injection site pruritus, Injection site nodule	France	

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Case ID	Initial Date Received By Dept	Age	Gender	Case Outcome	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0735472A	27-Jul-11	Infant	Female	Unresolved	Infanrix hexa, Infanrix-polio-HIB	DTPa-Polio-HIB (Non-GSK), Pneumococcal vaccines (Non-GSK)	0 Days	Extensive swelling of vaccinated limb, Injection site reaction, Injection site nodule, Injection site erythema, Injection site warmth, Injection site induration, Injection site pruritus, Hypersensitivity	France	
B0741005A	18-Aug-11	Infant	Female	Unresolved	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Months	Injection site nodule, Injection site pruritus, Hypertrichosis	France	
B0745076A	05-Sep-11	4 Months	Male	Improved	Infanrix hexa	Infanrix-polio-HIB	3 Weeks	Subcutaneous nodule, Injection site pruritus, Injection site eczema, Injection site induration, Injection site nodule	France	
B0746455A	12-Sep-11	5 Months	Male	Unresolved	Infanrix hexa, Infanrix-polio-HIB, Pneumococcal vaccines (Non-GSK)		0 Months	Injection site nodule, Injection site pruritus	France	
D0070379A	18-Feb-11	24 Months	Male	Unresolved	Infanrix hexa		2 Days	Injection site erythema, Injection site swelling, Injection site nodule, Pyrexia	Germany	Heart sounds abnormal

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Case ID	Initial Date Received By Dept	Age	Gender	Case Outcome	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0070846A	30-Mar-11	10 Months	Male	Unresolved	Infanrix hexa	Pneumococcal vaccines (Non-GSK), Sodium Fluoride	27 Days	Aspartate aminotransferase increased, Alanine aminotransferase increased, Injection site nodule, Injection site induration, Injection site erythema, Febrile convulsion, Soft tissue infection, Abscess sterile, Respiratory tract infection	Germany	Milk allergy
D0070912A	06-Apr-11	6 Months	Male	Unresolved	Infanrix hexa		0 Weeks	Injection site nodule, Scar	Germany	
D0072316A	08-Aug-11	9 Months	Female	Resolved	Infanrix hexa		0 Years	Injection site abscess sterile, Injection site nodule, Injection site erythema, Injection site swelling	Germany	Hypoplastic left heart syndrome, Aortic valve atresia, Coarctation of the aorta, Atrial septal defect, Patent ductus arteriosus
D0072316A	08-Aug-11	9 Months	Female	Resolved	Infanrix hexa		0 Months	Injection site abscess sterile, Injection site nodule, Injection site erythema, Injection site swelling	Germany	Hypoplastic left heart syndrome, Aortic valve atresia, Coarctation of the aorta, Atrial septal defect, Patent ductus arteriosus

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Case ID	Initial Date Received By Dept	Age	Gender	Case Outcome	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0637096A*	02-Mar-10	4 Months	Female	Resolved	Infanrix hexa		0 Days	Injection site nodule, Injection site erythema	Italy	

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6.5.2.5.5. Injection site urticaria

Three (3) cases of Injection site urticaria were received during the period (B0699204A, B0732577A and B0744335A). These cases are summarized in Section 6.5.2.11.7 Urticaria, Urticaria popular and Urticaria thermal.

6.5.2.5.6. Nodule

Three (3) cases of Nodule were received during the period:

- **B0701338A (France): Irritability, Sleep disorder, Pyrexia, Injection site induration, Nodule, Incorrect product storage**

  This case was reported by a pharmacist and a physician and described an incorrect product storage in a 4-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Medical conditions and concurrent medications were unspecified. On 21 February 2011, the subject received a 3rd dose of Infanrix hexa (batch, route and injection site unknown). Before administration, the vaccine was stored at room temperature during 15 days (incorrect product storage) At the time of reporting, no adverse effect was reported. Upon follow-up received on 04 March 2011 from the pharmacist: The subject weighed 6.8 kg and measured 61 cm. On the same day, he received one dose of Infanrix hexa (batch A21CA584B) and one dose of pneumococcal vaccine (Prevenar, non-gsk, batch E16268) both stored at room temperature during 15 days. One week after vaccination, the subject experienced fever at 38.5-39 degrees Celsius, irritability with sleep disorder and presented at one vaccine injection site (vaccine unspecified) an induration. At the time of reporting, Infanrix hexa was not readministered. Outcome of events and the reporter's assessment were unspecified. Upon follow-up received from the physician on 13 May 2011: Infanrix hexa and Prevenar were administered intramuscularly in thigh. The physician noticed fever at 38 degrees Celsius, nodule and sleep disorder for 48 hours. On an unspecified date, Infanrix hexa was readministered without recurrence of events. The physician considered the causal relationship between Infanrix hexa and the reported events as almost certain.

  Company comment: Injection site induration 1 week after 3rd vaccination with Infanrix hexa in a 4 month-old subject. The event resolved spontaneously.

- **B0726560A (Sweden): Nodule, Injection site extravasation, Abscess, Erythema**

  This case was reported by a physician and described the occurrence of nodule in a 3-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Concurrent vaccination included pneumococcal vaccines (Prevenar 13) (non-GSK manufacturer, intramuscular, left thigh) given on 20 December 2010. In October 2010, the subject received 1st dose dose of Infanrix hexa (intramuscular, unknown injection site, lot number not provided). At an unspecified time after vaccination with Infanrix hexa, the subject experienced nodule. On 20 December 2010, the subject received 2nd

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dose of Infanrix hexa (intramuscular, right thigh). At an unspecified time after vaccination with Infanrix hexa, the subject experienced an infiltrate with a size of a rice grain, which increased. In March 2011, 3 months after vaccination with Infanrix Hexan the subject experienced redness "like an abscess" which contained one table spoon of pus. At the time of reporting the outcome of the events was unspecified.

Company comment: Injection site nodule at unspecified time after vaccination with Infanrix hexa and Prevenar.

- **B0745840A (Italy): Injection site reaction, Nodule, Pyrexia**

  This case was reported by a regulatory authority (IT-Agenzia Italiana del Farmaco # 147350) and described the occurrence of injection site reaction in a 6-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevenar 13) for prophylaxis. On 14 February 2011, the subject received 2nd dose of Infanrix hexa (intramuscular, site of injection unknown) and 2nd dose of Prevenar 13 (intramuscular, site of injection unknown). On 14 February 2011, less than one day after vaccination with Infanrix hexa and Prevenar 13, the subject experienced injection site reaction, nodule (unspecified site) and fever (39.5 Deg.C.). The subject was treated with paracetamol. On 16 February 2011, the events were resolved. Follow-up received on 18 October 2011: No further informtion was expected. This case is closed.

  Company comment: Injection site reaction in a 6 month-old subject less than 1 day after 2nd injection with Infanrix hexa and Prevenar.

6.5.2.6. Immune system disorders

6.5.2.6.1. Anaphylactic shock

Three (3) cases of Anaphylactic shock were reported over the period. These cases are described below.

- **B0680987A (Belgium): Anaphylactic shock, Syncope, Apnoea, Bronchospasm, Blood pressure decreased, Pallor, Respiratory rate decreased, Crying, Hypoventilation**

  This case was reported by a physician and described the occurrence of anaphylactic shock in a 2-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), rotavirus vaccine (non-gsk) (RotaTeq) and pneumococcal vaccines (non-gsk) (Prevenar) for prophylaxis. The subject had no concomitant disease and no concomitant medication. The subject had no previous reaction to drug or allergy. On 20 October 2010, the subject received first, 1st dose of RotaTeq (oral), and then unspecified dose of Infanrix hexa (intramuscular) and after unspecified dose of Prevenar (intramuscular). On 20 October 2010, 1 minute after vaccination with Prevenar, within minutes of vaccination with Infanrix hexa and Rotateq, the subject experienced anaphylactic shock, syncope, bronchospasm, decreased blood pressure,

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pallor, respiration rate decreased, hypoventilation and possible apnea. The heart sounds were good. It took quite long before she fully recovered. She experienced no rash, no urticaria, no stridor and no wheezing. When the subject arrived at hospital, she was still pale but stable at cardio-respiratory level. No test was performed. The events lasted a few minutes. On 20 October 2010, the events were resolved, the subject had fully recovered. The physician considered the events were life threatening. The subject was treated with adrenaline (1mg/ml) 0,5 ml and 4 times respiration. The child's face brightened up and she started to cry. Her color came back and she breathed better again. But after 2 minutes, the baby became pale again. Again drowsy but recovered each time then began to cry again: was always so up and down. In the meantime ambulance was called. The subject was hospitalised for observation. At the time of reporting the events were resolved. The physician considered the events were almost certainly related to vaccination with Infanrix hexa, RotaTeq and Prevenar. This case has been identified as a duplicate of case B0685603A which was voided. This case was also reported by a physician via a sales representative.

Company comment: This 2-month-old female subject experienced anaphylactic reaction 1 minute after combined vaccination with Prevenar and within a few minutes after Infanrix hexa and RotaTeq (oral). This case fulfils Level 2 of diagnostic certainty of the Brighton Collaboration Anaphylaxis Working Ggroup criteria.

- **B0741646A (Italy): Anaphylactic shock, Stridor, Respiratory disorder, Pulse pressure decreased, Heart rate increased, Crying**

  This case was reported by a physician via a regulatory authority (IT-Agenzia Italiana del Farmaco # 146502) and described the occurrence of anaphylactic shock in a 2-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevenar 13) for prophylaxis. On 17 August 2011, the subject received 1st dose of Infanrix hexa (.5 ml, intramuscular, injection site unknown) and 1st dose of Prevenar 13 (.5 ml, intramuscular, injection site unknown). On 17 August 2011, less than one day after vaccination with Infanrix hexa and Prevenar 13, the subject experienced anaphylactic shock, slight laryngeal stridor, respiratory crisis, parvus and quick pulsus and weak weeping. The subject was hospitalised and the regulatory authority reported that the events were life threatening. The subject was treated with adrenaline, cardiac massage and oxygen. At the time of reporting, the events were improved. The regulatory authority reported that the events were possibly related to vaccination with Infanrix hexa and Prevenar 13.

  Company comment: This 2-month-old female subject experienced anaphylactic reaction less than 1 day after combined vaccination with Prevenar and Infanrix hexa. This case fulfils Level 3 of diagnostic certainty of the Brighton Collaboration Anaphylaxis Working Group criteria.

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- **D0071107A (Germany): Anaphylactic shock**

  This case was reported by a physician and described the occurrence of anaphylactic shock in an 8-month-old male subject (born 20 April 2007) who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. On 10 January 2008 the subject received 2nd dose of Infanrix hexa (unknown route and injection site). At an unspecified time after vaccination with Infanrix hexa, the subject experienced anaphylactic shock. This case was assessed as medically serious by GSK. At the time of reporting the outcome of the event was unspecified. Despite of requests no further information will be available.

  Company comment: This 8-month-old male subject experienced anaphylactic shock at an unspecified time after 2nd dose of Infanrix hexa. This report lacks important information such as anaphylaxis's symptoms, temporal sequence and treatment. This case fulfils Level 4 of diagnostic certainty of the Brighton Collaboration Anaphylaxis Working Group criteria.

6.5.2.6.2. Anaphylactic/Anaphylactoid reaction and Drug hypersensitivity

Four (4) cases of Anaphylactic reaction/Anaphylactoid reaction/Drug hypersensitivity were reported over the period:

- **B0698663A (Italy): Anaphylactic reaction, Circulatory collapse, Slow response to stimuli, Cyanosis, Hypotonia, Hypothermia, Pallor, Bradycardia, Oxygen saturation decreased, Pyrexia.**

  This case was reported by a physician and described the occurrence of anaphylaxis reaction in a 4-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Concurrent medical conditions included premature birth at 24 weeks (birth weight 700 g). The subject was born by cesarean section at 24 weeks + 6 days. He underwent mechanical ventilation until 2 December 2010. The persistence of the opening of the duct of Botallo was treated with cycles of ibuprofen and indomethacin, the ductus closed on 4 December 2010. The broncodisplasia of lung was treated with cortisone cycles and at the time of vaccination the subject was in good condition. Vaccinations ran the next in a protected environment. The medical family history included allergic reaction with Quincke's oedema due to cephalosporin (mother) and allergy to Novalgina (grandfather). Concurrent vaccination included respiratory syncytial virus vaccine (manufacturer unspecified; route and injection site unknown) given on an unspecified date. In February 2011, prior to the discharged, the subject received unspecified dose of Infanrix hexa (route and injection site unknown, batch number not provided). In February 2011, less than one day after vaccination with Infanrix hexa, the subject experienced collapse, hyporesponsiveness, hypotonia nos and hypothermia. The subject was hospitalised. Tests were performed and showed normal results. At the time of reporting, the events were resolved. The physician considered the events were possibly related to vaccination with Infanrix hexa. Follow-up information reported by a physician via a

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regulatory authority (IT-Agenzia Italiana del Farmaco # 134734): Concurrent medications included Palivizumab (Synagis), Frusemide (Lasix), Iron polymaltose (Intrafer), Multivitamins (Idroplurivit), Nutritional supplement (Reuterin) and Emollient (Folium). The subject was vaccinated with Infanrix hexa on 1st February 2011 (intramuscular, injection site unknown). On 1st February 2011, less than 1 day after vaccination with Infanrix hexa, the subject also developed pallid cyanosis, bradycardia, desaturation, fever and anaphylaxis reaction. On 2 February 2011, the events were resolved. Relevant tests were performed: an electrocardiogram was performed on 1st February 2011, X-ray, X-ray of the skull and C-reactive protein were performed on 2nd February 2011 and on 3rd February 2011, an electroencephalogram was performed. All these investigations showed normal results. The regulatory authority reported that the events were possibly related to vaccination with Infanrix hexa.

Company comment: This 4-month-old male subject with a history of premature birth (24 weeks) experienced anaphylactic reaction less than 1 day after vaccination with Infanrix hexa. This case fulfils Level 4 of diagnostic certainty of the Brighton Collaboration Anaphylaxis Working Group criteria.

- **D0072050A (Germany): Anaphylactic reaction, Swelling, Erythema, Crying, Petechiae**

  This case was reported by a physician via a sales representative and described the occurrence of anaphylactic reaction in a 3-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Co-suspect vaccination included pneumococcal vaccines (non-gsk) (Prevenar 13, Pfizer). On 12 July 2011 the subject received unspecified dose of Infanrix hexa (unknown route, unknown thigh) given contralaterally to unspecified dose of Prevenar 13 (unknown route, unknown thigh). On 12 July 2011, shortly after vaccination with Infanrix hexa and Prevenar 13, the subject experienced severe swelling with erythema on both legs up to groin. He was crying more than normal. The physician diagnosed anaphylactic reaction with swelling on both legs. The subject was hospitalised. At the time of reporting the outcome of the events was unspecified. The physician also informed German regulatory authority (Paul-Ehrlich-Institute) and public health agency. Written follow-up information was received on 22 July 2011 from physician. On 12 July 2011 the subject received 1st dose of Infanrix hexa (intramuscular, left thigh) and 1st dose of Prevenar 13 (intramuscular, right thigh). On 12 July 2011, less than one day after vaccination with Infanrix hexa and Prevenar 13, the subject experienced extensive swelling at both extremities and erythema. He was crying more than normal. On 13 July 2011, the subject developed petechiae. Anaphylactic reaction was not mentioned anymore. The subject was hospitalised. The subject was treated with cooling and prednisone (Rectodelt). On 12 July 2011, abnormal crying was resolved. On 13 July 2011, swelling was resolved and erythema improved. No outcome for petechiae was reported, but event lasted until 18 July 2011. The vaccination course with Infanrix hexa was discontinued. The physician considered swelling; erythema and crying were almost certainly related to vaccination with Infanrix hexa and Prevenar 13. Written follow-up information was received on 08

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August 2011 from Paul-Ehrlich-Institut (# DE-PEI-PEI2011025401) with no new medical information. No further information will be available.

Company comment: This 3-month-old male subject experienced a suspect anaphylactic reaction after 1st dose of Infanrix hexa. This case fulfils Level 5 of diagnostic certainty of the Brighton Collaboration Anaphylaxis Working Group criteria.

- **D0072500A (Germany): Anaphylactoid reaction, Hypersensitivity, Product quality issue, Urticaria, Rash, Apathy, Anaphylactic reaction, Erythema, Petechiae, Injection site erythema.**

  This case was initially reported by a pharmacist and described the occurrence of anaphylactoid reaction in a 13-week-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. The case was also received as pharmaceutical product complaint. On an unspecified date the subject received an unspecified dose of Infanrix hexa (0.5 ml, unknown). At an unspecified time post vaccination with Infanrix hexa, on an unknown date, the subject experienced severe allergic reaction. At the time of reporting the outcome of the event was unspecified. Follow-up information was received on 26 August 2011 from the quality assurance department. The event was now reported as anaphylactoid reaction. Follow-up information was received on 02 September 2011 from the quality assurance department. Based on all available data it was concluded that there was no evidence for a specific safety signal for the used lot of Infanrix hexa. Follow-up information was received on 16 September 2011 from the quality control department. All received returned samples conform to the description specifications. Based on QC results the pharmaceutical product complaint was considered to be unsubstantiated. Follow-up information from the reporting pharmacist has been requested. Follow-up information was received on 20 October 2011 from the vaccination responsible physician. Co-suspect vaccinations included 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer Pharma). On an unknown date in 2011 the subject received the first dose of Infanrix hexa (0.5 ml, unknown) and the first dose of Prevenar 13 (0.5 ml, unknown). At an unspecified time post vaccination with Infanrix hexa, on an unknown date, the subject experienced anaphylactoid reaction. The subject was hospitalised for an unknown period of time. At the time of reporting the outcome of anaphylactoid reaction was unspecified. The vaccination responsible physician considered that anaphylactoid reaction may be causally related to vaccination with Infanrix hexa and/or Prevenar 13. Follow-up information including a hospital report was received on 25 October 2011 from a physician. For the first time age and gender of the subject have been reported. The subject has no underlying or concurrent medical conditions or other risk factors. Previous vaccination with the first doses of combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) and 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer Pharma), given on 15 June 2011, was well tolerated. On 24 August 2011 at around 11:00 the subject received the second dose of Infanrix hexa (0.5 ml, unknown, unknown thigh) and the second dose of Prevenar 13 (0.5 ml,

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unknown, unknown thigh). Approximately 5 - 7 minutes post vaccination with Infanrix hexa and Prevenar 13, on 24 August 2011, the subject experienced generalized urticaria with apathy. The subject did not experience dyspnea or hypotension. According to the reporting physician these events were resolved after about four hours. The physician reported that the same batches of Infanrix hexa and Prevenar 13 had been used when the subject had received the first doses of Infanrix hexa and Prevenar 13 on 15 June 2011. On 24 August 2011 the subject was hospitalised for two days at a pediatric clinic for possible anaphylaxis post vaccination with the second doses of Infanrix hexa and Prevenar 13. According to anamnesis in the hospital the subject experienced urticaria at the head approximately 5 - 10 minutes post vaccination with Infanrix hexa and Prevenar 13, on 24 August 2011. Urticaria spread quickly over the whole body. But at the extremities the subject experienced mild exanthema (exanthema on extremities). An ambulance was called. The subject was transported to the pediatric clinic without complications. All previous vaccinations with not further specified vaccines have been well tolerated. As a neonate the subject received phototherapy for hyperbilirubinemia. One week prior to vaccination with the second doses of Infanrix hexa and Prevenar 13, on an unknown date in August 2011, the subject had suffered from rhinitis without fever. On 25 August 2011 the subject was discharged in good general condition with completely resolved urticaria for ambulatory follow-up. At the time of discharge from hospital the subject showed injection site redness. No further information will be available.

Company comment: This 13-week-old male subject experienced approximately 5 - 7 minutes after 1st vaccination with Infanrix hexa and Prevenar, generalized urticaria with apathy considered causally related to the vaccination. The subject did not experience anaphylaxis (dyspnea or hypotension). The case was also received as pharmaceutical product complaint and it was concluded that there was no evidence for a specific safety signal for the used lot of Infanrix hexa. This case fulfils Level 5 of diagnostic certainty of the Brighton Collaboration Anaphylaxis Working Group criteria.

- **B0712429A (Czech Republic): Salmonella sepsis, Rash generalised, Pyrexia, Diarrhoea, Drug hypersensitivity, Hypersensitivity**

  This case was reported by a physician and described the occurrence of salmonella enteritidis sepsis in a 7-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) and synflorix for prophylaxis. Since 12 December 2010, she was treated with Budesonide.Previous and/or concurrent vaccination included combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. ;GlaxoSmithKline;unknown;unknown given on 27 January 2011; synflorix ;GlaxoSmithKline;unknown;unknown given on 27 January 2011. No reactions after the 1st dose. Concurrent medications included Budesonide (Budiar). On 1 March 2011, the subject received 2nd dose of Infanrix hexa (administration site and route unknown), 2nd dose of Synflorix (administration site and route unknown). On 1 March 2011, less than one day after vaccination with Infanrix hexa and Synflorix, the subject experienced fever (39.4 deg.C). On 2 March

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2011, 1 day after vaccination with Infanrix hexa and Synflorix, the subject experienced generalised exanthema on the whole body, generalised allergic reaction and diarrhea. The subject was hospitalised for 13 days, from 2 to 14 March 2011. Blood tests were performed and showed pathological results: C-reactive protein: 8.3 mg/l and leucocytes: 27 Giga/l. The subject was treated with dimethindene maleate (Fenistil), prednisone (Prednison), and ibuprofen (Nurofen). After next dose of Nurofen, the exanthema repeated and worsened. An allergic reaction to Nurofen was diagnosed. On 6 March 2011, the diarrhea continued. She was afebrile and exanthema recovered. A microbiological cultivation of stool showed Salmonella enteritidis and on second blood tests, leucocytes was 33 Giga/l and c-reactive protein :121mg/l. The subject was admitted to Intensive Care Unit with the diagnosis of salmonelosis sepsis. She was treated with gentamicin sulphate (Gentamycin) and cefotaxime (Cefotaxim). On 14 March 2011, C-reactive protein was 6 mg/l. On 14 March 2011, salmonella enteritidis sepsis was resolved. Follow-up information received on 15 April 2011: Concurrent medical conditions included recurrent obstructive bronchitis since 3 months of age, but allergy had not been proved. As no additional information could be obtained, the case has been closed.

Company comment: This 7-month-old female subject experienced generalised allergic reaction (exanthema) and diarrhea 1 day after vaccination with Infanrix hexa and Synflorix. A concomitant Salmonella enteritis infection could have play a trigger role in the drug hypersensitivity.

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6.5.2.7. Infections and infestations

6.5.2.7.1. Abscess, Abscess limb, Incision site abscess, Injection site abscess, Injection site infection, Streptococcal abscess

During the reporting period, 25 cases were received including one of the following MedDRA Preferred Terms: Abscess (n=10), Abscess limb (n=1), Incision site abscess (n=2), Injection site abscess (n=12), Injection site infection (n=2), Streptococcal abscess (n=2). These cases are summarised in Table 14.

Table 14 Summary of Abscess-related cases received during the period

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0686567A	29-Nov-10	Resolved	9 Months	Unknown	Infanrix hexa		16 Days	Injection site abscess, Injection site oedema, Injection site swelling	Czech Republic	
B0696664A	28-Jan-11	Resolved	17 Months	Male	Infanrix hexa, Priorix		1 Days	Injection site infection, Erythema, Oedema, Feeling hot, C-reactive protein increased	France	
B0698641A	08-Feb-11	Resolved	3 Months	Male	Infanrix hexa		1 Weeks	Staphylococcal abscess, Streptococcal abscess, Injection site abscess	Czech Republic	
B0698651A	08-Feb-11	Resolved	4 Months	Male	Infanrix hexa	Infanrix hexa	2 Weeks	Staphylococcal abscess, Streptococcal abscess, Injection site abscess	Czech Republic	
B0702525A	25-Feb-11	Unresolved	16 Months	Male	Infanrix hexa		1 Days	Extensive swelling of vaccinated limb, Injection site erythema, Injection site warmth, Injection site induration, Injection site infection, Ill-defined disorder	France	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0707174A	21-Mar-11	Resolved	21 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Weeks	Staphylococcal abscess, Injection site abscess, Pyrexia, Injection site swelling, Leukocytosis, C-reactive protein increased, Injection site inflammation	France	Impaired self-care
B0718957A	12-May-11	Resolved	2 Months	Male	Infanrix hexa		Unknown	Injection site abscess, Injection site nodule, Injection site erythema	France	
B0726560A	24-May-11	Unknown	3 Months	Female	Infanrix hexa	Pneumococcal vaccines (Non-GSK)	Unknown	Nodule, Injection site extravasation, Abscess, Erythema	Sweden	
B0728595A	06-Jun-11	Resolved	2 Months	Female	Infanrix hexa	Rotavirus vaccine, Pneumococcal vaccines (Non-GSK)	14 Days	Injection site mass, Injection site abscess, Discomfort	South Africa	
B0740389A	12-Aug-11	Improved	10 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Abscess limb, Pyrexia, Oedema peripheral, Erythema, Pain, Inflammation	Italy	
B0740389A	12-Aug-11	Improved	10 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Abscess limb, Pyrexia, Oedema peripheral, Erythema, Pain, Inflammation	Italy	
B0748231A	15-Sep-11	Unresolved	4 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	6 Days	Groin abscess, Abscess	Czech Republic	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0748231A	15-Sep-11	Unresolved	4 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	6 Days	Groin abscess, Abscess	Czech Republic	
B0756153A	02-Oct-11	Unknown	4 Months	Female	Infanrix hexa		1 Weeks	Injection site abscess	Ecuador	
D0069806A	22-Dec-10	Unknown	Infant	Unknown	Infanrix hexa		Unknown	Injection site abscess	Germany	
D0069984A	13-Jan-11	Resolved	6 Months	Male	Infanrix hexa		0 Days	Injection site erythema, Injection site swelling, Abscess	Germany	
D0070332A	17-Feb-11	Resolved	11 Months	Male	Infanrix hexa		53 Days	Abscess	Germany	
D0070342A	17-Feb-11	Resolved	6 Months	Female	Infanrix hexa	Infanrix hexa	5 Days	Abscess	Germany	
D0071349A	12-May-11	Unresolved	26 Months	Female	Infanrix hexa		6 Months	Abscess, Granuloma	Germany	
D0071422B	18-May-11	Resolved with Sequelae	14 Months	Female	Infanrix hexa	Pneumococcal vaccines (Non-GSK)	6 Weeks	Injection site abscess, Injection site inflammation, Injection site swelling, Foreign body reaction, Incision site abscess	Germany	
D0072015A	12-Jul-11	Resolved with Sequelae	4 Months	Female	Infanrix hexa		0 Days	Abscess, Induration, Erythema, Product quality issue	Germany	
D0072769A	19-Sep-11	Unknown	4 Months	Male	Infanrix hexa		2 Days	Injection site abscess	Germany	
D0072948A	19-Sep-11	Unknown	4 Months	Male	Infanrix hexa		2 Days	Injection site abscess	Germany	
D0072966A	07-Oct-11	Unresolved	17 Months	Male	Infanrix hexa		82 Days	Abscess	Germany	
D0073011A	12-Oct-11	Resolved	8 Months	Male	Infanrix hexa		3 Days	Abscess	Germany	

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6.5.2.7.2. Cellulitis

Two (2) cases of Cellulitis were received during the period:

- **B0713564A (Serbia): Cellulitis, Erythema, Body temperature increased, Injection site swelling**

  This case was reported by a physician and described the occurrence of phlegmon in a 2-year-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Previous and/or concurrent vaccination included combined diphtheria, tetanus, acellular pertussis, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (GlaxoSmithKline) given on an unspecified date. No adverse events occurred after the 2 doses. Concurrent medical conditions included weak immune system. Due to this, the administration of the 3rd dose was postponed up to date. On 8 April 2011, the subject received 3rd dose of Infanrix hexa (intramuscular, unknown thigh, batch number not provided). On 10 April 2011, 2 days after vaccination with Infanrix hexa, the subject experienced intensive erythema, increased in local temperature and swelling injection site (10 cm diameter) above skin level. The subject was hospitalised and the diagnosis of phelgmon was made. No surgery was performed. He was treated with pharmacotherapy only. The subject was treated with ceftriaxone and antibiotics (Antibiotic). At the time of reporting, the events were unresolved, he was still in hospital. At the time of reporting, no additional data were available regarding his condition. Follow-up information received on 15 July 2011: As no additional information could be obtained, the case has been closed.

  Commpany comment: Phlegmon in a 2 year-old male subject 2 days after 3rd vaccination with Infanrix hexa. The subject was hospitalized and treated with antibiotics. The subject had a weak immunesystem (not further specified).

- **B0730177A (Spain): Cellulitis, Streptococcal bacteraemia, Local reaction, Pyrexia**

  This case was reported by a regulatory authority (ES-Agencia Esp de Medicamentos y Prod Sanitarios # ES-AGEMED-224093441) and described the occurrence of cellulitis in a 9-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) for prophylaxis. On 22 February 2011, the subject received an unspecified dose of Infanrix hexa (intramuscular, administration site unknown). On 1 March 2011, 7 days after vaccination with Infanrix hexa, the subject experienced fever. On 3 March 2011, 9 days after vaccination with Infanrix hexa, the subject experienced local reaction in lower limbs and cellulitis. On 5 March 2011, 11 days after vaccination with Infanrix hexa, the subject experienced streptococcal bacteremia. The subject was hospitalised from 5 to 16 March 2011 and the regulatory authority reported that the events were clinically significant (or requiring intervention). The diagnosis was cellulitis due to streptococcal bacteremia. The subject was treated with ibuprofen and antibiotics (Antibiotic). On 16 March 2011, cellulitis, streptococcal bacteremia and local reaction were resolved. In March 2011, fever was resolved. The regulatory

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authority reported that the events were probably related to vaccination with Infanrix hexa.

Commpany comment: Cellulitis in lower limbs and streptococcal bacteremia 9 days after vaccination with Infanrix hexa in a 9-month-old subject. The timeframe between injection and cellulitis seems long for a causal relationship. There is no other information about other possible sources of infection.

6.5.2.7.3. Encephalic infection

One (1) case of Encephalitic infection was received during the period (B0692285A) and is described in Section 6.5.2.9.5 Encephalitis, Encephalopathy and Encephalic infection.

6.5.2.7.4. Injection site cellulitis

Two (2) non-serious cases of Injection site cellulitis were receivedduring the period and are summarized in Table 15.

Table 15 Summary of cases of Injection site cellulitis received during the period

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0747623A	14-Sep-11	Unknown	6 Months	Male	Infanrix hexa		Unknown	Injection site cellulitis, Extensive swelling of vaccinated limb, Injection site oedema	Belgium	Multiple allergies
B0748879A	16-Sep-11	Unresolved	16 Months	Male	Infanrix hexa		1 Days	Injection site cellulitis, Injection site warmth, Injection site pain, Inflammation, Hypersensitivity, Injection site swelling, Injection site erythema, Injection site induration	Belgium	

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6.5.2.7.5. Meningitis aseptic

One (1) case of Meningitis aseptic was reported during the period:

- **B0714940A (France): Meningitis aseptic**

  This case was reported by the French regulatory authority (AFSSaPS number MA20110871) and described the occurrence of lymphocytic meningitis in a 4-month-old female subject who was vaccinated with combined diphtheria, tetanus, acellular pertussis, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrixquinta, GlaxoSmithKline) for prophylaxis. Medical history and concurrent medications, if any, were unspecified. On 26 March 2011, the subject received 2nd dose of Infanrixquinta (intramuscular, unknown injection site, batch number "121CD021B" as reported and A21CB021B according to sales data). On 30 or 31 March 2011 (inconsistent information), four or five days days after vaccination with Infanrixquinta, the subject experienced lymphocytic meningitis. On 03 April 2011, she was transferred to the intensive care unit. Analysis of nasal sample found PCR positive for Enterovirus. After symptomatic therapy, the subject's condition improved. Hospitalisation in intensive care unit lasted five days. The AFSSaPS reported that the event was life threatening. At the time of reporting the event was resolved without sequalae. The AFSSaPS considered the relationship between the event and the vaccination with Infanrixquinta was dubious, according to the French method of assessment. Upon follow-up received from the french center of pharmacovigilance on 09 May 2011: Suspect drug was changed to Infanrix hexa, the reporter confirmed the batch number but the name of the vaccine was unreadable on the vaccines record. Upon follow-up received from AFSSAPS on 16 May 2011: AFSSAPS had made the change from Infanrix Quinta to Infanrix Hexa on their database, as previously reported.

  Company comment: Lymfocytic meningitis in a 4 month-old female subject 4 or 5 days after vaccination with Infanrix hexa. The subject was hospitalized and the event recovered with symptomatic therapy. There is no additional information about investigation of other sources of infection. The AFSSaPS considered the relationship between the event and the vaccination dubious, according to the French method of assessment.

6.5.2.7.6. Meningitis pneumococcal

Two (2) cases of Meningitis pneumococcal were received during the period:

- **D0069889A (Germany) Meningitis pneumococcal, Grand mal convulsion, Epilepsy, Hydrocephalus, Subdural hygroma, Subdural empyema, Anaemia, Generalised oedema, Ileus paralytic, Conjunctivitis, Septic shock, Pneumonia primary atypical, Neurosurgery, Pyrexia, Abdominal distension, Ill-defined disorder, Restlessness, Hyperaesthesia, Oligodipsia, Eye movement disorder, Hypertonia, Tachycardia, Oxygen saturation decreased, Ascites, Respiratory arrest, Drug ineffective, Cyanosis, Splenomegaly**

  This case was reported by a physician and described the occurrence of pneumococcal meningitis in a 4-month-old male subject who was vaccinated with combined

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diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Co-suspect vaccines included 13-valent pneumococcal vaccines (non-gsk) (Prevenar 13, Pfizer) and rotavirus vaccine (non-gsk) (RotaTeq). The subject's medical history included premature birth at 36 weeks of gestation and congenital bacterial pneumonia (with sterile throat smear, abdominal aspirate and blood culture). The subject was healthy on the day of vaccination. On 1 October 2010 the subject received unspecified dose of Infanrix hexa (unknown route and application site), unspecified dose of Prevenar 13 (unknown route and application site) and unspecified dose of RotaTeq (oral). On 04 October 2010 the subject had increased body temperature (over 40 degC). A physician was consulted the next day, but clinical examination was without pathologic findings, except for abdominal distension. There were no neurological findings. The subject was treated with unspecified antipyretic measures. On 06 October 2010 the physician was again consulted with fever up to 40.5 degC and the patient was whining, whimpered, was restless, touch-sensitive and the drinking volume was reduced. After a short examination the subject began to seize. No drugs were administered. The subject had tonic seizures of all limbs, light-fixed pupils and open eyes with ocular deviation to top left. The subject was hospitalised on 06 October 2010 in reduced general condition with grand mal seizure and meningitis. The physician considered the events were life threatening and clinically significant (or requiring intervention). The subject showed convex, pulsating fontanel with a size of 3x4 cm, muscle hypertonus, positive meningitic signs (meningism, Laegue, Brudzinski and Kernig), tachycardia and distended abdomen. Bacterial meningitis was suspected. The patient was treated with sodium chloride and cefotaxime (Cefotaxim), phenobarbitone (Phenobarbital), oxybate sodium (Somsanit) for sedation. After the subject slept, seizures ceased. Lumbar puncture showed increased lumbar pressure and murky cerebrospinal fluid (CSF) with S. pneumoniae in rapid test. Treatment with cefotaxime (Cefotaxim), phenobarbitone (Phenobarbital), gentamicin sulphate (Gentamycin), dexamethasone and dipyrone (Metamizole sodium) was started. On 07 October 2010 the fever resolved and the patient drank well. Because of reduced stool excretion, the subject received frusemide (Lasix) for expulsion, simethicone (Sab simplex) and hyoscine butylbromide (Buscopan). Because of reduced oxygen saturation (87%) the subject received oxygen. Anemia was treated with Red blood cell concentrate. The patient's condition improved with stable oxygen saturation and good urine expulsion. On 08 October 2010 the subject showed impaired condition, reduced drinking volume, unchanged fontanel, negative pupil reaction, sensitivity to touch, restlessness and increasing abdominal tension. Abdominal sonogram showed ascites, treated with frusemide. Because of still high readiness for seizures, lumbar puncture was performed. Lumbar pressure was normal. Cerebrospinal fluid test showed Streptococcus pneumoniae. Inflammatory parameters (C-reactive protein (CRP) and white blood cell count) were increased. Treatment was changed to vancomycin and cefotaxime. The subject drank better and became calm. On 09 October 2010 the subject received bladder catheter and intestinal tube due to intestinal paralysis. On 11 October 2010 bladder catheter was removed and the dose of Phenobarbital reduced. The subject drank normally, but had thin stool. Physiotherapy was started. Within the next days the subject's condition improved and treatment drugs could be reduced. Additional treatment included escherichia coli (Mutaflor). On 14 October 2010 the

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subject developed conjunctivitis and was treated with benzalkonium chloride, ofloxacin (Floxal) and later with colistin and erythromycin lactobromide (Ecolicin). Restlessness was treated successfully with promethazine hydrochloride (Atosil). Because of cough, increased inflammatory parameters and increased body temperature, an X-ray was performed, which showed atypical pneumonia. On 18 October 2010 the subject had another tonic-clonic, generalised seizure with perioral fasciculation and breathing pause. Diazepam was without effect. After treatment with Phenobarbital the seizure ceased. Cranial sonogram showed extended inner and outer subarachnoid spaces. The subject was transferred to another hospital with the suspect of subdural empyema. Diagnoses in hospital included pneumococcal meningitis, symptomatic epilepsy, decreased cerebrospinal fluid resorption (hydrocephalus), generalized edema, septic shock and drug ineffectiveness. Magnetic resonance imaging (MRI) showed subdural hygroma and subdural empyema, at the right side more than at the left. The subject was treated with anti-epileptic medication and neurosurgical operation. On 18 October 2010 the subject underwent subdural-peritoneal shunt implantation. Epilepsy still required treatment. The reporting physician considered the events were probably related to Prevenar 13. Follow-up information was received on 21 January 2011 via Pfizer. The reporting physician stated that the result of serotype analysis was unknown. The following events were still unresolved: pneumococcal meningitis, epilepsy, hydrocephalus, subdural hygroma. The outcome of the following events was unknown to the physician: Grand mal attacks, subdural empyema, anaemia, edema, paralytic intestine, conjunctivitis, septic shock and pneumonia. The reporting physician considered the events were possibly related to Prevenar 13. Follow-up information was received on 16 May 2011 via Pfizer. The subject had no immunodeficiency. It was the first dose of Prevenar 13 (intramuscular) and Infanrix hexa and the third dose of RotaTeq. The reporter of this follow-up considered pneumococcal meningitis was unlikely related to Prevenar 13. A hospital report was provided, with similar information to the initial report. When admitted to hospital, the subject also showed peripheral cyanosis. Sonogram on 08 October 2010 also showed splenomegaly. According to follow-up information from 20 May 2011 pneumococcal meningitis was caused by streptococcus pneumonia serotype 19A.

Company comment: Pneumococcal meningitis in a 4-month-old male subject 5 days after first dose of Infanrix hexa and Prevenar third dose of RotaTeq. The subject required subdural-peritoneal shunt implantation due to ineffective antibiotic therapy. The outcome of sequellae (grand mal attacks) is unknown.

- **D0072024A (Germany) Meningitis pneumococcal, Gastroenteritis rotavirus, Respiratory syncytial virus infection, Pneumococcal sepsis, Pharyngitis, Somnolence, Pyrexia, Fluid intake reduced, Respiration abnormal, Crying, Diarrhoea, Cardiovascular insufficiency, Pallor, Tachypnoea, Anaemia, Thrombocytosis**

  This case was reported by a regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2011022521) and described the occurrence of pneumococcal meningitis with sepsis in a 3-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Co-

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suspect vaccination included 13-valent pneumococcal vaccine (non-GSK) (Prevenar 13, Pfizer). First vaccination with both vaccines was received on 13 April 2011. On 24 May 2011 the subject received 2nd dose of Infanrix hexa (intramuscular, right thigh), 2nd dose of Prevenar 13 (intramuscular, left thigh). On 25 May 2011, less than one day after vaccination with Infanrix hexa and Prevenar 13, the subject experienced pneumococcal meningitis with pneumococcal sepsis, rotavirus gastroenteritis and respiratory syncytial viral infection. The events were resolved after 14 days. The subject was hospitalised for 15 days and the events were life threatening. A hospital report was provided. The subject was hospitalised from 25 May to 08 June 2011. According to the report, the subject developed sleepiness, high fever and fluid intake reduced on the day of admission. An ambulance was consulted, where the subject showed abnormal respiration, crying and stinky, green diarrhea. When admitted to hospital the subject additionally showed circulatory depression and pale lips, as well as enteritic bowel sounds. Oxygen saturation was good. After treatment with sodium chloride (NaCl) the condition improved, but worsened again in the evening, with tachypnea. Cerebrospinal fluid test showed bacterial meningitis and the subject was treated with cefotaxime (Cefotaxim) and gentamicin sulphate (Gentamycin). The subject was transferred to an intensive care unit. The next 24 hours of monitoring were uneventful. Additional treatment included dipyrone (Novalgin), paracetamol and further fluid. Cerebrospinal fluid, blood test and throat swab showed masses of Streptococcus pneumonia. Rotavirus in stool and respiratory syncytial virus (RSV) in swab were positive. Inflammatory parameters were transiently increased. The subject had mild anemia and thrombocytosis, which were considered to be triggered by infection. Additionally the subject was diagnosed with pharyngitis. On 27 May 2011 fever resolved and on the next day the subject was transferred back to a normal unit. Further course was without complications and with continuous improvement. On 08 June 2011 the subject was discharged in good general condition. No further information will be available.

Company comment: Less than one day after combined vaccination with Infanrix hexa and Prevenar, this 3-month-old male subject experienced pneumococcal meningitis with sepsis. The subject recovered after 14 days of hospitalisation and parenteral antibiotherapy.

6.5.2.7.7. Meningitis viral

One (1) case of Meningitis viral was received during the period and is described in Section 6.5.1 Cases with a fatal outcome.

6.5.2.7.8. Osteomyelitis

One (1) case of Osteomyelitis was received during the period:

- **D0069814A (Germany): Osteomyelitis, Bone abscess.**

  This case was reported by a physician and described the occurrence of osteomyelitis in a 9-week-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae

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type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. On 29 October 2010 the subject received the first dose of Infanrix hexa (0.5 ml, unknown). Approximately six days post vaccination with Infanrix hexa, on 04 November 2010, the subject experienced osteomyelitis. The event was reported by the subject's father. The subject was hospitalised for 22 days from 12 November 2010 to 03 December 2010. At the time of reporting, on 21 December 2010, the outcome of the event was unspecified. Follow-up information was received on 04 January 2011 from the reporting physician. The subject has no underlying or concurrent medical conditions or other risk factors. The subject has received no previous vaccinations. On 29 October 2010 the subject received the first dose of Infanrix hexa (0.5 ml, intramuscular, right thigh). Approximately six days post vaccination with Infanrix hexa, on 04 November 2010, the subject experienced fractured femur left distal. Treatment included immobilising by plaster cast. Approximately 15 days post vaccination with Infanrix hexa, on 13 November 2010, the subject was diagnosed with osteomyelitis left at tibia metaphysic left medial with periosteal abscess. The subject was hospitalised on 12 November 2010 for surgery. Treatment included opening and draining of the abscess on 12 November 2010. At the time of follow-up reporting all events were resolved but control examinations have to be performed to exclude sequelae. The vaccination course with Infanrix hexa was discontinued. No further information will be available from the reporting physician. The same case was received on 21 July 2011 from the German regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2010038778).

Commpany comment: This 9-week-old male subject experienced osteomyelitis with bone abscess two weeks after 1st dose of Infanrix hexa. The subject had a left distal femur fracture 6 days post-vaccinaton and developed osteomyelitis at tibia metaphysic left medial with periosteal abscess (bone abscess) 14 days post-vaccination. The patient was hospitalised and treated treated surgically. All events have been resolved and control examinations are performed to exclude sequelae

6.5.2.7.9. Pneumococcal sepsis

One (1) case of Pneumococcal sepsis was received during the period (D0072024A) and is described in Section 6.5.2.7.6 Meningitis pneumococcal.

6.5.2.7.10. Salmonella sepsis

One (1) case of Salmonella sepsis was received during the period (B0712429A) and is described in Section 6.5.2.6.2 Anaphylactic/Anaphylactoid reaction and Drug hypersensitivity.

6.5.2.7.11. Sepsis

Four (4) cases of Sepsis were received during the period:

- **B0700040A (Sweden): Meningitis, Sepsis, Shock, Pneumococcal infection, Renal impairment, Hepatic function abnormal, Pyrexia, Diarrhea, Vomiting**

  See Section 6.5.1 Cases with a fatal outcome.

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- **D0069502A (Germany): Oedema peripheral, Sepsis, Swelling, Erythema**

  This case was reported by a physician via a sales representative and described the occurrence of bilateral leg swelling in a 20-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) and 10 valent pneumococcal conjugate vaccine (Synflorix, GlaxoSmithKline) for prophylaxis. Concurrent medical conditions included ocular neoplasm. Concurrent medications included treatment with ketamine (Ketanest) three days prior to vaccination with Infanrix hexa and Synflorix, on 08 November 2010. Previous vaccinations had been performed by another paediatrician. On 11 November 2010 the subject received the fourth dose of Infanrix hexa (0.5 ml, intramuscular, unknown application site at left side) and the fourth dose of Synflorix (0.5 ml, intramuscular, unknown application site at right side), contralaterally. Less than one week post vaccination with Infanrix hexa and Synflorix, on an unknown date between 11 November 2010 and 18 November 2010, the subject experienced bilateral leg swelling. Approximately one day post vaccination with Infanrix hexa and Synflorix, on 12 November 2010, the subject experienced swelling and erythema (no site specified). On an unknown day in November 2010 the subject was hospitalised for two days for this event. Sepsis was suspected (possible sepsis). The subject was treated with amoxicillin trihydrate + potassium clavulanate (Amoxiclav) for sepsis. On the next day, on an unknown day in November 2010, the subject was discharged from hospital. At the time of reporting, on 19 November 2010, the outcome of the events was unspecified. Follow-up information was received on 06 December 2010 from the reporting physician. After about six days, on 17 November 2010, all events were resolved. The vaccination courses with Infanrix hexa and Synflorix were discontinued. No further information will be available.

  Company comment: Less than one week post vaccination with Infanrix hexa and Synflorix the 20 month-old subject experienced bilateral leg swelling and erythema. Sepsis was suspected but not confirmed. No etiological agent causing sepsis was reported. The subject recovered after hospitalization and antibiotherapy.

- **D0069690A (Germany): Injection site swelling, Injection site erythema, Sepsis**

  This case was reported by a physician, via sales representative and described the occurrence of suspected sepsis in an 18-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. According to initial information, on 06 December 2010 the subject received the fourth dose of Infanrix hexa (left leg). Concurrently a dose of Synflorix was administered to the right leg. On an unspecified date within the following three days the subject developed swelling and redness at the injection site of Infanrix hexa. The reaction was the size of an adult's palm. Otherwise the subject was fit. There was no whining or fever. The subject was treated with cetirizine hydrochloride and cefaclor. At the time of reporting the outcome of the events was unspecified. Follow-up information was received on 29 December 2010 from the reporting physician by means of a completed questionnaire: Previous vaccinations with Infanrix hexa were well tolerated. On 06 December 2010 the

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subject received the fourth dose of Infanrix hexa (intramuscular, left thigh). Concurrently a dose of Synflorix was administered contraleterally. The following day, on 07 December 2010, the subject developed swelling and redness at the injection site. The subject was treated with cetirizine hydrochloride and cefaclor (CEC) for suspected sepsis (not reported as an event, provided as indication of the treatment drug). On 10 December 2010 swelling and redness resolved. On an unspecified date in December 2010 the subject fully recovered.

Company comment: Site injection complication within 3 days post-vaccination with Infanrix hexa and Synflorix. complication. Sepsis was suspected but not confirmed and no etiological agent was reportedThe event resolved after antibiotherapy.

- **D0072852A (Germany): Circulatory collapse, Sepsis, Shock, Crying, Pallor**

  See Section 6.5.1 Cases with a fatal outcome.

6.5.2.7.12. Septic shock

One case of Septic shock was received during the period (D0069889A) and is described in Section 6.5.2.7.6 Meningitis pneumococcal.

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6.5.2.8. Musculoskeletal and connective tissue disorders

6.5.2.8.1. Muscle spasms

Eight (8) cases of Muscle spasms were received during the period. In one case, muscle spasms were associated with an hypotonic-hyporesponsive episode and in another case with hypertonia. The muscle spasms were resolved in 2/8 cases. These cases are summarised in Table 16.

Table 16 Summary of cases of Muscle spasms received during the period

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0686677A	26-Nov-10	Resolved	4 Months	Male	Infanrix hexa		0 Days	Hypotonic-hyporesponsive episode, Screaming, Apathy, Unresponsive to stimuli, Sleep disorder, Muscle tightness, Abdominal pain, Decreased activity, Hypertonia, Ill-defined disorder, Hypotonia, Developmental delay, Muscle spasms, Restlessness, Crying	Poland	Abdominal pain
B0695552A	21-Jan-11	Unknown	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Hours	Infantile spasms, Slow response to stimuli, Hypertonia, Staring, Tremor, Clonus, Muscle spasms, Joint hyperextension, Adenovirus test positive, Pyrexia, Crying	Italy	
B0702855A	24-Feb-11	Unknown	5 Months	Female	Infanrix hexa		0 Days	Muscle spasms, Pyrexia, Escherichia urinary tract infection	Greece	
B0720309A	19-May-11	Unknown	2 Months	Female	Infanrix hexa, Rotavirus vaccine, Pneumococcal vaccines (Non-GSK)		0 Days	Muscle contracture, Muscle spasms, Erythema, Staring, Heart rate increased	Belgium	

B0745247A	06-Sep-11	Resolved	20 Months	Male	Infanrix hexa		2 Days	Crying, Muscle spasms, Injection site erythema	Czech Republic	
D0070495A	04-Mar-11	Unresolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		2 Days	Restlessness, Muscle spasms, Insomnia, Crying	Germany	Functional gastrointestinal disorder
D0070972A	11-Apr-11	Unknown	2 Months	Female	Infanrix hexa		0 Days	Muscle spasms, Underdose	Germany	
D0072455A	19-Aug-11	Unresolved	6 Months	Male	Infanrix hexa	Pneumococcal vaccines (Non-GSK)	0 Days	Restlessness, Pyrexia, Insomnia, Decreased appetite, Muscle spasms, Crying, Agitation, Fatigue, Rash, Vaccination complication, Herpes virus infection, Exanthema subitum	Germany	

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6.5.2.8.2. Soft tissue necrosis

One (1) case of Soft tissue necrosis was reported during the period:

- **D0069239A (Germany): Soft tissue necrosis, Debridement, Incorrect route of drug administration**

  This case was reported by a regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2010030686) and described the occurrence of soft tissue necrosis in a 1-year-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. On an unspecified date in 2010, approximately six month prior to initial reporting, the subject received unspecified dose of Infanrix hexa (unknown route, right thigh). In 2010, approximately 6 months after vaccination with Infanrix hexa, the subject experienced sterile necrosis in subcutis of thigh (soft tissue necrosis). The subject was hospitalised on 19 July 2010 for 5 days for local excision of necrotic tissue. In 2010, the events were resolved. The paediatrician considered that the events were related to vaccination with Infanrix hexa. The paediatrician stated that this was the second subject with necrosis in his praxis and he had increased rates of swelling post vaccination since approximately two years. According to the surgery report, the subject had abscess forming fat tissue necrosis subcutaneous on right thigh after an older subcutaneous injection (intramuscular formulation administered by other route). This was surgically removed on 20 July 2010, without any complications. The wound was treated with gentamicin sulphate (Sulmycin). When the subject was discharged, the wound was not irritated. No further information will be available.

  Company comment: Sterile soft tissue necrosis of the thigh in a 1-year-old male subject approximately 6 months after vaccination with Infanrix hexa. The complication recovered after adequate surgery. The surgery report states possible relation to incorrect route of drug administration (intramuscular formulation administered subcutaneously).

6.5.2.9. Nervous system disorders

6.5.2.9.1. Cerebral atrophy and Cerebral ischemia

Three (3) cases of Cerebral atrophy/Cerebral ischemia were reported during the period:

- **B0686639A (Italy): Epilepsy, Cerebral ischaemia, Partial seizures**

  This case was reported by a physician via a regulatory authority (IT-Agenzia Italiana del Farmaco # 128180) and described the occurrence of epileptic seizure in a 3-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Concurrent medications included Bisolvon. On 8 November 2010, the subject received unspecified dose of Infanrix hexa (intramuscular, injection site unknown). On 18 November 2010, 10 days after vaccination with Infanrix hexa, the subject experienced epileptic seizure. The subject was hospitalised where cardiac monitoring

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was made. Relevant tests were performed: electroencephalogram showed epileptiform abnormalities in the right hemisphere and nuclear magnetic resonance with contrast liquid showed ischemic injury due to hypoxia in the right hemisphere. The subject was treated with anti-inflammatory (Anti inflammatory) and anticonvulsant (Anticonvulsants). At the time of reporting, the outcome of the event was unspecified. The regulatory authority reported that the event was possibly related to vaccination with Infanrix hexa. Follow-up information received on 2 December 2010: The vaccination performed on 8 November 2010, was 1st dose of Infanrix hexa. Nuclear magnetic resonnance resulted as hypoxic ischemic lesion in the right hemisphere. At the time of follow-up, the subject was still under control, and other clinical exams were planned little time later. Follow-up information received on 6 June 2011: On 1st June, at the clinical control, are no longer present motor focal seizures. The subject made her anticonvulsivant therapy.

Company comment: This 3-month-old female subject experienced partial seizures 10 days after 1st vaccination with Infanrix hexa. Complementary exams revealed a hypoxic ischemic lesion in the right hemisphere. The time sequence before partial seizures made the possible relationship to the product dubious.

- **B0716780A (Italy): Cardiac arrest, Multi-organ failure, Pneumonia aspiration, Cerebral ischaemia, Sudden infant death syndrome, Unresponsive to stimuli, Peripheral coldness, Staring, Musculoskeletal stiffness, Pyrexia, Somnolence.**

  See Section 6.5.1 Cases with a Fatal Outcome.

- **D0070024A (Germany): Infantile spasms, Developmental delay, Posture abnormal, Restlessness, Crying, Hypotonia, Microcephaly, Cerebral atrophy, Bone marrow failure, Vomiting, Dehydration, Hypokalaemia, Pancytopenia.**

  This case was reported by a public department for welfare and social affairs and described the occurrence of West's syndrome in a 4-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. On 8 May 2009 and 5 June 2009 the subject received 1st dose and 2nd dose of Infanrix hexa (unknown route and application site). The drug was reported as Infanrix, but the lot numbers clearly identified Infanrix hexa. At an unspecified time after vaccination with Infanrix hexa, the subject experienced convulsion disorder and developmental delay. It was unclear after which vaccination the events appeared. This case was assessed as medically serious by GSK. At the time of reporting the outcome of the events was unspecified. Co-suspect vaccination included pneumococcal vaccine (non-GSK) (Prevenar, Wyeth). On 5 June 2009 the subject received 2nd dose of Infanrix hexa (unknown route and application site), 2nd dose of Prevenar (unknown route and application site). On 09 June 2009 the subject suffered a bruise on forehead from a clay bowel falling down. Neurologic test was normal. On 17 July 2009 the subject received 3rd dose of Infanrix hexa (unknown route and application site), 3rd dose of Prevenar (unknown route and application site). Examination before vaccination was normal. The subject developed normally according to the parents. On 24 July 2009, 7 days after vaccination with Infanrix hexa and Prevenar, the parents reported about trunk bowing and feared about imperforate anus or faecal concretion. The subject was

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hospitalised on 30 July 2009. The events were disabling. The subject was diagnosed with West's syndrome, severe developmental delay, axial hypotonia and microcephaly. During pregnancy the mother had vena-cava syndrome with a single syncope. The subject was the first and only child and was born spontaneously in 40 weeks of gestation with a weight of 3570 g, a size of 56 cm and an APGAR score of 9/10/10. The subject had a first convulsion on the day of second vaccination, on 05 June 2009 in the evening. On 30 July 2009 the subject was hospitalised with West's syndrome. Electroencephalogram (EEG) showed hypsarrhythmia. Magnetic resonance tomogram (MRT) in August 2009 was normal. The subject was treated with clonazepam, phenobarbitone (Phenobarbital), pyridoxine hydrochloride (Vitamin B6) and folic acid, but without effect. Under treatment with sulthiame (Sultiame) and levetiracetam the convulsions improved in frequency and severity. After treatment with tetracosactrin acetate (Synacthen) and prednisolone (Prednisolon) hypsarrhythmia ceased. The subject finally received levetiracetam and valproate. After discharge in August 2009 the subject was free from convulsions, but they recurred in September 2009. Vigabatrin was given. At the age of 7 months the subject's development was one months behind. From 30 November 2009 to 03 February 2010 the subject was treated in a specialised centre for epilepsy. In December 2009 and January 2010 the EEG results showed epileptic activity, especially posterior at both sides. Treatment with topiramate was started. Convulsions resolved under cyclic treatment with dexamethasone and omeprazole. In June 2010, at the age of 17 months, the subject had a developmental age of 7 months, with statomotor and psychomental development delay. In August 2010 the subject was hospitalised with severe vomiting (not keeping any nutrition) and exsiccation. Laboratory tests showed hypokalemia and pancytopenia. All medication was stopped. Treatment with phenobarbitone (Luminal) and antibiotics was started. MRT showed dilated subarachnoid spaces in terms of cerebral atrophy. After bone marrow puncture in another hospital drug induced bone marrow depression was suspected. This resolved in further course and blood test normalised. The last examination report was from 30 November 2010, where the physician stated that EEG again showed increased generalised epileptic activity. No further information will be available.

Company comment: This 4-month-old female had a convulsion less than 1 day after 2nd dose of Infanrix hexa and Prevenar 55 days post-vaccination, she was diagnosed with West's syndrome severe developmental delay, axial hypotonia and microcephaly. The time sequence of signs apparition remained unclear but there is a medical anamnesis of neonatal convulsion unrelated to vaccination.

6.5.2.9.2. Seizures and Epilepsy

Seizures/Convulsions

During the period, 118 individual case reports were received including one of the following MedDRA preferred terms: **Clonic convulsion** (n=4), **Clonus** (n=8), **Convulsion** (53), **Febrile convulsion** (n=44[1]), **Grand mal convulsion** (n=15),

[1] Including two cases received prior to this PSUR period but not included in a previous PSUR (B0674885A and B0631888A).

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Myoclonus (n=10), **Partial seizures** (n=3), **Seizure like phenomena** (2), **Tonic clonic movements** (2) and **Tonic convulsion** (n=1). In some instances more than one MedDRA preferred term was included to describe the same event. These cases are summarised in Table 17.

Table 17 Summary information for complete 'Seizures/Convulsion' data set (n=118)

Patient age (n=113)	Range	months	2-72
	Median	months	9.19
Patient gender (n=111)	Male	n	58
	Female	n	53
Report type	Spontaneous	n	118
Type of convulsion	Febrile*	n	74
	Afebrile	n	44
Time to onset of event (n=114)	Range	days	0-27
	Number < 1 day	n	105
Outcome (n=117)	Resolved	n	78
	Improved	n	7
	Fatal	n	2
	Unresolved	n	8
	Unknown	n	22
Concomitant vaccine(s)	administered	n	13

* Based on the presence of the following preferred terms in a seizure case:

- Febrile convulsion

OR

- Convulsion and Pyrexia in the same case.

Indeed some febrile seizures were described with the MedDRA PTs 'Convulsion' and 'Pyrexia' rather than with the PT 'Febrile convulsion'.

Epilepsy

During the period, 19 individual case reports were received including at least one of the following MedDRA preferred terms: **Complex partial seizures** (1), **Epilepsy** (9), **Infantile spasms** (6), **Petit Mal Epilepsy** (3) and **Status epilepticus** (2). These cases are summarized in Table 18, Table 19, Table 20 and Table 21.

Table 18 Summary information for complete 'Epilepsy' data set (n=19)

Patient age (n=19)	Range	months	2-18
	Median	months	6.6
Patient gender (n=18)	Male	n	9
	Female	n	9
Report type	Spontaneous	n	19
Time to onset of event (n=19)	Range	Days	0-45
	Number < 1 day	n	12
Outcome (n=19)	Resolved	n	5
	Improved	n	1
	Unresolved	n	6
	Unknown	n	7
Concomitant vaccine(s)	administered	n	3

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Table 19 Summary of cases of Epilepsy and Petit mal epilepsy received during the period (n=11)

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0686208A	25-Nov-10	Unknown	3 Months		Infanrix hexa		0 Months	Encephalitis, Epilepsy	Italy	
B0686639A	26-Nov-10	Unknown	3 Months	Female	Infanrix hexa	Bisolvon	10 Days	Epilepsy, Cerebral ischaemia, Partial seizures	Italy	
B0700168A	16-Feb-11	Unknown	5 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Epilepsy, Petit mal epilepsy, Staring, Clonus, Dyskinesia, Pyrexia	Italy	
B0713436A	11-Apr-11	Resolved	5 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Petit mal epilepsy, Blepharospasm, Dyskinesia	Italy	
B0720048A	13-May-11	Unresolved	6 Months	Female	Infanrix hexa, Synflorix		1 Days	Epilepsy, Infantile spasms, Tearfulness, Dyskinesia	Czech Republic	
B0737600A	04-Aug-11	Unknown	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		12 Days	Epilepsy, Convulsion	Latvia	
D0069341A	05-Nov-10	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Hours	Circulatory collapse, Apnoea, Loss of consciousness, Pallor, Bradycardia, Salivary hypersecretion, Cyanosis, Epilepsy, Partial seizures, Foaming at mouth, Hypotonia, Cardiac arrest, Vomiting, Dyskinesia, Eye movement disorder, Productive cough, Depressed	Germany	Atrial septal defect

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0069889A	10-Jan-11	Unresolved	4 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK), Rotavirus vaccine (Non-GSK)		3 Days	Meningitis pneumococcal, Grand mal convulsion, Epilepsy, Hydrocephalus, Subdural hygroma, Subdural empyema, Anaemia, Generalised oedema, Ileus paralytic, Conjunctivitis, Septic shock, Pneumonia primary atypical, Neurosurgery, Pyrexia, Abdominal distension	Germany	Premature baby, Pneumonia bacterial, Conjunctivitis infective
D0070286A	12-Feb-11	Unknown	1 Years	Female	Priorix Tetra, Infanrix hexa		6 Days	Petit mal epilepsy, Staring, Dyskinesia	Germany	
D0072920A	04-Oct-11	Unknown	15 Months	Male	Infanrix hexa, Synflorix		6 Hours	Febrile convulsion, Epilepsy, Rash, Pyrexia, Dyskinesia, Salivary hypersecretion, Eye movement disorder, Somnolence, Pallor, Tachycardia, Injection site erythema, Injection site swelling	Germany	
R0014765A	30-Nov-10	Improved	4 Months	Male	Meningitis ACWY tetanus toxoid vaccine, Infanrix hexa, Synflorix		7 Days	Epilepsy	Spain	

Table 20 Summary of cases of Status epilepticus received during the period

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0710868A	29-Mar-11	Resolved	11 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Status epilepticus, Loss of consciousness, Apnoea, Convulsion, Vomiting, Skin warm, Staring, Hypotonia, Hyporesponsive to stimuli, Crying, Erythema, Upper respiratory tract infection, Pyrexia, Hypertonia, Postictal state, Malaise, Listless	Netherlands	
D0070499A	04-Mar-11	Resolved	18 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Synflorix	1 Days	Convulsion, Endotracheal intubation, Status epilepticus, Pyrexia, Febrile convulsion	Germany	

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Table 21 Summary of cases of Complex partial seizures and Infantils spasms

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0684471A	10-Nov-10	Unresolved	7 Months	Female	Infanrix hexa	Infanrix hexa	2 Months	Infantile spasms	Italy	
B0695552A	21-Jan-11	Unknown	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Hours	Infantile spasms, Slow response to stimuli, Hypertonia, Staring, Tremor, Clonus, Muscle spasms, Joint hyperextension, Adenovirus test positive, Pyrexia, Crying	Italy	
B0720048A	13-May-11	Unresolved	6 Months	Female	Infanrix hexa, Synflorix		1 Days	Epilepsy, Infantile spasms, Tearfulness, Dyskinesia	Czech Republic	
B0728516A	24-Jun-11	Resolved	12 Months	Male	Infanrix hexa, MMR vaccine (Non-GSK)		1 Days	Febrile convulsion, Loss of consciousness, Tremor, Complex partial seizures, Grand mal convulsion, Pyrexia	Italy	
D0069378A	09-Nov-10	Unresolved	5 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		45 Days	Infantile spasms, Cerebral disorder	Germany	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0070024A	19-Jan-11	Unknown	4 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa	0 Days	Infantile spasms, Developmental delay, Posture abnormal, Restlessness, Crying, Hypotonia, Microcephaly, Cerebral atrophy, Bone marrow failure, Vomiting, Dehydration, Hypokalaemia, Pancytopenia	Germany	Contusion, Ingrowing nail
D0071841A	27-Jun-11	Unresolved	4 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Encephalopathy, Infantile spasms, Lennox-Gastaut syndrome, Dyskinesia, Developmental delay, Eye movement disorder, Motor dysfunction, Posture abnormal, Fatigue, Hyperhidrosis, Crying, Pallor, Diarrhoea, Musculoskeletal stiffness, Depressed level of consci	Germany	Umbilical cord around neck, Bronchitis, Pharyngitis, Rhinitis, Klebsiella infection, Hypotonia

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6.5.2.9.3. Demyelination and Demyelinating polyneuropathy

Two (2) cases of Demyelination/Demyelinating polyneuropathy were received during the period:

- **B0689246A (Saudia Arabia): Demyelination, Extrapyramidal disorder, Neurological symptom, Irritability, Crying, Pyrexia, Strabismus.**

  This case was reported by a physician via a sales representative and described the occurrence of demyelination in a 4-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevenar) for prophylaxis. On an unspecified date the subject received unspecified dose of Infanrix hexa (intramuscular, unknown injection site), unspecified dose of Prevenar (intramuscular, unknown injection site). Lot numbers not provided. The same day at night, less than one day after vaccination with Infanrix hexa and Prevenar, the subject experienced crying and fever. The 3rd day after vaccination, the baby showed irritability and acute neurological symptoms. The subject was hospitalised and the physician considered the events were disabling. An NMR was performed and showed pigmentations in the brain but no sign of infection. The subject was treated with azithromycin (Zitromax), dimethindene maleate (Fenistil) and antipyretic (Antipyretics). At the time of reporting, fever and crying were resolved but the other events were improved. The physician considered the events were possibly related to vaccination with Infanrix hexa and Prevenar. Follow up information received on 26 December 2010: Concurrent medications included Acyclovir (Zovirax) and Corticosteroid (Corticosteroids) for 3 weeks. In November 2010, the subject received 2nd dose of Infanrix hexa and 2nd dose of Prevenar. In November 2010, the subject experienced extra pyramidal symptoms, neurological symptom, irritability, crying, fever and eye squint. Relevant tests were performed (CT brain, CSF, CBC, EEG) but the results were not provided. An NMR was performed and showed patches of demyelination in the brain but no sign of infection. The final diagnosis was post vaccination acute demyelination. At the time of reporting, the events were improved. No additional information has been received. The case has been closed on 4 August 2011.

  Company comment: This 4-month-old male subject experienced post vaccination acute demyelination (diagnosed at MRI) with acute neurological symptoms (extra pyramidal signs, irritability, crying, fever and eye squint) starting less than one day after 2nd dose of Infanrix hexa and Prevenar

- **D0069554A (Germany): Guillain-Barre syndrome, Congenital neuropathy, Demyelinating polyneuropathy, Hip deformity, Foot deformity, Motor developmental delay.**

  See Section 6.5.2.9.6 Guillain-Barré syndrome.

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6.5.2.9.4. Depressed level of consciousness

Twenty four (24) cases of Depressed level of consciousness were reported during the period and are summarised in Table 22.

Table 22 Summary of cases of Depressed level of consciousness received during the period

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0683333A	05-Nov-10	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Hours	Presyncope, Loss of consciousness, Depressed level of consciousness, Staring, Hypotonia, Pallor, Crying, Pyrexia, Pain, Mental impairment, Vomiting, Muscle contractions involuntary, Myoclonus, Abdominal abscess, Irritability, Hypotonic-hyporesponsive epis	Netherlands	Gastrooesophageal reflux disease, Choking
B0692285A	06-Jan-11	Unknown	21 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Encephalitic infection, Convulsion, Dyskinesia, Fatigue, Pyrexia, Hypertonia, Depressed level of consciousness, Electroencephalogram abnormal	France	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0701374A	18-Feb-11	Resolved	2 Months	Male	Infanrix hexa, Rotavirus vaccine, Pneumococcal vaccines (Non-GSK)	Rotavirus vaccine, Pneumococcal vaccines (Non-GSK)	3 Hours	Hypotonic-hyporesponsive episode, Loss of consciousness, Depressed level of consciousness, Unresponsive to stimuli, Cyanosis, Cough, Ill-defined disorder, Fatigue, Adverse event, Vomiting, Eyelid disorder, Crying, Somnolence	Switzerland	
B0707035A	15-Mar-11	Resolved	3 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Unknown	Depressed level of consciousness, Crying, Pyrexia, Injection site inflammation, Injection site pain, Insomnia, Nasopharyngitis	Netherlands	
B0712012A	04-Apr-11	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Hours	Depressed level of consciousness, Skin warm, Staring, Hypotonia, Respiration abnormal, Crying, Pyrexia, Injection site pain	Netherlands	
B0712712A	05-Apr-11	Resolved	13 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Hours	Loss of consciousness, Depressed level of consciousness, Convulsion, Gaze palsy, Respiration abnormal, Pallor, Hypotonia, Drooling, Cyanosis, Pyrexia, Vomiting	Netherlands	
B0712989A	08-Apr-11	Resolved	3 Months	Male	Infanrix hexa		2 Minutes	Depressed level of consciousness, Pallor, Crying, Somnolence, Malaise	Netherlands	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0717794A	06-May-11	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		36 Hours	Loss of consciousness, Apnoea, Depressed level of consciousness, Gaze palsy, Pallor, Cyanosis, Hypotonia, Peripheral coldness, Pyrexia	Netherlands	
B0719423A	16-May-11	Resolved	9 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Depressed level of consciousness, Inflammation, Pain, Injected limb mobility decreased, Pyrexia, Crying	Netherlands	
B0727317A	17-Jun-11	Unknown	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		2 Days	Depressed level of consciousness, Hypotonic-hyporesponsive episode, Pallor, Ill-defined disorder, Feeling abnormal, Pyrexia	Netherlands	
B0732346A	11-Jul-11	Unknown	2 Months	Female	Infanrix hexa, Synflorix		4 Hours	Depressed level of consciousness, Pyrexia, Somnolence	Netherlands	
B0741007A	16-Aug-11	Unresolved	10 Months	Female	Infanrix hexa		Immediate	Respiratory arrest, Depressed level of consciousness, Breath holding, Crying, Eye movement disorder, Skin discolouration, Pallor	Netherlands	Caesarean section
B0746088A	08-Sep-11	Improved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		3 Seconds	Depressed level of consciousness, Crying, Injection site inflammation, Pallor, Hypotonia, Oligodipsia, Somnolence, Respiratory disorder	Netherlands	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0750040A	20-Sep-11	Resolved	2 Months	Female	Infanrix hexa, Synflorix		7 Hours	Presyncope, Febrile convulsion, Depressed level of consciousness, Hypertonia, Myoclonus, Pallor, Pyrexia, Musculoskeletal stiffness	Netherlands	
B0755401A	07-Oct-11	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Depressed level of consciousness, Pyrexia, Inflammation, Pain, Vomiting, Somnolence, Diarrhoea, Staring	Netherlands	
B0756437A	18-Oct-11	Resolved	2 Months	Male	Infanrix hexa, Synflorix		5 Minutes	Depressed level of consciousness, Staring, Pallor	Netherlands	
D0069325A	04-Nov-10	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		8 Hours	Depressed level of consciousness, Hypotonic-hyporesponsive episode, Pallor, Fatigue, Eye movement disorder	Germany	
D0069341A	05-Nov-10	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Hours	Circulatory collapse, Apnoea, Loss of consciousness, Pallor, Bradycardia, Salivary hypersecretion, Cyanosis, Epilepsy, Partial seizures, Foaming at mouth, Hypotonia, Cardiac arrest, Vomiting, Dyskinesia, Eye movement disorder, Productive cough, Depressed	Germany	Atrial septal defect

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0071099A	19-Apr-11	Resolved	11 Weeks	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Hypotonic-hyporesponsive episode, Body temperature increased, Crying, Asthenia, Pallor, Depressed level of consciousness, Pharyngeal erythema	Germany	
D0071366A	13-May-11	Unknown	12 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Convulsion, Depressed level of consciousness, Gaze palsy, Hypochromic anaemia, Pyrexia, Injection site erythema, Musculoskeletal stiffness, Iron deficiency	Germany	
D0071441A	19-May-11	Improved	15 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Convulsion, Depressed level of consciousness, Staring, Pyrexia, Asthenia, Upper respiratory tract infection, Vaccination complication	Germany	
D0071549A	27-May-11	Unresolved	4 Months	Male	Synflorix, Infanrix hexa		0 Days	Encephalitis, Bronchitis, Lactic acidosis, Hyperglycaemia, Convulsion, Injection site induration, Pyrexia, Somnolence, Hypotonia, Depressed level of consciousness, Respiration abnormal, Cough, Pallor, Lip haematoma, General physical health deterioration,	Germany	Pneumonia respiratory syncytial viral, Respiratory tract infection

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0071841A	27-Jun-11	Unresolved	4 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Encephalopathy, Infantile spasms, Lennox-Gastaut syndrome, Dyskinesia, Developmental delay, Eye movement disorder, Motor dysfunction, Posture abnormal, Fatigue, Hyperhidrosis, Crying, Pallor, Diarrhoea, Musculoskeletal stiffness, Depressed level of consci	Germany	Umbilical cord around neck, Bronchitis, Pharyngitis, Rhinitis, Klebsiella infection, Hypotonia
D0073004A	11-Oct-11	Unknown	16 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		48 Hours	Convulsion, Pallor, Gaze palsy, Depressed level of consciousness, Joint hyperextension	Germany	

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6.5.2.9.5. Encephalitis, Encephalopathy and Encephalic infection

Five (5) cases of Encephalitis/Encephalopathy/Encephalic infection were received during the period:

- **B0686208A (Italy): Encephalitis, Epilepsy.**

  This case was reported by a physician via a sales representative and described the occurrence of possible encephalitis in a 3-month-old subject of unspecified gender who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Subject's medical history was negative. On 8 November 2010 the subject received 2nd dose of Infanrix hexa (unknown), lot number not provided. Less than one month after vaccination with Infanrix hexa, the subject experienced possible encephalitis and epileptic seizure. The subject was hospitalised. At the time of reporting the outcome of the events was unspecified.

  Company comment: A 3-month-old subject experienced encephalopathy less than one month after 2nd dose of Infanrix hexa. Due to a lack of data, this case cannot be medically assessed.

- **D0070015A (Germany): Ataxia, Balance disorder, Encephalitis, Gait disturbance, Pyrexia, Upper respiratory tract infection, Otitis media acute, Cerebellar ataxia.**

  This case was reported by a German regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2010038217) and described the occurrence of ataxia in a 16-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Co-suspect vaccinations included 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer Pharma). Past medical history was not provided. Previous vaccinations including three doses of combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) and three doses of 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer Pharma), given on 28 September 2009, 04 January 2010 and 20 April 2010, were well tolerated. On 09 December 2010 the subject received the fourth dose of Infanrix hexa (0.5 ml, subcutaneous, right thigh) and the fourth dose of Prevenar 13 (0.5 ml, subcutaneous, left thigh), contralaterally. Approximately one day post vaccination with Infanrix hexa and Prevenar 13, on 10 December 2010, the subject experienced ataxia and tendency to fall towards the right side (balance disorder). The report suspected cerebellitis and/or encephalitis. The subject was hospitalised for an unknown period of time. In hospital cerebrospinal fluid (CSF) examination, electroencephalogram (EEG), cranial magnetic resonance tomogram (cMRT) and metabolic diagnoses were performed to confirm the events but the result of these examinations have not been provided. At the time of initial reporting, on 14 December 2010, the events were unresolved. The vaccination courses with Infanrix hexa and Prevenar 13 were discontinued. The vaccine was reported as diphtheria and tetanus toxoids and acellular pertussis vaccine (Infanrix,

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GlaxoSmithKline), but according to lot number the subject was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline). Less than one day post vaccination with Infanrix hexa and Prevenar 13, on 09 December 2010, the subject experienced high fever of up to 39 degC. The following days the subject only showed subfebrile temperature of 37.5 degC. Approximately one day post vaccination with Infanrix hexa and Prevenar 13, on 10 December 2010, the subject experienced conspicuous staggering which improved over the next days. On 13 December 2010 the subject experienced conspicuous gait disturbance and was hospitalised for this event. Examinations, performed on 10 December 2010, showed upper respiratory tract infection. Cranial computed tomogram (CCT) was normal without pathogenic changes. Cerebrospinal fluid (CSF) showed increased CSF protein. CSF cell count could not be determined due to bloody and in parts coagulated CSF sample. Infection diagnostic of CSF were negative; CSF and blood cultures were sterile. Metabolic diagnostics were normal. Cranial magnetic resonance tomogram (cMRT) was normal. Electroencephalogram (EEG) showed beta superimposition due to medication and a conspicuous phase with a short group of irregular spike-slow-wave-complexes left frontocentral, control EEG was recommended. During course of hospitalisation the subject recovered and ataxia was clinically completely improved. During course of hospitalisation the subject showed high fever due to underlying respiratory tract infection. Regular laboratory examinations showed normal inflammatory parameters. Therefore the subject needed no treatment with antibiotics. The hospital physician(s) considered either post infectious cerebellar ataxia due to underlying respiratory tract infection, postvaccinal cerebellitis due to time context or otogenic ataxia associated with serous otitis media both sides (right more than left). On 18 December 2010 the subject was discharged from hospital in stable general condition against medical advice. No further information was available. At the time of follow-up reporting, on 21 December 2010, the events were resolved.

Company comment: This 16-month-old male subject experienced post infectious cerebellar ataxia due to underlying respiratory tract infection in the course of Infanrix hexa vaccination. A postvaccinal cerebellitis was compatible with the time sequence (one day post-vaccination with Infanrix hexa and Prevenar) but the ataxia was associated with serous otitis media both sides and finally recovered.

- **D0071549A (Germany): Encephalitis, Bronchitis, Lactic acidosis, Hyperglycaemia, Convulsion, Injection site induration, Pyrexia, Somnolence, Hypotonia, Depressed level of consciousness, Respiration abnormal, Cough, Pallor, Lip haematoma, General physical health deterioration,**

  This case was reported by a regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2011015875) and described the occurrence of viral meningoencephalitis in a 4-month-old male subject who was vaccinated with 10 valent pneumococcal conjugate vaccine (Synflorix, GlaxoSmithKline), combined diphtheria, tetanus-acellular pertussis, hepatitis B and inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa) for prophylaxis. Former vaccinations included Synflorix on 04 March 2011 (same lot number), which was well tolerated. On 7 April 2011 the subject received 2nd dose of Synflorix (unknown route, right

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thigh), 1st dose of Infanrix hexa (unknown route, left thigh). On 7 April 2011, less than one day after vaccination with Infanrix hexa and Synflorix, the subject experienced injection site induration. In the evening the subject had fever. This had resolved the next day and the subject was normal. On 10 April 2011 the subject developed somnolence. The subject was hospitalised for 25 days and the events were life threatening. The subject was diagnosed with viral meningoencephalitis. On 06 May 2011 the events were still unresolved. A hospital report was provided. According to this, the subject's medical history included respiratory syncytial virus pneumonia in January 2011. Since then there were recurrent respiratory infections. When the father wanted to give him the second baby bottle that morning, he found the subject with flaccid muscle tone and nonresponsive (could not be woken up), with rattling respiration. The subject had been lying at the side due to mild cough, but the face was not covered. When admitted, the subject was in reduced and instable general condition, with moaning, snapping breath, flaccid muscle tone, pale, non-responsive, without reaction to pain stimuli and had prolonged recapillarisation time. There was an extended hematoma at the lip at the right, but no other signs for injury. The subject had severe pulmonary obstruction (obstructive bronchitis diagnosed), lactic acidosis and hyperglycemia. First treatment included fluid substitution. Lactic acidosis quickly normalised. Blood glucose normalised on the second day and in further course all controls of lactate, blood glucose, blood gases and metabolic screening were normal. The subject was cardio-respiratory stable. Because of suspected encephalitis treatment with ampicillin trihydrate (Ampicillin), gentamicin sulphate (Gentamicin), cefotaxime (Cefotaxim) and acyclovir (Aciclovir) was started. Imaging diagnostics and electroencephalogram (EEG) confirmed the diagnosis of meningoencephalitis. As cerebrospinal fluid test showed 41 lymphocytic cells and respiratory infection, a viral genesis was suspected. After confirmation of negative bacteriological results, antibiotic treatment was stopped after three days. Aciclovir was continued for three weeks. On the second day the subject developed cerebral seizure and was treated with phenobarbitone (Phenobarbital). In further course there were no convulsions, but daily electroencephalogram (EEG) showed epileptic potentials and general changes in terms of retardation. Before discharge, EEG was still pathologic with missing sleeping structure and discrete multifocal irritability, but without seizure potentials. The subject was discharged with improved general condition, but still abnormal EEG and multiple neurologic abnormalities, including decreased spontaneous motor movement, frequent fisting, missing head control, missing active and targeted movements and no active sounding.

Company comment: This is a case of viral meningoencephalitis in a 4-month-old male subject. First symptoms occured 3 days post vaccination with Infanrix hexa and Synflorix. The subject suffered from multiple neurologic sequellae. The hospital physician did not consider that the events were a reaction to vaccination.

- **B0692285A (France): Encephalitic infection, Convulsion, Dyskinesia, Fatigue, Pyrexia, Hypertonia, Depressed level of consciousness, Electroencephalogram abnormal**

  This case was reported by the French regulatory authority (AF SSPS reference LL20100605) and described the occurrence of post infectious encephalitis in a 21-

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month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (Prevenar, non-gsk) for prophylaxis. Medical condition was unspecified. On 08 December 2010, the subject received unspecified doses of Infanrix hexa (batch, route and injection site unknown) and of Prevenar (batch, route and injection site unknown). The subject experienced fever. On 09 December 2010, the subject was very tired and slept a lot. On 10 December 2010, the subject presented with convulsive status resistant to diazepam (Valium) and phenytoin (Dilantin) but effectively treated by midazolam hydrochloride (Hypnovel). Since that date, convulsion crisis recurred with abnormal movements, as pedaling, and hypertonia associated with a loss of contact (coded decreased level of consciousness). HSV1, HSV2, VZV, Epstein Barr virus and cytomegalovirus tests were negative. On 11 December 2010, an abnormal electroencephalogram was recorded with a very slow down line with a slight right hemispheric predominance without focusing suggestive of encephalitis. On 13 December 2010, HSV test was negative. Stool analysis revealed presence of campylobacter jejunii. Physicians concluded to post infectious encephalitis. The subject was hospitalised. At the time of reporting, the outcome of the events was unknown.

Company comment: Post-infectious encephalitis (campylobacter jejuni) in a 21-month-old female subject. Intermittend convulsive crises starting 2 days after vaccination with Infanrix hexa and Prevenar. According to AFSSaPS, the causal relationship between Infanrix hexa and Prevenar and the reported events is dubious.

- **D0071841A (Germany): Encephalopathy, Infantile spasms, Lennox-Gastaut syndrome, Dyskinesia, Developmental delay, Eye movement disorder, Motor dysfunction, Posture abnormal, Fatigue, Hyperhidrosis, Crying, Pallor, Diarrhoea, Musculoskeletal stiffness, Depressed level of consciousness.**

  This case was reported by a physician and described the occurrence of epileptic encephalopathy in a 4-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. No epilepsy was known in the family. Co-suspect vaccination included pneumococcal vaccine (non-GSK) (Prevenar, Pfizer). On 9 February 2011 the subject received 1st dose of Infanrix hexa (unknown route and application site), 1st dose of Prevenar (unknown route and application site). In the end of February or beginning of March 2011, less than one month after vaccination with Infanrix hexa and Prevenar, the subject experienced decreased contact activity, eyes rolling, smacking and motor dysfunction. The subject was hospitalised and diagnosed with epileptic encephalopathy with regressive dyskinetic movement disorder and myocloni. Electroencephalogram (EEG) showed potentials typical for epilepsy. Magnetic resonance tomogram (MRT) of head was without pathologic findings. The family consulted another hospital, where the subject was diagnosed with West syndrome / Lennox Gastaut syndrome. The hospital report was not available to the reporting physician. There were no concurrent medical conditions or concurrent medications (Prevenar was not mentioned in the case follow-up). Infanrix hexa was given intramuscular, unknown gluteal. The subject developed convulsive disease /

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West syndrome. The subject was hospitalised and the physician considered the events were disabling. The vaccination course with Infanrix hexa was discontinued. Follow-up information was received on 05 August 2011 via the German regulatory authority (PEI). The subject was born with umbilical cord around neck, but APGAR score was 10. In the evening after vaccination with Infanrix hexa and Prevenar, the subject could not keep the head straight (head posture abnormal) and had rolling eyes and restless head. The next day the subject developed sweating, tiredness and after three days high-pitched crying and regression of development (loss of known skills, speech and body control). In second week the subject was twitching and developed West syndrome. Medical stabilisation was difficult. At last (in July 2011), the subject was treated with sultiam (Ospolot). The subject had developed well until vaccination. Starting in the evening after vaccination and throughout the next three weeks, the subject developed problems holding the head with waggling the head, tiredness, pallor, diarrhea, sweating, stiff neck, was not responsive, stopped laughing, became more and more stiff, with high-pitched crying, twitching, headache and abdominal pain. The subject was hospitalised from 07 to 18 March 2011, 30 March to 09 April 2011, 16 to 18 May 2011 and 18 May to 10 June 2011. The hospital reports stated the following. The subject had two healthy siblings. After normal pregnancy, the subject was born spontaneously with a weight of 4040 g. Newborn screening and childhood examinations U1 to U3 were normal. On 31 December 2010 the subject had bronchitis, pharyngitis and purulent rhinitis. High amounts of Klebsiella pneumoniae were found in nose swab. U4 showed trunk hypotonia and physiotherapy was prescribed. On the same day vaccination was administered. After vaccination the subject's development was regressive, with less contact, tiredness, not responsive, rolling eyes, no sounding, loss of skills. When first hospitalised, the subject had hypotonia and movement disorder, but no infection, fever or diarrhea. Diagnoses included epileptic encephalopathy with developmental regression, West syndrome, dyskinetic movement disorder and muscular hypotonia. Electroencephalogram (EEG) was pathologic with hypsarrhythmia. Several convulsions were observed in hospital. Metabolic tests were normal, except for mildly increased methylmalonic acid in urine. Tests for amino acids in urine and plasma, acylcarnitin pattern in blood and lysosomal enzymes excluded GM1/2 gangliosidosis, CLN1/2 and Morbus Krabbe and showed no signs for metabolic diseases. Glutamin in plasma was mildly increased. Echocardiogram showed no cardiac hypertrophy. Treatment with vigabatrin (Sabril) was without effect and stopped by the parents without dose reduction. Treatment with pyridoxine hydrochloride (Vitamin B6) and calcium folinate (Folinic acid) was without effect. The parents started homeopathic treatment and quantum medicine with diverting harmful substances. During these measures harmful germs were reported, including lactobacillus acidophilus, lamblia, fungi, pseudomonas aeruginosa and multiple diseases, against which vaccination was possible, like Haemophilus influenzae. The parents refused medical treatment, because the disease had been caused by vaccination and anticonvulsive treatment had not been good for the child, causing constipation, which had to be removed with treatment for "gastritis" and "reflux" by a non-medical practitioner. The hospital physician strongly advised to start medical anticonvulsive treatment. After health care for the subject had been taken over by a youth welfare office and EEG was highly pathologic, treatment with steroids was started. This was followed by sulthiame (Ospolot). Timely relation to vaccination

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was clear, but causal relation could not be assessed. Alternative causes were viral encephalitis (Cocksackie virus antibody found, which could also be maternal). A paediatrician was consulted for second assessment. The paediatrician had examined the subject on 31 December 2010 due to bacterial airways infection. At that time there were no neurologic symptoms. During examination on 22 March 2011, the subject was highly disabled, with disturbed perception, no reaction to stimuli, no contact to persons and extremely low muscle tone. The physician considered encephalitis most likely. Mercury intoxication, as suspected by the parents, was excluded.

Company comment: This 4-month-old female subject was diagnosed with West Syndrome/ Lennox-Gastaut syndrome less than one month after 1st dose of Infanrix hexa and Prevenar. Causal relationship to vaccination could not be formerly assessed and other etiologies were considered (metabolic, viral encephalitis).

6.5.2.9.6. Guillain-Barré syndrome

Two (2) cases of Guillain-Barré syndrome were received during the period:

- **B0691863A (Italy): Guillain-Barre syndrome, Neuropathy peripheral, Pyrexia, General physical health deterioration, Restlessness, Asthma, Decreased appetite, Gait disturbance, Dysstasia, Nuchal rigidity, Hyperaemia, Dysphonia, Hyporeflexia, Hypotonia, Asthenia**

  This case was reported by a regulatory authority (IT-Agenzia Italiana del Farmaco # 130966) and described the occurrence of Guillain Barre syndrome in a 15-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevnar) for prophylaxis. On 8 September 2010 the subject received unspecified dose of Infanrix hexa (intramuscular, unknown, lot number not provided), unspecified dose of Prevnar (intramuscular, unknown). On 10 September 2010, 2 days after vaccination with Infanrix hexa and Prevnar, the subject experienced fever (NOS). On 22 September 2010, the patient expirenced peripheral neuritis. On a date as yet unspecified, the patient experienced Guillain Barre syndrome. On 01 December 2010, he had recovered from the fever and peripheral neuritis and on a date as yet unspecified, he had recovered from Guillain Barre syndrome. The subject was hospitalised. Relevant test results included a CSF analysis and an NMR but no results were provided. The subject was treated with normal immunoglobulin (Immunoglobulin). The regulatory authority reported that the events were possibly related to vaccination with Infanrix hexa and Prevnar. Follow-up information received on 03 January 2011: The vacine lot number for Infanrix Hexa was provided (A21FA780A). Follow-up information received on 19 April 2011: The child was hospitalized for the first time from 25 September 2010 till 30 September 2010 and from 08 October 2010 till 15 October 2010. Discharge letter: hospitalization from 25 September 2010 to 30 September 2010 Diagnosis: Guillain Barre Syndrome Medical history: patient was taken to emergency room. due to ingravescent fever since 10 September 2010 (vaccination date 08 September 2010). Since the start of fever the child presented with ingravescent general condition, with restlessness, asthenia,

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decreased appetite. Since 22 September 2010 showed unsteady walk, with difficulty in maintaining erect position. On admission, the child was in a poor general condition and was unable to maintain standing position. He presented a pale-grayish complexion, decreased trophism, capillary refill inferior to 2 seconds. He presented also moderate skin hydration, hyperaemic pharynx and dysphonia as well as difficult breathing with chest wall retraction. Thorax examination showed reduced air intake, spare wheezes and rales. Clinical pattern suggestive of peripheral neuropathy with global asthenia. To be re-evaluated within 30 days. Course of hospitalization and prescribed therapy: during the first period of hospitalization the child showed clinical worsening with increased nuchal rigidity. For this reason, rachicentesis was performed. Then the child was treated with antibiotics. In the next days, marked improvement of general condition, associated with a still incomplete improvement of neurological condition, osteotendon reflexes, tone, walking and nucal rigidity. The child was discharged in moderately good condition. Advice at discharge: antibiotic therapy: amoxi-clavulanic acid (Augmentin) 2ml 3xD until 04 October 2010 inclusive. Discharge letter: hospitalization from 08 October 2010 to 15 October 2010: Diagnosis: Guillain Barre Syndrome Medical history: patient already hospitalized for peripheral neuritis. At follow up visits the child's neurological condition had not improved. Therefore, a new hospitalization was decided in order to perform NMR of the brain and spinal cord under sedation, followed by therapy with immunoglobulins i.v. On admission: fair general condition, pale complexion, decreased trophism, capillary refill above 2 seconds, moderate skin hydration. Pink pharynx, normal breathing. Neurological visit: hypotonic child, shows difficulty in movement of upper limbs, no walking, no erect standing, no signs of meningeal irritation. Lab tests (08 October 2010): RBC 4.74 tera/L; HB 123 g/L; Ht 38%, MCV 79.2 fl/cell; PLT 476 giga/L; WBC 17.0 giga/L (neutrophils 9.9, leucocytes 5.6, monocytes 1.1 giga/L). CRP 0.7 mg/dL. Glycemia, albumin and ions normal. Lab tests (11 October 2010): RBC 9.90 tera/L; CRP< 0.5 mg/dL. Na 132 mEq/L. PT, aPTT normal. Brain/spinal chord NMR negative. Course of hospitalization and Prescribed therapy: on admission date, the child was drowsy and with leucocytosis, likely due to dehydration. He was treated with rehydrating solution; the next day therapy with immunoglobulins i.v. (400mg/Kg/die for 5 days) was started. Pre-treatment with Trimeton (chlorpheniramine). No adverse reactions observed. Neurological visit: upper limbs improvement observed. Further clinical improvement can be expected, which will be monitored closely through follow up visits.

Company comment: This case does not provide any supportive evidence for GBS diagnosis except for the clinical description. Rresults of diagnostic tests supportive of the diagnosis were not provided: CSF, EMG, NCS, and no investigation results of other possible etiology such as herpes infection. The febrile context 48 hours after vaccination could have triggered the occurrence of the neurologic syndrome that started 2 weeks after vaccination with Infanrix and Prevenar. Clinical neurological improvement after multiple hospitalization and therapy is reported. This case fulfils the Level 4 of diagnostic certainty of Brighton Collaboration GBS Working group criteria.

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- **D0069554A (Germany): Guillain-Barre syndrome, Congenital neuropathy, Demyelinating polyneuropathy, Hip deformity, Foot deformity, Motor developmental delay**

  This case was reported by a regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2010034653) and described the occurrence of Guillain Barre syndrome in a 2-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Later vaccinations included pneumococcal vaccine (Prevenar, Wyeth) in December 2006, January 2007 and November 2007, combined measles, mumps and rubella vaccine, live, attenuated on 27 February 2008, meningococcal vaccine (NeisVac-C, Baxter Healthcare) on 24 February 2009, hepatitis A vaccine (Havrix pediatric, GSK) in July 2009. On 22 August 2006, 26 September 2006 and 24 October 2006 the subject received 1st dose, 2nd dose and 3rd dose of Infanrix hexa (unknown route, unknown thigh). At an unspecified time after vaccination with Infanrix hexa, the subject experienced Guillain Barre syndrome (GBS). The subject developed GBS during infancy, but it was not clarified after which vaccination. The subject was hospitalised. At the time of reporting the event was unresolved. Follow-up information was received on 19 January 2011 via the German regulatory authority (PEI). Later vaccinations also included another dose of Infanrix hexa on 01 August 2007, combined measles, mumps and rubella vaccine, live, attenuated (Priorix, GSK) in June 2007 and varicella vaccine (Varivax) in June 2007. Ambulatory orthopaedic examination was performed on 23 October 2007. During early childhood the subject showed stato-motor developmental delay and was diagnosed with hydrocepahalus internus. The subject had first problems, later diagnosed as coxa valga and antetorta at both sides and pes valgus. The subject received regular physiotherapy. From 09 March to 20 April 2010 the subject was hospitalised for rehabilitation measures. The following was reported for anamnesis: The subject was born in 40+5 weeks of gestation by emergency caesarean section, after complications because of unusual position. At birth the subject had a weight of 3540 g, a size of 50 cm and an Apgar score of 10/10. The subject was breast-fed for eight months and received vitamin D and fluor prophylaxis for 20 months. The subject was seldom ill, but had three-day fever once. There were no allergies. The subject had congenital hydrocephalus internus and mild Dandy-Walter disease variant, but no other malformations. The subject still received regular physiotherapy and had Swash-Orthesis at night until January 2010. During hospitalisation from 04 to 07 August 2010 a muscle conduction velocity (MLG) examination showed signs for severe polytopic demyelinating neuropathy. In a medical report from 21 October 2010 the diagnosis was polyneuropathy, differential diagnosis congenital hypomyelinating neuropathy. No further information will be available.

  Company comment: This case fulfils the Level 4 of diagnostic certainty of Brighton Collaboration GBS Working group criteria. The physician did not consider GBS as primary possible diagnosis and stated a chronic inflammatory demyelinating polyneuropathy (CIDP) has to be considered more likely, although the course of disease was unusual. Other differential diagnoses have been postulated (congenital hypomyelinating neuropathy).

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6.5.2.9.7. Hemiparesis

One (1) case of Hemiparesis was received during the period (D0071075A) and is described in Section 6.5.2.9.12 Thalamus haemorrhage.

6.5.2.9.8. Lennox-Gastaut syndrome

One (1) case of Lennox-Gastaut syndrome was received during the period (D0071841A) and is described in Section 6.5.2.9.5 Encephalitis, Encephalopathy and Encephalic infection.

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6.5.2.9.9. Loss of consciousness

Thirty five (35) cases of Loss of consciousness were reported during the period and are summarized in Table 23. This table also includes one case received prior to the period of this report but never included in a previous PSUR (B0591710A). This case's ID is marked by a '*' in Table 23.

Table 23 Summary of cases of Loss of consciousness received during the period

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0682745A	03-Nov-10	Unresolved	6 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Hours	Convulsion, Loss of consciousness, Gaze palsy, Pallor, Pyrexia, Crying	Netherlands	
B0683333A	05-Nov-10	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Hours	Presyncope, Loss of consciousness, Depressed level of consciousness, Staring, Hypotonia, Pallor, Crying, Pyrexia, Pain, Mental impairment, Vomiting, Muscle contractions involuntary, Myoclonus, Abdominal abscess, Irritability, Hypotonic-hyporesponsive epis	Netherlands	Gastrooesophageal reflux disease, Choking
B0687865A	07-Dec-10	Resolved	11 Months	Male	Infanrix hexa	Priorix	2 Days	Loss of consciousness, Gaze palsy, Pallor, Hypotonia	Italy	
B0691167A	23-Dec-10	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Apnoea, Loss of consciousness, Erythema, Hypertonia	Italy	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0692220A	04-Jan-11	Resolved	11 Months	Male	Infanrix hexa		1 Days	Syncope, Loss of consciousness, Febrile convulsion, Eye movement disorder, Opisthotonus, Pallor, Pyrexia	Italy	
B0692681A	07-Jan-11	Resolved	18 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		4 Hours	Febrile convulsion, Loss of consciousness, Pallor, Tremor, Hypotonia, Peripheral coldness, Respiratory disorder, Cyanosis, Chills, Postictal state, Pyrexia	Netherlands	Nasopharyngitis, Cough, H1N1 influenza, Eczema
B0695521A	19-Jan-11	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		8 Hours	Loss of consciousness, Pallor, Hypotonia, Feeling cold, Somnolence	Netherlands	
B0701374A	18-Feb-11	Resolved	2 Months	Male	Infanrix hexa, Rotavirus vaccine, Pneumococcal vaccines (Non-GSK)	Rotavirus vaccine, Pneumococcal vaccines (Non-GSK)	3 Hours	Hypotonic-hyporesponsive episode, Loss of consciousness, Depressed level of consciousness, Unresponsive to stimuli, Cyanosis, Cough, Ill-defined disorder, Fatigue, Adverse event, Vomiting, Eyelid disorder, Crying, Somnolence	Switzerland	
B0702744A	24-Feb-11	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Loss of consciousness, Pyrexia	Italy	

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0705098A	08-Mar-11	Resolved	2 Months	Female	Infanrix hexa		Immediate	Presyncope, Bradycardia, Hypotonia, Injection site pain, Loss of consciousness, Cyanosis	France	
B0706275A	10-Mar-11	Resolved	4 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Grand mal convulsion, Loss of consciousness, Staring, Hypertonia, Erythema, Gastrooesophageal reflux disease, Regurgitation	Italy	
B0709210A	22-Mar-11	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		8 Hours	Loss of consciousness, Pallor, Pyrexia	Italy	
B0709247A	24-Mar-11	Resolved	6 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Hours	Loss of consciousness, Pallor, Hypotonia, Hypotonic-hyporesponsive episode, Vomiting	Netherlands	
B0710868A	29-Mar-11	Resolved	11 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Status epilepticus, Loss of consciousness, Apnoea, Convulsion, Vomiting, Skin warm, Staring, Hypotonia, Hyporesponsive to stimuli, Crying, Erythema, Upper respiratory tract infection, Pyrexia, Hypertonia, Postictal state, Malaise, Listless	Netherlands	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0712712A	05-Apr-11	Resolved	13 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Hours	Loss of consciousness, Depressed level of consciousness, Convulsion, Gaze palsy, Respiration abnormal, Pallor, Hypotonia, Drooling, Cyanosis, Pyrexia, Vomiting	Netherlands	
B0715332A	21-Apr-11	Resolved	15 Months	Female	Infanrix hexa, Meningococcal polysaccharide vaccine group C (Non-GSK)		0 Days	Cyanosis, Loss of consciousness, Apnoea, Hypotonia, Crying	Italy	
B0715581A	27-Apr-11	Resolved	2 Months	Female	Infanrix hexa	Pneumococcal vaccines (Non-GSK)	Hours	Hypertonia, Loss of consciousness, Cyanosis, Clonus, Eye disorder, Apathy, Convulsion	France	
B0716232A	27-Apr-11	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Syncope, Loss of consciousness, Pallor	Italy	
B0716294A	28-Apr-11	Resolved	13 Months	Male	Infanrix hexa, Meningococcal polysaccharide vaccine group C (Non-GSK)		0 Days	Febrile convulsion, Cyanosis, Loss of consciousness, Clonus, Salivary hypersecretion, Hypertonia	Italy	
B0716724A	28-Apr-11	Resolved	2 Months	Female	Infanrix hexa		0 Days	Loss of consciousness, Hypotonic-hyporesponsive episode, Hypotonia, Diarrhoea	Poland	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0717794A	06-May-11	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		36 Hours	Loss of consciousness, Apnoea, Depressed level of consciousness, Gaze palsy, Pallor, Cyanosis, Hypotonia, Peripheral coldness, Pyrexia	Netherlands	
B0721081A	19-May-11	Resolved	2 Months	Unknown	Infanrix hexa, Rotavirus vaccine (Non-GSK)		2 Days	Unresponsive to stimuli, Loss of consciousness, Hypotonic-hyporesponsive episode, Apathy, Restlessness, Somnolence, Crying	Poland	
B0722809A	27-May-11	Resolved	3 Months	Female	Synflorix, Infanrix hexa		0 Days	Loss of consciousness, Convulsion, Cyanosis, Somnolence, Body temperature increased, Crying	Czech Republic	Postmature baby, Neonatal asphyxia, Low birth weight baby, Resuscitation
B0724363A	06-Jun-11	Resolved	4 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Loss of consciousness, Pyrexia, Pallor, Arrhythmia	Italy	Pharyngitis, Conjunctivitis
B0726312A	08-Jun-11	Resolved	10 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Cyanosis, Loss of consciousness, Hypotonia	Italy	
B0728516A	24-Jun-11	Resolved	12 Months	Male	Infanrix hexa, MMR vaccine (Non-GSK)		1 Days	Febrile convulsion, Loss of consciousness, Tremor, Complex partial seizures, Grand mal convulsion, Pyrexia	Italy	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0732350A	11-Jul-11	Resolved	3 Months	Male	Synflorix, Infanrix hexa	Ranitidine hydrochloride, Domperidone	4 Hours	Loss of consciousness, Apnoea, Hypotonic-hyporesponsive episode, Pallor, Hypotonia	Netherlands	Hyperbilirubinaemia, Meconium stain, Gastrooesophageal reflux disease, Cardiac murmur
B0741462A	19-Aug-11	Resolved	3 Months	Unknown	Infanrix hexa	Rotavirus vaccine	Immediate	Hypotonic-hyporesponsive episode, Loss of consciousness, Somnolence, Pallor, Hypotonia, Crying	Poland	
B0744808A	05-Sep-11	Resolved	5 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		19 Days	Loss of consciousness, Nystagmus, Opisthotonus, Eye movement disorder, Pyrexia, Vomiting	Italy	Binocular eye movement disorder, Dermatitis atopic
B0756155A	17-Oct-11	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Sleep apnoea syndrome, Loss of consciousness, Cyanosis, Neutropenia, Salivary hypersecretion, Hyperpyrexia	Italy	Premature baby, Regurgitation
B0757269A	18-Oct-11	Resolved	2 Months	Unknown	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		10 Minutes	Loss of consciousness, Hypotonia, Somnolence	France	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0069341A	05-Nov-10	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Hours	Circulatory collapse, Apnoea, Loss of consciousness, Pallor, Bradycardia, Salivary hypersecretion, Cyanosis, Epilepsy, Partial seizures, Foaming at mouth, Hypotonia, Cardiac arrest, Vomiting, Dyskinesia, Eye movement disorder, Productive cough, Depressed	Germany	Atrial septal defect
D0070819A	28-Mar-11	Resolved	4 Months	Female	Rotavirus vaccine, Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Hypotonic-hyporesponsive episode, Pyrexia, Vomiting, Loss of consciousness, Restlessness, Hyperhidrosis, Abnormal faeces, Hypotonia, Eye movement disorder, Fatigue, Abdominal distension, Pharyngeal erythema	Germany	
D0071146A	26-Apr-11	Resolved	12 Weeks	Female	Infanrix hexa, Rotavirus vaccine, Pneumococcal vaccines (Non-GSK)		2 Hours	Apparent life threatening event, Pallor, Loss of consciousness, Erythema, Respiratory arrest, Somnolence	Germany	

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0071516A	25-May-11	Resolved	3 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		30 Minutes	Loss of consciousness	Germany	Plagiocephaly , Posture abnormal, Twin pregnancy
B0591710A*	04-Sep-09	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		6 Hours	Loss of consciousness, Hypotonia, Vomiting, Pallor, Cyanosis, Drooling	Netherlands	

6.5.2.9.10. Somnolence

Fifty nine (59) cases of Somnolence were received during the period. The outcome was favourable and the event resolved in 42 cases (including one time with sequelae). In 19 cases, the event reported was recorded in a non serious case description. These cases are summarized in Table 24.

Table 24 Summary of cases of Somnolence received during the period

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0682304A	20-Oct-10	Resolved	2 Months	Male	Infanrix hexa		0 Days	Somnolence, Pyrexia	Italy	
B0682373A	25-Oct-10	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Pyrexia, Somnolence	Italy	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0683335A	05-Nov-10	Fatal	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		3 Minutes	Meningitis viral, Convulsion, Yellow skin, Cyanosis, Dehydration, Diarrhoea, Somnolence, Crying, Vomiting	Netherlands	
B0683346A	05-Nov-10	Unknown	4 Months	Male	Boostrix, Infanrix hexa	Oral fluid	24 Hours	Wrong drug administered, Overdose, Somnolence, Irritability	Australia	
B0686044A	25-Nov-10	Resolved	3 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		4 Hours	Hypotonia, Somnolence	Italy	
B0686455A	23-Nov-10	Unknown	2 Months		Infanrix hexa, Rotavirus vaccine		3 Days	Hypotonic-hyporesponsive episode, Abdominal pain, Vaccination complication, Restlessness, Crying, Somnolence	Poland	
B0687574A	03-Dec-10	Unknown	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Pyrexia, Somnolence	Italy	
B0687791A	06-Dec-10	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Somnolence	Italy	
B0689223A	14-Dec-10	Unknown	10 Weeks	Unknown	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Immediate	Pallor, Somnolence, Injection site erythema, Injection site oedema, Injection site inflammation	France	
B0695521A	19-Jan-11	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		8 Hours	Loss of consciousness, Pallor, Hypotonia, Feeling cold, Somnolence	Netherlands	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0696866A	28-Jan-11	Resolved	1 Months		Infanrix hexa, Pneumococcal vaccines (Non-GSK)		3 Days	Anaemia, Hypotonic-hyporesponsive episode, Apathy, Thirst decreased, Respiratory tract infection, Somnolence	Poland	
B0701374A	18-Feb-11	Resolved	2 Months	Male	Infanrix hexa, Rotavirus vaccine, Pneumococcal vaccines (Non-GSK)	Rotavirus vaccine, Pneumococcal vaccines (Non-GSK)	3 Hours	Hypotonic-hyporesponsive episode, Loss of consciousness, Depressed level of consciousness, Unresponsive to stimuli, Cyanosis, Cough, Ill-defined disorder, Fatigue, Adverse event, Vomiting, Eyelid disorder, Crying, Somnolence	Switzerland	
B0702321A	22-Feb-11	Resolved	10 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Euphoric mood, Somnolence	Italy	
B0702562A	25-Feb-11	Resolved	10 Weeks	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK), Rotavirus vaccine (Non-GSK)		18 Hours	Hypotonic-hyporesponsive episode, Somnolence, Pallor, Incorrect route of drug administration, Neurological examination abnormal	France	Anaemia
B0705201A	08-Mar-11	Resolved	2 Months	Male	Infanrix hexa	Calcium salt	0 Days	Somnolence, Urticaria, Acne	Romania	
B0706016A	08-Mar-11	Resolved	2 Months	Female	Infanrix hexa		3 Hours	Hypotonic-hyporesponsive episode, Cyanosis, Somnolence, Crying, Restlessness, Pyrexia, Hypotonia, Anxiety, Lividity	Poland	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0706503A	11-Mar-11	Fatal	2 Months	Female	Infanrix hexa		1 Days	Shock, Respiratory arrest, Cardiac arrest, Pyrexia, Somnolence, Hypotonia, Vomiting, Crying, Apnoea	Thailand	Cytogenetic abnormality
B0708789A	21-Mar-11	Resolved	2 Months	Male	Infanrix hexa		30 Minutes	Crying, Somnolence, Decreased appetite	Poland	
B0712001A	04-Apr-11	Resolved	7 Weeks	Female	Infanrix hexa		1 Days	Somnolence, Injection site reaction	Poland	
B0712989A	08-Apr-11	Resolved	3 Months	Male	Infanrix hexa		2 Minutes	Depressed level of consciousness, Pallor, Crying, Somnolence, Malaise	Netherlands	
B0716780A	02-May-11	Fatal	5 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Cardiac arrest, Multi-organ failure, Pneumonia aspiration, Cerebral ischaemia, Sudden infant death syndrome, Unresponsive to stimuli, Peripheral coldness, Staring, Musculoskeletal stiffness, Pyrexia, Somnolence	Italy	
B0716859A	18-Apr-11	Resolved	5 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Gait disturbance, Stupor, Somnolence	Italy	
B0717816A	06-May-11	Resolved	4 Months	Unknown	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		13 Hours	Respiration abnormal, Oligodipsia, Skin discolouration, Chills, Somnolence, Pyrexia, Injection site pain	Netherlands	
B0719542A	16-May-11	Unknown	1 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Decreased activity, Hypotonia, Somnolence	Poland	Pneumonia

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0720694A	19-May-11	Resolved	19 Months	Unknown	Infanrix hexa		0 Days	Hypotonic-hyporesponsive episode, Pyrexia, Crying, Somnolence	Poland	
B0721081A	19-May-11	Resolved	2 Months	Unknown	Infanrix hexa, Rotavirus vaccine (Non-GSK)		2 Days	Unresponsive to stimuli, Loss of consciousness, Hypotonic-hyporesponsive episode, Apathy, Restlessness, Somnolence, Crying	Poland	
B0722375A	26-May-11	Resolved	22 Months	Unknown	Infanrix hexa, Synflorix		Hours	Hypotonic-hyporesponsive episode, Pain in extremity, Gait disturbance, Body temperature increased, Somnolence	Poland	
B0722407A	24-May-11	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		14 Hours	Gaze palsy, Hypertonia, Pyrexia, Dyskinesia, Somnolence, Feeling hot	Netherlands	
B0722809A	27-May-11	Resolved	3 Months	Female	Synflorix, Infanrix hexa		0 Days	Loss of consciousness, Convulsion, Cyanosis, Somnolence, Body temperature increased, Crying	Czech Republic	Postmature baby, Neonatal asphyxia, Low birth weight baby, Resuscitation
B0727512A	16-Jun-11	Resolved	4 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Malaise, Injection site inflammation, Crying, Pyrexia, Somnolence	Netherlands	
B0728546A	23-Jun-11	Resolved	2 Months	Female	Infanrix hexa	Pneumococcal vaccines (Non-GSK)	7 Hours	Pyrexia, Decreased appetite, Somnolence, Fatigue	France	Febrile convulsion, Breast feeding

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0730356A	30-Jun-11	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Hyporeflexia, Somnolence, Vomiting	Italy	
B0731377A	16-Jun-11	Resolved	5 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Hyperpyrexia, Erythema, Crying, Decreased appetite, Somnolence	Italy	
B0732140A	22-Jun-11	Unknown	4 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		3 Days	Malaise, Fatigue, Crying, Pyrexia, Diarrhoea, Nasopharyngitis, Somnolence	Netherlands	
B0732346A	11-Jul-11	Unknown	2 Months	Female	Infanrix hexa, Synflorix		4 Hours	Depressed level of consciousness, Pyrexia, Somnolence	Netherlands	
B0732350B	02-Sep-11	Resolved	6 Months	Male	Synflorix, Infanrix hexa	Paracetamol, Domperidone, Esomeprazole	3 Hours	Hypotonic-hyporesponsive episode, Crying, Pallor, Hypotonia, Somnolence, Unresponsive to stimuli	Netherlands	Gastrooesophageal reflux disease
B0734272A	20-Jul-11	Resolved	1 Months	Female	Rotavirus vaccine, Infanrix hexa		0 Days	Hypotonic-hyporesponsive episode, Somnolence, Hypotonia, Body temperature decreased	Poland	
B0741462A	19-Aug-11	Resolved	3 Months	Unknown	Infanrix hexa	Rotavirus vaccine	Immediate	Hypotonic-hyporesponsive episode, Loss of consciousness, Somnolence, Pallor, Hypotonia, Crying	Poland	
B0741965A	24-Aug-11	Resolved	6 Months	Male	Infanrix hexa, Synflorix		45 Minutes	Somnolence	Romania	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0746088A	08-Sep-11	Improved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		3 Seconds	Depressed level of consciousness, Crying, Injection site inflammation, Pallor, Hypotonia, Oligodipsia, Somnolence, Respiratory disorder	Netherlands	
B0750925A	22-Sep-11	Resolved	4 Months	Female	Infanrix hexa	Pneumococcal vaccines (Non-GSK), Rotavirus vaccine, Domperidone, Omeprazole	0 Days	Convulsion, Crying, Somnolence, Staring, Abnormal behaviour, Dyskinesia	Singapore	Gastrooesophageal reflux disease
B0752361A	29-Sep-11	Resolved with Sequelae	17 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		9 Days	Type 1 diabetes mellitus, Diabetic ketoacidosis, Polydipsia, Polyuria, Somnolence, Tachypnoea, Increased appetite, Vomiting, Dermal cyst, Ketosis, Lip dry, Dehydration, Lymphadenopathy	Italy	Growth retardation
B0752371A	29-Sep-11	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Cyanosis, Escherichia infection, Oxygen saturation decreased, C-reactive protein increased, Weight decreased, Decreased appetite, Hypotonic-hyporesponsive episode, Somnolence	Italy	Milk allergy
B0754309A	22-Sep-11	Resolved	11 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Pyrexia, Restlessness, Decreased appetite, Somnolence	Italy	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0755401A	07-Oct-11	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Depressed level of consciousness, Pyrexia, Inflammation, Pain, Vomiting, Somnolence, Diarrhoea, Staring	Netherlands	
B0756166A	14-Oct-11	Resolved	1 Months	Male	Infanrix hexa		1 Days	Body temperature increased, Hypotonic-hyporesponsive episode, Somnolence	Poland	
B0756934A	06-Oct-11	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Mobility decreased, Apathy, Somnolence	Italy	
B0757269A	18-Oct-11	Resolved	2 Months	Unknown	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		10 Minutes	Loss of consciousness, Hypotonia, Somnolence	France	
D0069309A	03-Nov-10	Unknown	4 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Febrile convulsion, Pyrexia, Musculoskeletal stiffness, Gaze palsy, Somnolence, Transaminases increased, Pharyngeal erythema, Tympanic membrane hyperaemia	Germany	Cardiac murmur
D0070292A	14-Feb-11	Resolved	3 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK), Rotavirus vaccine (Non-GSK)		3 Days	Convulsion, Eye movement disorder, Dyskinesia, Pallor, Somnolence	Germany	Premature baby

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0070873A	01-Apr-11	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK), Rotavirus vaccine (Non-GSK)		0 Days	Hypotonic-hyporesponsive episode, Pallor, Somnolence	Germany	
D0070921A	07-Apr-11	Resolved	2 Months	Female	Infanrix hexa		0 Days	Kawasaki's disease, Pyelonephritis, Pyrexia, Infection, Somnolence, Fluid intake reduced, General physical health deterioration, Pallor, Ill-defined disorder, Rash, Conjunctivitis, Erythema, Enanthema, Chapped lips, Hypertrophy of tongue papillae	Germany	Pyrexia, Premature baby, Haemangioma congenital, Streptococcal infection
D0071075A	18-Apr-11	Unknown	3 Months	Male	Rotavirus vaccine, Infanrix hexa, Synflorix		1 Days	Thalamus haemorrhage, Convulsion, Facial paresis, Hemiparesis, Hypophagia, Restlessness, Pyrexia, Screaming, Somnolence, Pallor, Hyperaesthesia, Eyelid oedema, Abdominal distension, Hypotonia, Apnoea, Gaze palsy	Germany	
D0071096A	18-Apr-11	Resolved	5 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Grand mal convulsion, Muscle twitching, Somnolence, Pyrexia	Germany	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0071146A	26-Apr-11	Resolved	12 Weeks	Female	Infanrix hexa, Rotavirus vaccine, Pneumococcal vaccines (Non-GSK)		2 Hours	Apparent life threatening event, Pallor, Loss of consciousness, Erythema, Respiratory arrest, Somnolence	Germany	
D0071548A	27-May-11	Unknown	8 Months	Female	Infanrix hexa, Synflorix		1 Days	Convulsion, Gaze palsy, Cyanosis, Vaccination complication, Restlessness, Feeling hot, Staring, Muscle twitching, Dyspnoea, Hypotonia, Somnolence, General physical health deterioration, Body temperature increased	Germany	
D0071549A	27-May-11	Unresolved	4 Months	Male	Synflorix, Infanrix hexa		0 Days	Encephalitis, Bronchitis, Lactic acidosis, Hyperglycaemia, Convulsion, Injection site induration, Pyrexia, Somnolence, Hypotonia, Depressed level of consciousness, Respiration abnormal, Cough, Pallor, Lip haematoma, General physical health deterioration,	Germany	Pneumonia respiratory syncytial viral, Respiratory tract infection

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0072024A	13-Jul-11	Unknown	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Meningitis pneumococcal, Gastroenteritis rotavirus, Respiratory syncytial virus infection, Pneumococcal sepsis, Pharyngitis, Somnolence, Pyrexia, Fluid intake reduced, Respiration abnormal, Crying, Diarrhoea, Cardiovascular insufficiency, Pallor, Tachypno	Germany	
D0072920A	04-Oct-11	Unknown	15 Months	Male	Infanrix hexa, Synflorix		6 Hours	Febrile convulsion, Epilepsy, Rash, Pyrexia, Dyskinesia, Salivary hypersecretion, Eye movement disorder, Somnolence, Pallor, Tachycardia, Injection site erythema, Injection site swelling	Germany	

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6.5.2.9.11. Syncope and Presyncope

Fifteen (15) cases of Syncope/Presyncope were received during the period and are summarised in Table 25.

Table 25 Summary of cases of Syncope/Presyncope received during the period

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0680987A	22-Oct-10	Resolved	2 Months	Female	Infanrix hexa, Rotavirus vaccine (Non-GSK), Pneumococcal vaccines (Non-GSK)		Minutes	Anaphylactic shock, Syncope, Apnoea, Bronchospasm, Blood pressure decreased, Pallor, Respiratory rate decreased, Crying, Hypoventilation	Belgium	
B0682378A	25-Oct-10	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Erythema, Pallor, Presyncope, Pyrexia	Italy	
B0683333A	05-Nov-10	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Hours	Presyncope, Loss of consciousness, Depressed level of consciousness, Staring, Hypotonia, Pallor, Crying, Pyrexia, Pain, Mental impairment, Vomiting, Muscle contractions involuntary, Myoclonus, Abdominal abscess, Irritability, Hypotonic-hyporesponsive epis	Netherlands	Gastrooesophageal reflux disease, Choking
B0687818A	07-Dec-10	Resolved	11 Months	Female	Infanrix hexa	Infanrix hexa	0 Days	Syncope	Italy	Drug hypersensitivity

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0692220A	04-Jan-11	Resolved	11 Months	Male	Infanrix hexa		1 Days	Syncope, Loss of consciousness, Febrile convulsion, Eye movement disorder, Opisthotonus, Pallor, Pyrexia	Italy	
B0699755A	14-Feb-11	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Unresponsive to stimuli, Syncope, Pallor	Ireland	
B0705098A	08-Mar-11	Resolved	2 Months	Female	Infanrix hexa		Immediate	Presyncope, Bradycardia, Hypotonia, Injection site pain, Loss of consciousness, Cyanosis	France	
B0716232A	27-Apr-11	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Syncope, Loss of consciousness, Pallor	Italy	
B0733127A	06-Jul-11	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Presyncope, Hypotonia, Pallor, Pyrexia, Vomiting, Irritability	Italy	
B0733860A	18-Jul-11	Resolved	5 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Presyncope, Syncope, Pallor, Hypotonia, Vomiting	Italy	
B0750040A	20-Sep-11	Resolved	2 Months	Female	Infanrix hexa, Synflorix		7 Hours	Presyncope, Febrile convulsion, Depressed level of consciousness, Hypertonia, Myoclonus, Pallor, Pyrexia, Musculoskeletal stiffness	Netherlands	
B0756838A	17-Oct-11	Resolved	2 Months	Male	Infanrix hexa, Synflorix		2 Minutes	Presyncope, Pallor, Hyperhidrosis, Feeling cold, Heart rate increased	Netherlands	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0069604A	02-Dec-10	Resolved	6 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Immediate	Hypotonic-hyporesponsive episode, Syncope, Skin discolouration, Pallor, Crying, Unresponsive to stimuli, Cardiovascular disorder	Germany	
D0069784A	20-Dec-10	Resolved	12 Weeks	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Crying, Respiratory disorder, Presyncope, Pyrexia, Fatigue, Apathy, Dyskinesia, Inappropriate affect, Decreased interest, Initial insomnia, Diarrhoea	Germany	
D0072433A	18-Aug-11	Resolved	6 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Synflorix, Vigantol	0 Days	Syncope, Cyanosis, Restlessness, Pallor, Vomiting, Hypotonia, Unresponsive to stimuli	Germany	

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6.5.2.9.12. Thalamus haemorrhage

One (1) case of Thalamus haemorrhage was received during the period:

- **D0071075A (Germany): Thalamus haemorrhage, Convulsion, Facial paresis, Hemiparesis, Hypophagia, Restlessness, Pyrexia, Screaming, Somnolence, Pallor, Hyperaesthesia, Eyelid oedema, Abdominal distension, Hypotonia, Apnoea, Gaze palsy.**

  This case was reported by a regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2011011270) and described the occurrence of thalamic bleeding in a 3-month-old male subject who was vaccinated with live attenuated human rotavirus vaccine (Rotarix, GlaxoSmithKline), combined diphtheria, tetanus-acellular pertussis, hepatitis B and inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa) for prophylaxis. On 24 March 2011 the subject received 1st dose of Rotarix (liquid, oral), 1st dose of Infanrix hexa (intramuscular, unknown injection site). On 29 March 2011, 5 days after vaccination with Infanrix hexa and Rotarix, the subject experienced thalamic bleeding of capsula interna at the right side. The subject was hospitalised. A hospital report was received on 01 June 2011 via the German regulatory authority (PEI). The subject was hospitalised from 29 March to 11 April 2011, and then transferred to another unit. Pregnancy, birth and further development of the infant had been normal. On 24 March 2011 the subject received Rotarix and Infanrix hexa. On 25 March 2011 the subject had fever up to 37.7 degC, but else no symptoms. In the night from 28 to 29 March 2011 the subject developed restlessness, screaming, reduced food intake and was hard to wake up. A paediatrician was consulted and the subject was admitted to hospital with the suspect of acute abdomen. In hospital acute abdomen was excluded. Sonogram showed recent thalamic bleeding at the right and the subject was transferred to the reporting hospital for further diagnostics. When transferred, the subject was pale with marble skin, sensitive to touch, but without hematoma or petechiae. The subject had lid edema and abdominal distension, but normal bowel sounds. There were neurological deficits. Cranial magnetic resonance tomogram (MRT) confirmed right-sided bleeding in thalamic centre region and capsula interna. A malformation of vessels was excluded. Extended hematologic diagnostics excluded factor deficiency and thrombophilia and the genesis of bleeding kept unclear. There was no sign for viral infection. Only rotavirus antigen was found in stool, which was caused by rotavirus vaccination. In further course, electroencephalogram (EEG) showed regional function disorder and increased predisposition for convulsions and the subject was treated with phenobarbitone (Phenobarbital). EEG on 06 April 2011 showed mild improvement. Initial neurologic symptoms included decreased muscle tone at the left with increased tendency for stretching of extremities at the left. The subject also had gaze palsy to the right. Additional diagnoses in hospital included cerebral convulsion, peripheral facial paresis and left-sided hemiparesis. The subject was treated with dextrose (Glucose), electrolytes, phytomenadione (Konakion), midazolam hydrochloride (Dormicum), paracetamol, chloral hydrate, and ergocalciferol (Vigantoletten). Intensive physiotherapy was started for compensation of neurologic deficits. Outstanding vaccination with Pneumococcal vaccine (unknown manufacturer) was performed stationary on 09 April 2011. After this, the subject developed solitary episodes of apnea, but without affection of other vital

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parameters. The physician stated that there will probably be mental or motor sequelae. The hospital physician did not consider a causal relation of thalamic bleeding to vaccination. No further information will be available.

Company comment: This 3-month year old male subject experienced a thalamic bleeding of the right capsula interna with multiple neurological complications 5 days after 1st vaccination with Infanrix hexa and Rotarix. The treating physician did not suspect a causal relationship.

6.5.2.9.13. VIth nerve paralysis

One (1) case of VIth nerve paralysis was received during the period:

- **B0681066A (Belgium): VIth nerve paralysis, Strabismus.**

  This case was reported by a healthcare professional and described the occurrence of sixth nerve paralysis in a 15-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) and meningococcal polysaccharide vaccine group c (non-gsk) (Menjugate) for prophylaxis. Previous and/or concurrent vaccination included dtpa-polio-hib (non-gsk) ;Sanofi Pasteur MSD;unknown;unknown given on an unspecified date. On 13 September 2010, the subject received 1st dose of Infanrix hexa (administration site and route unknown) and an unspecified dose of Menjugate (unknown). The subject had previously received 3 doses of Pentavac during his first year. The 4th dose was administered with Infanrix hexa (which contained vaccine against hepatitis B virus). On 5 October 2010, 22 days after vaccination with Infanrix hexa and Menjugate, the subject experienced paralysis of cranial nerve VI external oculomotor on left eye. No fever was experienced. On 6 and 8 October 2010, the subject was seen by the opthalmologist who decided to transfer him to the emergency department. The subject was hospitalised till 12 October 2010. On 11 October 2010, several tests were performed under general anesthesia. All the tests were negative: cerebral magnetic resonance imaging, blood test, lumbar puncture and ocular fundus. No treatment was administered. According to the neurologist, the event was not due to a problem of the brain but possibly due to Infanrix hexa and Menjugate and asked to stop vaccination against hepatits B virus. At the time of reporting, the event was unresolved. There was a paralysis of the left cranial nerve VI considered as a post viral paralysis or post vaccinal. During the hospitalisation, left paralysis of cranial nerve VI persisted without deterioration and without improvement. The subject didn't show other sign of neurological lesions. He remained with excellent general status, the appetite was excellent. The investigation performed by him didn't show for the moment any cause for the paralysis. He should be followed by his ophthalmologist in order to determine whether any treatment was requested. Some oligoclonal bands were noted in the cerebrospinal fluid with uncertain significance. It was advised to the parents to discontinue temporary the vaccination and to reevaluate this condition in the future.

  Company comment: Post-infectious or post-vaccinal paralysis of cranial nerve VI in a 15-month-old male subject 22 days after vaccination with Infanrix hexa and Menjugate. Time to onset seems long for causality.

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6.5.2.9.14. VIIth nerve paralysis

Two (2) cases of VIIth nerve paralysis were received during the period:

- **B0728966A (France): VIIth nerve paralysis, Pain in extremity, Mobility decreased, Oedema peripheral, Erythema, Pyrexia, Facial asymmetry.**

  This case was reported by a pediatrician, via a GSK sales representative, and described the occurrence of paralysis of mouth in a 23-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Subject's father experienced rythm disorder after Influenza vaccination (nos) please see linked case B0728963A (same family, same reporter). In 2011, the subject received an unspecified dose of Infanrix hexa (batch, route and injection site unknown). About 48 hours after vaccination with Infanrix hexa, the subject experienced paralysis of mouth, limb pain with limb decreased mobility. This case was assessed as medically serious by GSK. At the time of reporting, the outcomes of the events were unspecified. Previous vaccination included one dose of Priorix given on 22 November 2010 and one dose of Prevenar given on 13 September 2010. The subject had a febril reaction after this vaccination with Prevenar. On 19 May 2011, the subject received a fourth dose of Infanrix hexa in thigh probably in the left side. On 20 May 2011, the subject had fever at 39 degrees Celsius wich within 24 hours and elusive lower limbs edema and redness (red plaques). On 21 May 2011, 48 hours after vaccination, the subject developped intermittent and flabby right facial asymmetry at mouth level. Several hospital consultations at pediatric unit were made (without hospitalization). Asymmetry persisted but improved and occurred mainly when the subject was tired. It was more visible when he smiled. On 23 June 2011 at consultation, asymmetry persisted. Neurological investigations were planned. On 04 July 2011, the subject was hospitalized for bilateral eyelid edema, not related to vaccination according to the physician. The reporter's assessment was not provided.

  Company comment: This 23-month-old male subject experienced intermittent facial paresis starting 48 hours after combined vaccination with Infanrix hexa and Prevenar. A febrile reaction to Prevenar occurred 24 hours prior to the symptoms.

- **D0071922A (Germany): VIIth nerve paralysis, Facial paresis**

  This case was reported by a physician via a sales representative and described the occurrence of central facial paresis left in a 4-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Co-suspect vaccinations included 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer Pharma). Less than one day post vaccination with the third doses of Infanrix hexa and Prevenar 13, on 22 March 2011, the subject experienced the first episode of asymmetrical crying face (asymmetrical status facial side drooping). Approximately 49 days with the third doses of Infanrix hexa and Prevenar 13, on 10 May 2011, the subject experienced another episode of asymmetrical crying face (asymmetrical status facial side drooping). Approximately 69 days with the third doses of Infanrix hexa and Prevenar

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13, on 30 May 2011, the subject experienced a very severe episode of asymmetrical crying face (asymmetrical status facial side drooping) and was hospitalised for an unknown period of time. In hospital the subject was diagnosed with central facial paresis left of unknown origin by a neuropaediatrician. Ultrasound and cranial computed tomogram (CCT) as well as motor function tests were normal. The reporting physician considered that the event may cause permanent damage. The reporting physician considered that the event was possibly related to vaccination with Infanrix hexa. Family anamnesis included Weber's disease (Sturge-Weber syndrome) of the mother which had already caused amputation of one leg, abnormal nodules of the 8-year-old sister which needed surgical treatment, and lipomyelomeningocele of the twin sister which needed surgical treatment followed by physiotherapy. Since the subject was two months old the subject showed reduced movement of the left side of the face when crying. The subject was diagnosed with facial paresis left. By anamnesis and differential diagnosis no involvement of the cranial branch was observed. No cause of the event could be determined. Birth anamnesis was normal. Mental and motor development was normal. The hospital physicians considered that the event was at the moment no serious neurological disease and recommended monitoring of the event. No further information will be available.

Company comment: This 4-month-old male subject experienced 2 episodes of transient facial nerve palsy less than one day and 69 days after vaccination with 3rd dose of Infanrix hexa. There was no compelling evidence that the event was causally related to the combined vaccination with Infanrix hexa and Prevenar.

6.5.2.10. Repiratory, thoracic and mediastinal disorders

6.5.2.10.1. Apparent life threatening event

Four (4) cases of Apparent life threatening event were received during the period:

- **B0691130A (France): Apnoea, Bradycardia, Oxygen saturation decreased, Blood pressure decreased, Apparent life threatening event, Urine output decreased, Cholinergic syndrome, Eye movement disorder, Gastrooesophageal reflux disease, Aspiration**

  This case was reported by the French regulatory authority (AFSSaPS reference ST20100963) and described the occurrence of apnea in a 1-month and 29 day-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) and pneumococcal vaccine (Prevenar, non-gsk) for prophylaxis. Concurrent medical conditions included prematurity (born at 27 weeks of amenorrhea). The subject weighed 2.25 kg. On 15 December 2010, at about 11:00 the subject received a 1st dose of Infanrix hexa (intramuscular, batch and injection site unknown) and a 1st dose of Prevenar (intramuscular, batch and injection site unknown). On 15 December 2010 at about 16:00, approximately five hours after vaccination with Infanrix hexa and Prevenar, the subject presented with several episodes of apnea with bradycardia and oxygen desaturation which required a mechanical ventilation (Continuous positive airway pressure) and at 19:00 intubation as apnea, bradycardia and desaturation persisted. On 16 December 2010, the subject

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remained dependent on mechanical ventilation. Blood pressure and diuresis decreased. The subject was treated with dopamine at 7.5 g/kg/min. At 17:00, blood pressure and diuresis normalized. The subject remained intubated. The AFSSAPS also coded a near sudden infant death syndrome. The subject was hospitalised and the regulatory authority reported that the events were life threatening. At the time of reporting, the events were unresolved. According to the French method of assessment, the AFSSaPS considered the causal relationship between Infanrix hexa and Prevenar and the reported events as dubious. Upon follow-up received on 11 January 2011: Birth weight of the subject was 1192 g. Medical condition included neonatal apnea treated with cafeine until 30 November 2010 and with doxapram chlorhydrate (Dopram). On 15 December 2010, a possible pulmonary inhalation was considered, as the subject might had reflux. Clinical course was favourable. At the time of reporting, the events were resolved. Upon follow-up received on 17 January 2011: Contacted by phone, the intensive care pediatrician reported a severe vagal hypertonia demonstrated by oculomotor reflexes disturbance. At an unknown date, the subject had bilateral inguinal hernia surgery. At this time, he was treated with atropine.

Company comment: Case of near sudden infant death syndrome in a prematurely born 2- month-old male subject 5 hours after first vaccination with Infanrix hexa and Prevenar. The subject was hospitalized and recovered completely. According to the French method of assessment, the AFSSaPS considered the causal relationship between Infanrix hexa and Prevenar and the reported events as dubious.

- **B0707044A (Netherlands): Anaemia, Milk allergy, Gastrooesophageal reflux disease, Body temperature increased, Gastrointestinal motility disorder**

  This case was reported by a regulatory authority (NL-College ter Beoordeling van Geneesmiddelen # NL-LRB-118313) and described the occurrence of apparent life threatening event in a 2-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) and pneumococcal vaccines (non-GSK) (Prevenar) for prophylaxis. Concurrent medical conditions included anemia (depth and underlying cause unspecified), recurrent elevated body temperature, defecation disorder (undulating defecation frequency), suspected cow's milk allergy and suspected gastroesophageal reflux. Concurrent medications included Ranitidine hydrochloride (Zantac), Domperidone (Motilium) and Macrogol 4000 (Forlax). On 28 February 2011 the subject received 1st dose of Infanrix hexa (intramuscular, unknown injection site), 1st dose of Prevenar (intramuscular, unknown injection site). Lot numbers were not provided. On 1 March 2011, 8 hours after vaccination with Infanrix hexa and Prevenar, the subject experienced apparent life threatening event. The subject was hospitalised. At the time of reporting the event was improved. The regulatory authority reported that the event was possibly related to vaccination with Infanrix hexa and Prevenar. No further information is expected, the regulatory Authority has provided GSK with all the available information for the time being, if they ever get any further information they will send it to GSK. Therefore the case has been closed.

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Company comment: Apparent life threatening event in a 2-month-old male subject 8 hours after combined 1st vaccination with Infanrix hexa and Prevenar. There is insufficient information to assess this case.

- **D0071146A (Germany) Apparent life threatening event, Pallor, Loss of consciousness, Erythema, Respiratory arrest, Somnolence**

  This case was reported by a physician, via Pfizer Pharma GmbH, and described the occurrence of near miss sudden infant death syndrome in a 12-week-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) and live attenuated human rotavirus vaccine (Rotarix, GlaxoSmithKline) for prophylaxis. Co-suspect vaccinations included 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer Pharma). There was no relevant medical history. On 13 April 2011 the subject received the first dose of Infanrix hexa (0.5 ml, intramuscular, right thigh), the first dose of Prevenar 13 (0.5 ml, intramuscular, left thigh), contralaterally, and the first dose of Rotarix (0.5 ml, unknown formulation, oral). Post vaccination the subject was sleepy. Approximately two and a half hours post vaccination with Infanrix hexa, Prevenar 13 and Rotarix, on 13 April 2011, the subject experienced near miss sudden infant death syndrome with pallor, loss of consciousness, skin red and stopped breathing. The physician considered the events were life threatening. After measures by the grandmother with lifting up and shaking, the subject regained consciousness and the conditions normalised. Since 15 April 2011 the subject was monitored for breathing and heart sounds. Additionally the subject received supply with "vital fire". At the time of reporting, on 19 April 2011, a events were resolved. The physician considered the events were possibly related to vaccination with Infanrix hexa, Prevenar 13 and Rotarix. Follow-up information was received on 05 May 2011 via Pfizer. Vaccination was on 13 April 2011 at 13:00. The physician considered that the events were clinically significant (or requiring intervention). Follow-up information was received on 31 October 2011 via case D0073203A received from a German regulatory authority (DE-Paul-Ehrlich-Institut). Approximately five hours post vaccination with the second dose of Rotarix, given on 26 May 2011, the subject experienced similar events (severe pallor, decreased heart and respiratory function) which have repeatedly triggered monitor alarm. For additional information please see case D0073203A. No further information will be available.

  Company comment: Case of near sudden death infant syndrome in a 3-month-old female subject 2 hours after first dose of Infanrix hexa, Prevenar and Rotarix. The event resolved spontaneously. A similar event was reported 5 hours after the second dose of Rotarix.

- **D0071421A (Germany) Apparent life threatening event, Altered state of consciousness, Hypothyroidism, Neutropenia, Staring, Hypotonia, Pallor, Respiratory arrest, Crying**

  This case was reported by a regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2011015251) and described the occurrence of apparent life threatening event in a 4-month-old male subject who was vaccinated with synflorix (GlaxoSmithKline) for prophylaxis. Co-suspect vaccination included combined diphtheria, tetanus-

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acellular pertussis, hepatitis B and inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa). Past medical history was not provided. Concurrent medications included D-fluoretten. On 29 March 2011 the subject received 1st dose of Synflorix (intramuscular, unknown gluteal) and 1st dose of Infanrix hexa (intramuscular, unknown gluteal). On 2 April 2011 in the evening, 4 days after vaccination with Infanrix hexa and Synflorix, the subject was suddenly staring, eyes did not roll back. Muscle tone was flaccid and complexion pale. The subject's mother explained it "like dead" (consciousness disturbed). After stimulation the subject started breathing again and crying. The subject was admitted to hospital and hospitalized for 5 days. At admission to hospital the subject was in stable general condition, awake and conscious. Therapy and course The subject was admitted to hospital because of possible apparent life threatening event lasting for seconds. Monitoring was inconspicuously during stationary stay. No repeated similar event appeared. The examinations performed including metabolism diagnostics showed no pathological finding. Metabolism disturbance and central regulatory disturbance could be excluded. The subject showed latent hypothyroidism (inconspicuously peripheral thyroid parameters) and temporary neutropenia, The subject was treated with potassium iodide (Jodid). On 06 April 2011 the subject was discharged from hospital in good general condition. No further information will be available.

Company comment: Case of possible apparent life threatening event lasting for a few seconds in a 4-month-old male subject 4 days after combined vaccination with Infanrix hexa and Synflorix. Extensive examinations found no pathology. The event resolved spontaneously.

6.5.2.10.2. Asphyxia

One (1) case of Asphyxia was reported during the period (B0705290A) and is described in Section 6.5.1 Cases with a fatal outcome.

6.5.2.10.3. Respiratory arrest

Seven (7) cases of Respiratory arrest were received during the period:

- **B0706503A (Thailand): Shock, Respiratory arrest, Cardiac arrest, Pyrexia, Somnolence, Hypotonia, Vomiting, Crying, Apnoea.**

  See Section 6.5.1 Cases with a Fatal Outcome.

- **B0710929A (Netherlands): Hypotonic-hyporesponsive episode, Respiratory arrest, Crying**

  This case was reported by a regulatory authority (NL-College ter Beoordeling van Geneesmiddelen # NL-LRB-118929) and described the occurrence of hypotonic-hyporesponsive episode in a 2-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) and pneumococcal vaccines (non-gsk) (Prevenar) for prophylaxis. She was born at 35.4 weeks, she grew slowly and will be examined for achalasia. On 11 March 2011, the subject received 1st dose of Infanrix hexa (intramuscular,

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administration site unknown, batch number not provided) and 1st dose of Prevenar (intramuscular, unknown). On 11 March 2011, within minutes of vaccination with Infanrix hexa and Prevenar, the subject experienced hypotonic-hyporesponsive episode. She stopped crying and seemed to fall asleep, she was white and stopped breathing. After touching her cheek, she started to cry and regained colour, but then the same happened again. These episodes repeated themselves 5 times. The subject was hospitalised for one day. In the hospital, she was well again. At the time of reporting, the events were resolved. The regulatory authority reported that the events were probably related to vaccination with Infanrix hexa and Prevenar. No further information is expected, the regulatory Authority has provided GSK with all the available information for the time being, if they ever get any further information they will send it to GSK.

Company comment: Case suggestive of breath holding spells in a 2-month-old female subject minutes after vaccination with first dose of Infanrix hexa and Prevenar. The event resolved spontaneously. The subject was hospitalized for 1 day but no information on examinations was included.

- **B0741007A (Netherlands): Respiratory arrest, Depressed level of consciousness, Breath holding, Crying, Eye movement disorder, Skin discolouration, Pallor**

  This case was reported by a regulatory authority (NL-College ter Beoordeling van Geneesmiddelen # NL-LRB-126405) and described the occurrence of stopped breathing in a 10-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) for prophylaxis. The subject's medical history included planned cesarean section birth with weight of 5000g. On 9 August 2011, the subject received 4th dose of Infanrix hexa (.5 ml, intramuscular, injection site unknown, batch number not provided). On 9 August 2011, immediately after vaccination with Infanrix hexa, the subject was crying for 1 minute. After 1 minute of crying, she stopped breathing and her eyes turned backwards. She did not react for 10 seconds, her face was purple, but turned white shortly after this. When she was taken on the arm, she started breathing again and cried. She was very pale and grew less pale after she was lied down. After half an hour, she went homewards, still somewhat pale. This case was assessed as medically serious by GSK. At the time of reporting, the breath holding spells, stopped breathing and not responsiveness were resolved and the outcome of other events was unspecified. Face turned white was unresloved. The regulatory authority reported that the breath holding spells was probably related to vaccination with Infanrix hexa. No further information is expected, the regulatory Authority has provided GSK with all the available information for the time being, if they ever get any further information they will send it to GSK.

  Company comment: Case suggestive of breath holding spells in a 10-month-old female subject minutes after vaccination with 4th dose of Infanrix hexa. The event resolved spontaneously.

- **D0069889A (Germany): Meningitis pneumococcal, Grand mal convulsion, Epilepsy, Hydrocephalus, Subdural hygroma, Subdural empyema, Anaemia, Generalised oedema, Ileus paralytic, Conjunctivitis, Septic shock, Pneumonia**

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primary atypical, Neurosurgery, Pyrexia, Abdominal distension, Ill-defined disorder, Restlessness, Hyperaesthesia, Oligodipsia, Eye movement disorder, Hypertonia, Tachycardia, Oxygen saturation decreased, Ascites, Respiratory arrest, Drug ineffective, Cyanosis, Splenomegaly

See Section 6.5.2.7.6 Meningitis pneumococcal.

- **D0070901A (Germany):Circulatory collapse, Respiratory arrest, Cyanosis, Hypotonic-hyporesponsive episode, Screaming, Agitation, Hypotonia, Peripheral coldness, Ill-defined disorder, Fatigue, Pyrexia**

  This case was reported by a regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2011009758) and described the occurrence of circulatory collapse in a 12-week-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline for prophylaxis. Co-suspect vaccinations included 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer). Previous vaccinations were well tolerated. On 22 March 2011 the subject received 1st dose of Infanrix hexa (unknown route, left thigh), together with 1st dose of Prevenar 13 (unknown route, right thigh). On the same day, the subject experienced hypotonic-hyporesponsive episode with circulatory collapse. The event was resolved after 1 minute. The subject was hospitalised for observation. Electroencephalogram showed normal findings. A seizure was excluded. The reporting Health Professional was uncertain whether the event was life threatening. Follow-up was received from the regulatory authority on 25 August 2011, including a hospital report. The subject was hospitalised for 2 days from 22 to 23 March 2011. Possible affect spasm was diagnosed. On 22 March 2011, the subject experienced screaming and inability to calm down. On the arm of the mother, the subject suddenly experienced atonia and stopped breathing. The skin of the face was cyanotic (cyanosis). There was no clonus. The subject had cold skin. After 1-2 minutes, the events were resolved. Afterwards, the subject opened his eyes and was whining and tired. There was no vomiting. Body temperature was 37.6 degC (fever). There was no family history of chronic diseases or convulsive disorder. On admission examination, neurological examinations showed normal findings. During monitoring in the hospital there were no unusual neurological findings and no further spasm. On discharge from hospital the subject was in good general condition. Follow-up was received from the regulatory authority on 26 August 2011, including a questionnaire. There was no concurrent medical condition. There were no anamnestic characteristics. On 22 March 2011 the subject received 1st dose of Infanrix hexa (intramuscular, left thigh), together with 1st dose of Prevenar 13 (intramuscular, right thigh). On 22 March 2011, 7 hours after vaccination with Infanrix hexa and Prevenar 13, the subject experienced circulatory collapse and hypotonic-hyporesponsive episode. The event was resolved after stimulation, after approximately 1 minute. The subject was hospitalised. Blood-taking and electroencephalogram were performed and showed normal findings. The reporting physician considered that the events were related to vaccination with Infanrix hexa and Prevenar 13. The vaccination course with Infanrix hexa was discontinued. No further information will be available.

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Company comment: Case suggestive of breath holding spells in a 12-week-old male subject 7 hours after vaccination with 1st dose of Infanrix hexa and Prevenar. The event resolved after stimulation. The subject was hospitalized and no pathology was found.

- **D0071146A (Germany) Apparent life threatening event, Pallor, Loss of consciousness, Erythema, Respiratory arrest, Somnolence**

  See Section 6.5.2.10.1 Apparent life threatening event.

- **D0071421A (Germany) Apparent life threatening event, Altered state of consciousness, Hypothyroidism, Neutropenia, Staring, Hypotonia, Pallor, Respiratory arrest, Crying**

  See Section 6.5.2.10.1 Apparent life threatening event.

6.5.2.11. Skin and subcutaneous tissue disorders

6.5.2.11.1. Angioedema

Four (4) cases of angioderma were reported over the period. These cases are described below.

- **B0691862A (Italy): Angioedema**

  This case was reported by a regulatory authority (IT-Agenzia Italiana del Farmaco # 130512) and described the occurrence of angioedema (face) in a 5-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevnar 13) for prophylaxis. On 17 December 2010 the subject received unspecified dose of Infanrix hexa (.5 ml, intramuscular, unknown), unspecified dose of Prevnar 13 (.5 ml, intramuscular, unknown). On 17 December 2010, less than one day after vaccination with Infanrix hexa and Prevnar 13, the subject experienced angioedema (face). This case was assessed as medically serious by GSK. Relevant test results included C-reactive protein (1.18 mg/dl), LDH (261 IU/L) and WBC (9590/mm3). On 18 December 2010, the event was resolved. The regulatory authority reported that the event was possibly related to vaccination with Infanrix hexa and Prevnar. No additional information could be obtained and this case has been closed.

  Company comment: Angioedema of the face in a 5-month-old female subject less than 1 day after combined vaccination with Infanrix hexa and Prevenar. The event resolved spontaneously within 1 day.

- **B0730009A (Italy): Angioedema, Urticaria**

  This case was reported by a regulatory authority (IT-Agenzia Italiana del Farmaco # 143398) and described the occurrence of angioedema in a 13-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) for prophylaxis. On 4 May 2011, the subject

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received 1st dose of Infanrix hexa (intramuscular, administration site unknown). On 4 May 2011, less than one day after vaccination with Infanrix hexa, the subject experienced angioedema and urticaria of right thigh. This case was assessed as medically serious by GSK. The subject was treated with ice. At the time of reporting, the outcome of the events was unspecified.

Company comment: This case lacks data on the subject's medical history and other possible diagnosis.

- **B0741876A (Italy): Angioedema**

  This case was reported by a regulatory authority (IT-Agenzia Italiana del Farmaco # 146655) and described the occurrence of giant urticaria in a 11-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Concurrent vaccination included pneumococcal vaccines (non-gsk) given on 17 August 2011. On 17 August 2011, the subject received unspecified dose of Infanrix hexa (unknown route of administration, unknown site of injection). On 17 August 2011, less than one day after vaccination with Infanrix hexa, the subject experienced giant urticaria. This case was assessed as medically serious by GSK. The subject was treated with betamethasone (Bentelan) and oxatomide (Tinset). At the time of reporting, the event was improved

  Company comment: This case lacks data on the subject's medical history and other possible diagnosis.

- **B0749275A (Italy): Angioedema, Hyperaemia, Pyrexia**

  This case was reported by a regulatory authority (IT-Agenzia Italiana del Farmaco # 147929) and described the occurrence of giant urticaria in a 5-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) and pneumococcal vaccines (non-gsk) (Prevenar 13) for prophylaxis. Concurrent vaccination included combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. ;GlaxoSmithKline;unknown;unknown given on 20 June 2011. No adverse events occurred. On 18 August 2011, the subject received 2nd dose of Infanrix hexa (administration site and route unknown) and an unspecified dose of Prevenar 13 (unknown). On 18 August 2011, less than one day after vaccination with Infanrix hexa and Prevenar 13, the subject experienced giant urticaria, hyperemic pharynx and fever (40 deg.C). This case was assessed as medically serious by GSK. The subject was treated with amoxicillin trihydrate (Amoxicillin) from 19 to 29 August 2011. On 28 August 2011, the events were resolved.

  Company comment: Case of angioedema in a 5-month-old female subject less than 1 day after vaccination with Infanrix Hexa and Prevenar. The event resolved after 10 days of antibiotherapy. The context of pyrexia might have triggered the event.

In addition, one (1) case of Acute haemorrhagic oedema of infancy was received during the period:

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- **B0743733A (Argentina) Acute haemorrhagic oedema of infancy, Malaise, Tachycardia, Purpura, Pyrexia, Rash, Toxic skin eruption.**

  This case was reported by a physician and described the occurrence of acute hemorrhagic edema of infancy in a 7-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Relevant medical history was not reported. Previous and/or concurrent vaccination included pneumococcal vaccines (non-gsk) given on 20 August 2011. On 20 August 2011, the subject received 3rd dose of Infanrix hexa (unknown route of administration, unknown site of injection). On 21 August 2011, within hours of vaccination with Infanrix hexa, the subject experienced high fever, exanthema and malaise. On 21 August 2011, he was taken to the emergency room where he was diagnosed with acute hemorrhagic edema of infancy. On 22 August 2011, he was examined by his pediatrician who noticed that the subject was tachychardic. He also presented a purpuric exanthema, his fever persisted and he had edema of the four limbs. The doctor assumed that the subject had a toxicodermia and treated him with corticoisteroids and antihistaminics. He controlled the subject 24 hours afterwards. He indicated evaluation by a dermatologist. The subject was not hospitalized. This case was assessed as medically serious by GSK. On 23 August 2011, the pediatrician reported that the subject responded well to the treatment. He had no fever and the edema has diminished. The purpuric lesions were fainter. Given the improvement of the subject, his mother did not consult a dermatologist. At the time of reporting, the events were improved. This case was closed since no additional information could be obtained.

  Company comment: Hemorrhagic edema of infancy (fever exanthema and malaise) in a 7-month-old male subject (acute less than 1 day after 3rd dose of Infanrix hexa. Due to the lack of medical data, the time sequence and assessment of causality remain dubious.

6.5.2.11.2. Erythema multiforme

Two (2) cases of Erythema multiforme were received during the period:

- **D0069303A (Germany): Erythema multiforme**

  This case was reported by a physician, via a web site, and described the occurrence of erythema exsudativum multiforme minor in a 9-month-old subject of unspecified gender who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Co-suspect vaccinations included pneumococcal vaccine (non-GSK) (Prevenar, Wyeth). The subject's medical history included mild schonlein-henoch purpura after an infection when being 7 months old. On an unspecified date approximately in July 2010, the subject received 3rd dose of Infanrix hexa (unknown route and application site), together with 3rd dose of Prevenar (unknown route and application site). One day after vaccination with Infanrix hexa and Prevenar, the subject experienced erythema exsudativum multiforme minor. Laboratory values and IgE were normal. This case was assessed

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as medically serious by GSK. At the time of reporting, on 2 November 2010, the outcome of the event was unspecified. No further information will be available.

Company comment: A 9-month-old subject developed minor erythema multiforme after 3rd dose of Infanrix hexa. This case lacks data on the subject's medical history, data confirming the diagnosis (biopsy), and other possible diagnoses.

- **D0072847A (Germany): Erythema multiforme, Urticaria, Arthropod bite, Swelling, Erythema, Pyrexia, Hypertonia, Herpes simplex, Rash, General physical health deterioration**

  This case was reported by a physician and described the occurrence of erythema exsudativum multiforme in a 2-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Co-suspect vaccine included rotavirus vaccine (RotaTeq). There were no concurrent medications, no concurrent medical conditions or any other risk factors. On 15 July 2011 the subject received 1st dose of Infanrix hexa (intramuscular, left gluteal). An unspecified time after vaccination the subject experienced urticaria. On 12 August 2011 the subject received 2nd dose of Infanrix hexa (intramuscular, left gluteal) and unspecified dose of RotaTeq (oral). In the evening the subject experienced fever. The subject was hospitalized from 17 August 2011 to 21 August 2011 because of parainfectious erythema exsudativum multiforme and differential diagnosis urticaria. The subject was admitted to hospital by the rescue service. The mother reported that the subject showed several mosquito bites in the morning. The subject was treated with zinc oxide and vileda. In the evening the subject's mother used chamomile bath for the first time. At admission to hospital the subject showed swelling and erythema on whole body. There was no shortness of breath. The subject was drinking well. The subject was in good nutrient condition and showed reduced general condition. There was no itching. Ear, nose and throat were bland. Urticarial maculopapular exanthema was on whole body with maximum on trunk. Flexion tone was increased. Internal and neurological examination was age-corresponding inconspicuously. Laboratory tests showed increased IgM values for Herpes II (9 U per ml). The subject was treated with intravenous infusion, intravenously with prednisolone and with cetirizine hydrochloride drops. The exanthema was intermittent. Because of herpes II serology finding the physician suspected erythema exsudativum multiforme. The subject was discharged from hospital on 21 August 2011 with improving exathema. Latest on 24 August 2011 all events were resolved. On 20 September 2011 the subject received 3rd dose of Infanrix hexa (intramuscular, left gluteal) and unspecified dose of RotaTeq (oral). On the same day the subject experienced fever. From 24 September 2011 on the subject developed rash with increasing efflorescences. The subject was treated in emergency admission on 25 September 2011. Urticarial multiform exanthema was diagnosed as suspected vaccination reaction. The subject was treated with prednisolone acetate. In September 2011, the events were resolved. According to treating physician urticaria was unlikely related to vaccination with Infanrix hexa. No further information will be available.

  Company comment: A 2-month-old subject developed erythema multiforme 5 days after 2nd dose of Infanrix hexa and RotaTeq. This case lacks data confirming the

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diagnosis (biopsy), and other possible diagnosis. Conversely, a medical history of Herpes type II and recent mosquito multiple bites was noted. Causal relationship with the vaccination was unlikely.

6.5.2.11.3. Henoch-Schonlein purpura

Two (2) cases of Henoch-Schonlein purpura were received during the period:

- **B0710915A (France): Henoch-Schonlein purpura, Contusion**

  This case was reported by a consumer and described the occurrence of rheumatic purpura in a 5-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. A physician or other health care professional has not verified this report. Concurrent medical conditions included a cold on 10 March 2011. First dose of Infanrix hexa associated with pneumococcal vaccine (Prevenar) was well tolerated. On 22 March 2011, the subject received a 2nd dose of Infanrix hexa (batch and route unknown, unknown thigh). On 27 March 2011, 5 days after vaccination with Infanrix hexa, the subject's mother noticed the presence of bruises on all vaccinated leg from knee to toes and on the other leg with a lower intensity (coded bruises on bilateral lower legs). At emergency service, where blood and urine analyses were performed (results not provided), the physician diagnozed a rheumatic purpura. According to the mother, the physician said that it was not very probable that rheumatic purpura was related to vaccination with Infanrix hexa and might be related to a virus infection. The subject was not hospitalized and was discharged without any treatment. On 04 April 2011, a few bruises persisted and purpura was clearly improved. This case was assessed as medically serious by GSK. At the time of reporting, the events were improved.

  Company comment: Case of a possible Henoch-Schonlein purpura in a 5-month-old subject 5 days after 2nd vaccination with Infanrix and Prevenar. This case lacks laboratory confirmation of the diagnosis.

- **D0070216A (Germany): Henoch-Schonlein purpura, Thrombocytopenia, Petechiae, Pyrexia, Upper respiratory tract infection, Anaemia**

  This case was reported by a physician, via a sales representative, and described the occurrence of Schoenlein-Henoch purpura in a nearly 9-month-old subject of unspecified gender who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. The subject was born as hypoplastic neonate with cyanosis and hypoglycaemia, after treatment with ampicillin due to premature rupture of the amnion. The subject's family were smokers. Former vaccinations were well tolerated. On 1 April 2010 the subject received 3rd dose of Infanrix hexa (intramuscular, left thigh). On an unspecified date in April 2010 the subject developed generalised exanthema and fever of 39 degC. On 29 April 2010 the subject was hospitalised with Schoenlein-Henoch purpura and thrombocytopenia. At the time of reporting all events were resolved. After the next vaccination with Infanrix hexa the events did not recur. The physician considered

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Schoenlein-Henoch purpura and thrombocytopenia were probably related to vaccination with Infanrix hexa. The subject was hospitalised from 29 April to 03 May 2010. According to the hospital report, the subject was diagnosed with thrombocytopenia and infection of the upper airways. When admitted to hospital the subject had petechial exanthema and mild fever. There was no previous infection. The subject had no cough, diarrhea, vomiting or denial of food. The subject had thrombocytopenia with an initial platelet count of 21 Gpt/L. This increased to 98 Gpt/l in further course without treatment. There was a mild initial anemia, but haemoglobin and hematocrit values increased in further course. Additionally a mildly increased c-reactive protein (CRP) was found. The subject was treated with ibuprofen and fluoride + Vitamin D (Zymafluor D). When the subject was discharged, the events were nearly resolved.

Company comment: A nearly 9-month-old subject experienced HSP with 3rd dose of Infanrix Hexa. The subject had an upper respiratory infection prior to this event. The case lacks other laboratory data (antibody testing, plasma D-dimers, PT, etc) to confirm the diagnosis.

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6.5.2.11.4. Petechiae

Twenty nine (29) cases of Petechiae were reported during the period, out of which 20 cases were quoted as serious. In 11/20 serious cases a haematologic disorder was associated: (Idiopathic or non specified) thrombocytic purpura (n=7), thrombocytopenia (n=.3), hemorrhagic diathesis (n=1). These cases are summarized in Table 26.

Table 26 Summary of cases of Petechiae received during the period

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0684234A	09-Nov-10	Unknown	10 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		10 Days	Idiopathic thrombocytopenic purpura, Thrombocytopenia, Rhinitis, Petechiae, Pyrexia	Italy	
B0686840A	30-Nov-10	Resolved	5 Months	Male	Infanrix hexa		3 Hours	Idiopathic thrombocytopenic purpura, Febrile convulsion, Clonic convulsion, Tremor, Dyskinesia, Petechiae, Platelet count decreased, Pyrexia	Czech Republic	Cytomegalo virus viraemia, Familial risk factor, Myocardial infarction
B0693767A	07-Jan-11	Improved	6 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		18 Days	Thrombocytopenic purpura, Petechiae, Haematoma, Epistaxis, Splenomegaly, Thrombocytopenia, Gingival bleeding	France	
B0693944A	13-Jan-11	Resolved	4 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Thrombocytopenic purpura, Petechiae, Haematoma	Czech Republic	
B0694143A	18-Jan-11	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Thrombocytopenia, Petechiae, Pyrexia	Italy	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0700205A	14-Feb-11	Improved	4 Months	Female	Infanrix hexa		1 Days	Petechiae	Italy	
B0703972A	04-Mar-11	Resolved	11 Weeks	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK), Vitamin K		1 Days	Vasodilatation, Petechiae, Erythema, Skin warm	France	
B0705987A	09-Mar-11	Unknown	8 Months	Male	Infanrix hexa		1 Months	Idiopathic thrombocytopenic purpura, Haemorrhage, Platelet count decreased, Petechiae, Fall, Increased tendency to bruise, Upper respiratory tract infection	Ireland	
B0709033A	22-Mar-11	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		10 Minutes	Slow response to stimuli, Hypotonia, Rash macular, Petechiae, Ecchymosis, Conjunctival haemorrhage, Rash, Joint hyperextension	Italy	
B0714101A	18-Apr-11	Resolved	3 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		2 Hours	Pyrexia, Skin warm, Petechiae	Netherlands	
B0715209A	20-Apr-11	Resolved	13 Months	Female	Infanrix hexa		5 Days	Erythema nodosum, Arthralgia, Petechiae	Netherlands	Respiratory syncytial virus infection
B0724575A	07-Jun-11	Unknown	19 Months	Male	Infanrix hexa, MMR vaccine (Non-GSK)		20 Days	Thrombocytopenic purpura, Thrombocytopenia, Petechiae, Injection site haematoma	France	Bronchiolitis, Upper respiratory tract infection

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0727162A	16-Jun-11	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Immediate	Skin discolouration, Screaming, Oedema peripheral, Skin tightness, Oedema genital, Petechiae, Pyrexia, Crying, Injection site pain	Netherlands	
B0728665A	24-Jun-11	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		8 Hours	Viral infection, Petechiae, Pyrexia, Vomiting	Netherlands	
B0728714A	20-Jun-11	Resolved	6 Months	Male	Infanrix hexa, Synflorix		3 Hours	Lividity, Ecchymosis, Anxiety, Petechiae, Erythema, Crying, Body temperature increased, Hypersensitivity, Restlessness	Poland	
B0729750A	13-Jun-11	Resolved	14 Months	Male	Infanrix hexa, MMR vaccine (Non-GSK)	Cefaclor	0 Days	Petechiae	Italy	Otitis media acute
B0731112A	05-Jul-11	Unknown	2 Months	Male	Infanrix hexa, Rotavirus vaccine (Non-GSK), Pneumococcal vaccines (Non-GSK), Meningococcal vaccine	Domperidone, Ranitidine hydrochloride, Carbocisteine	0 Days	Apnoea, Skin discolouration, Pallor, Rash macular, Erythema, Fatigue, Pyrexia, Vomiting, Cough, Crying, Petechiae, Hyperhidrosis, Hypersensitivity, Hypotonic-hyporesponsive episode, General physical health deterioration	Brazil	Neonatal hypoxia, Gastrooesophageal reflux disease
B0737478A	30-Mar-11	Resolved	4 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		8 Hours	Haemorrhagic diathesis, Petechiae, Pyrexia	Poland	
B0740099A	11-Aug-11	Resolved	4 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Hours	Idiopathic thrombocytopenic purpura, Petechiae, Diarrhoea, Inflammation, Pyrexia	Netherlands	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0756825A	11-Oct-11	Improved	2 Months	Female	Infanrix hexa, Synflorix		2 Days	Petechiae, Skin discolouration	Netherlan ds	
D0070216A	04-Feb-11	Resolved	9 Months	Male	Infanrix hexa		28 Days	Henoch-Schonlein purpura, Thrombocytopenia, Petechiae, Pyrexia, Upper respiratory tract infection, Anaemia	Germany	Respiratory fume inhalation disorder, Hypoglycae mia neonatal, Ill-defined disorder, Cyanosis neonatal
D0070397A	21-Feb-11	Resolved	3 Months	Male	Rotavirus vaccine, Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Haemorrhagic diathesis, Ecchymosis, Petechiae, Upper respiratory tract infection	Germany	Ventricular septal defect, Atrial septal defect
D0071125A	21-Apr-11	Unknown	3 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	D-fluoretten	12 Days	Thrombocytopenia, Gastroenteritis rotavirus, Leukopenia, Petechiae, Haematoma, Ureteric stenosis, Pyelocaliectasis	Germany	
D0071437A	18-May-11	Unknown	4 Months	Female	Infanrix hexa		0 Days	Petechiae, Skin discolouration	Germany	
D0072050A	14-Jul-11	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Anaphylactic reaction, Swelling, Erythema, Crying, Petechiae	Germany	
D0072425A	17-Aug-11	Resolved	24 Months	Male	Infanrix hexa, Priorix		7 Days	Thrombocytopenia, Petechiae, Haematoma	Germany	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0072500A	25-Aug-11	Unknown	13 Weeks	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK), Sodium Fluoride	5 Minutes	Anaphylactoid reaction, Hypersensitivity, Product quality issue, Urticaria, Rash, Apathy, Anaphylactic reaction, Erythema, Petechiae, Injection site erythema	Germany	Hyperbilirubinaemia, Phototherapy, Rhinitis
D0072611A	06-Sep-11	Resolved	3 Months	Male	Infanrix hexa		5 Hours	Petechiae, Haematoma	Germany	
D0072699A	13-Sep-11	Resolved	5 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Unknown	Petechiae, Oedema peripheral	Germany	

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6.5.2.11.5. Purpura

Three (3) cases of Purpura were received during the period:

- **B0705315A (France): Purpura, Pyrexia, Injection site erythema, Injection site oedema, Injection site induration, Rash macular.**

  This case was reported by a pharmacist and a physician and described the occurrence of fever in a 16-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Previous vaccinations with such type of vaccine were well tolerated. On 03 March 2011, the fourth dose of Infanrix hexa was administered intramuscularly in unknown thigh (probably the right). On 07 March 2011, the subject received a booster dose of Infanrix hexa (batch A21CA784A, route and injection site unknown). Twelve hours later, the subject experienced severe fever (40-41 degrees Celsius) during 24 hours, mild induration at injection site during 3 days and mild petechial purpura of extremities associated with erythematous macules (coded rash erythematous macular) which lasted 3 days. On 10 March 2011, platelets were at 217000/mm3. The subject was treated with paracetamol (Doliprane). The reporter considered that the events were clinically significant (or requiring intervention) and resolved. The reporter considered the events as almost certainly related to vaccination with Infanrix hexa.

- **B0743959A (Italy): Purpura.**

  This case was reported by a regulatory authority (IT-Agenzia Italiana del Farmaco # 146768) and described the occurrence of purpura in a 3-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevenar 13) for prophylaxis. On 18 May 2011, the subject received unspecified dose of Infanrix hexa (unknown administration route, unspecified injection site) and unspecified dose of Prevenar 13 (unknown administration route, unspecified injection site). On 18 May 2011, less than one day after vaccination with Infanrix hexa and Prevenar 13, the subject experienced purpura on face and extremities. At the time of reporting, the outcome of the event was unspecified. No more information was expected. Therefore, this case has been closed.

- **B0743733A (Argentina) Acute haemorrhagic oedema of infancy, Malaise, Tachycardia, Purpura, Pyrexia, Rash, Toxic skin eruption**

  See Section 6.5.2.11.1 Angioderma.

6.5.2.11.6. Subcutaneous nodule

Two (2) non-serious cases of Subcutaneous nodule were received during the period:

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- **B0740908A (Poland): Injection site reaction, Subcutaneous nodule.**

  This case was reported by a physician and described the occurrence of injection site reaction in a 4-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) for prophylaxis. No adverse event was reported after the two previous doses of Infanrix hexa. On 21 July 2011, the subject received 3rd dose of Infanrix hexa (intramuscular, unknown injection site). On 22 July 2011, 1 day after vaccination with Infanrix hexa, the subject experienced injection site reaction (3cm diameter). On 15 August 2011, injection site reaction resolved. 3 weeks after vaccination with Infanrix hexa, a subcutaneous hard nodule (5x10cm) was perceptible on injection site. At the time of reporting the outcome of the subcutaneous hard nodule was unspecified. The physician reported that the injection site reaction was almost certainly related to vaccination with Infanrix hexa.

- **B0745076A (France): Subcutaneous nodule, Injection site pruritus, Injection site eczema, Injection site induration, Injection site nodule.**

  This case was reported by a dermatologist and described the occurrence of subcutaneous nodule in a two-year-old subject of unspecified gender who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), combined diphtheria, tetanus, acellular pertussis and inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrixquinta) for prophylaxis. Medical history and concurrent medications were unspecified. On an unspecified date, the subject received 1st dose of Infanrix Hexa (unknown batch, route and injection site). One month later, on an unspecified date, the subject received 2nd dose of Infanrix Quinta (unknown batch, route and injection site). One month later, on an unspecified date in 2011, the subject received 3rd dose of Infanrix Hexa (unknown batch, route and injection site) (inappropriate age at vaccine administration). In 2011, three weeks after vaccination with Infanrix Hexa, the subject experienced pruritus and eczematiform aspect at injection site with subcutaneous nodules. At the time of reporting, the events subcutaneous nodule, injection site pruritus and injection site eczema were unresolved. Causality assessment was not provided. Upon follow-up received on 27 September 2011: First dose of Infanrix hexa was administered on 09 November 2010 intramuscularly in left thigh. On 02 August 2011, an ultrasound scan showed an aspect of an unspecified fibrous granuloma (coded injection site granuloma) on 10 cm with scratching lesions. At the time of reporting, events were improved and Infanrix hexa was not readministered. The dermatologist considered the events were almost certainly related to vaccination with Infanrix hexa.

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6.5.2.11.7. Urticaria, Urticaria papular and Urticaria thermal

Sixty seven (67) cases of Urticaria/Urticaria papular/Urticaria thermal were received during the period, out of which 18 were serious. Summary information for the complete set of reports is shown in Table 27 and Table 28. These tables also include one case received prior to the period of this report but never included in a previous PSUR (D0066224A). This case's ID is marked by a '*' in Table 28.

Table 27 Summary of information complete data set (n=68)

Patient age (n=65)	Range	months	2-33
	Median	months	7.5
Patient gender (n=63)	Male	n	34
	Female	n	29
Report type	Spontaneous	n	68
Time to onset of event	Range (hour)	hours	0-48
	Median days less than 1 day	n	47
Outcome (n=68)	Resolved	n	48
	Improved	n	5
	Unresolved	n	2
	Unknown	n	13
Concomitant vaccine	administered	n	5

Table 28 Cases of Urticaria, Urticaria papular and Urticaria thermal received during the period

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0682359A	20-Oct-10	Resolved	2 Months	Female	Infanrix hexa		0 Days	Urticaria	Italy	
B0682837A	29-Oct-10	Unknown	4 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		2 Days	Urticaria	Italy	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0684237A	09-Nov-10	Resolved	11 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		4 Days	Urticaria	Italy	
B0684873A	16-Nov-10	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Urticaria	Italy	
B0686074A	25-Nov-10	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Cyanosis, Urticaria	Italy	
B0687294A	02-Dec-10	Unknown	16 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Urticaria	France	
B0689830A	17-Dec-10	Resolved	20 Months		Infanrix hexa		0 Days	Injection site erythema, Body temperature increased, Urticaria	Poland	
B0690266A	20-Dec-10	Resolved	6 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Erythema, Urticaria, Pyrexia	Italy	
B0692086A	30-Dec-10	Improved	1 Years	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Urticaria, Pyrexia	Italy	
B0692144A	04-Jan-11	Resolved	2 Years	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Urticaria, Pyrexia	Italy	
B0692145A	04-Jan-11	Improved	11 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Erythema, Urticaria, Injection site pain	Italy	
B0692425A	06-Jan-11	Resolved	3 Months	Female	Infanrix hexa, EMLA		2 Days	Urticaria	France	
B0696210A	26-Jan-11	Resolved	11 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Eyelid oedema, Localised oedema, Urticaria	Italy	Pyrexia, Cough

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0696865A	28-Jan-11	Resolved	3 Months	Male	Infanrix hexa		0 Days	Urticaria	Italy	
B0697023A	26-Jan-11	Unknown	4 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Urticaria	Italy	
B0697049A	26-Jan-11	Unknown	3 Months	Male	Infanrix hexa, Synflorix		1 Weeks	Impetigo, Urticaria papular, Rash erythematous, Rash vesicular, Rash pruritic, Rash macular	Sweden	
B0699683A	11-Feb-11	Unknown	4 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Urticaria	Italy	
B0701038A	17-Feb-11	Resolved	14 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Rash papular, Urticaria, Injection site oedema	Italy	
B0701091A	18-Feb-11	Resolved	1 Years	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Rash maculo-papular, Urticaria, Injection site oedema, Injection site erythema	Italy	
B0703168A	23-Feb-11	Resolved	13 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Urticaria, Pyrexia	Italy	
B0705201A	08-Mar-11	Resolved	2 Months	Male	Infanrix hexa	Calcium salt	0 Days	Somnolence, Urticaria, Acne	Romania	
B0709029A	24-Mar-11	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Pyrexia, Urticaria	Netherlands	
B0709851A	25-Mar-11	Resolved	3 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Lansoprazole, Arnica flower, Fluoride salt	15 Minutes	Urticaria	Italy	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0709866A	25-Mar-11	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Chamomile	15 Minutes	Urticaria	Italy	
B0714105A	12-Apr-11	Resolved	3 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Urticaria, Decreased appetite	Italy	
B0714276A	13-Apr-11	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Minutes	Rash, Urticaria	Italy	Atopy
B0714303A	13-Apr-11	Unknown	1 Years	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Urticaria	Italy	
B0722859A	26-May-11	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Sodium Fluoride, Colecalciferol	0 Days	Urticaria	Italy	
B0723046A	24-May-11	Resolved	1 Years	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Urticaria, Pyrexia	Italy	
B0724189A	12-May-11	Resolved	5 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Urticaria, Pyrexia	Italy	
B0726175A	19-May-11	Resolved	20 Months	Unknown	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Injection site warmth, Injection site reaction, Urticaria, Pyrexia	Poland	
B0726356A	08-Jun-11	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Urticaria	Italy	
B0726435A	08-Jun-11	Improved	15 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Face oedema, Urticaria, Pyrexia	Italy	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0726556A	20-May-11	Resolved	2 Months	Male	Infanrix hexa, Rotavirus vaccine		1 Days	Urticaria, Rash	Poland	
B0729166A	20-Jun-11	Resolved	3 Months	Female	Infanrix hexa, Meningococcal polysaccharide vaccine group C (Non-GSK), Synflorix		3 Weeks	Pemphigoid, Leukocytosis, Thrombocytosis, Blister, Scab, Skin lesion, Pruritus, Eosinophilia, Urticaria	Spain	
B0729681A	29-Jun-11	Unknown	16 Months	Female	Infanrix hexa		4 Hours	Urticaria, Pyrexia, Diarrhoea	France	
B0729732A	13-Jun-11	Resolved	13 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Blister, Urticaria, Pyrexia	Italy	
B0730009A	30-Jun-11	Unknown	13 Months	Female	Infanrix hexa		0 Days	Angioedema, Urticaria	Italy	
B0731863A	08-Jul-11	Resolved	6 Months	Male	Infanrix hexa, Meningococcal polysaccharide vaccine group C (Non-GSK), Pneumococcal vaccines (Non-GSK)		1 Days	Urticaria, Tonsillitis	Ireland	
B0732862A	30-Jun-11	Resolved	2 Months	Female	Infanrix hexa, Rotavirus vaccine, Pneumococcal vaccines (Non-GSK)		3 Minutes	Skin warm, Urticaria papular, Erythema, Urticaria	Belgium	
B0733556A	13-Jul-11	Resolved	2 Months	Male	Infanrix hexa		0 Days	Urticaria	Italy	
B0735456A	21-Jul-11	Resolved	4 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	0 Days	Allergy to vaccine, Urticaria, Pyrexia, Rash maculo-papular	Italy	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0737088A	03-Aug-11	Resolved	2 Months	Male	Infanrix hexa, Infanrix-polio-HIB	Pneumococcal vaccines (Non-GSK), Bacillus Calmette-Guerin Vaccine (Non-GSK)	15 Minutes	Urticaria, Rash macular, Hypersensitivity	France	
B0739944A	11-Aug-11	Resolved	6 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Urticaria	Italy	
B0742850A	25-Aug-11	Resolved	2 Months	Unknown	Infanrix hexa, Infanrix-polio-HIB	Pneumococcal vaccines (Non-GSK)	1 Days	Urticaria	France	
B0743870A	01-Sep-11	Resolved	33 Months	Male	Infanrix hexa	Antihistamine	0 Days	Hypersensitivity, Pyrexia, Face oedema, Urticaria, Injection site inflammation	France	Penile oedema, Pyrexia, Bronchiolitis, Bronchitis
B0744411A	02-Sep-11	Resolved	2 Months	Female	Priorix, Infanrix hexa		5 Days	Oedema, Diarrhoea, Vomiting, Urticaria, Transaminases increased, Drug administered to patient of inappropriate age, Papule, Crying, Pain	France	
B0745839A	05-Sep-11	Improved	4 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Pyrexia, Urticaria	Italy	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0745845A	08-Sep-11	Resolved	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Urticaria, Dyspnoea	Italy	
B0747658A	15-Sep-11	Unknown	27 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Urticaria	Italy	
B0750855A	20-Sep-11	Resolved	1 Years	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Urticaria	Italy	
B0754395A	27-Sep-11	Improved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		2 Hours	Urticaria	Italy	
B0756170A	14-Oct-11	Resolved	19 Months	Unknown	Infanrix hexa		0 Days	Injection site reaction, Injection site warmth, Pyrexia, Urticaria	Poland	
B0757243A	21-Oct-11	Unknown	2 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Urticaria	France	
D0066224A *	26-Jan-10	Resolved	4 Months	Female	Infanrix hexa, Synflorix		3 Days	Urticaria	Germany	
D0069348A	05-Nov-10	Resolved	4 Months	Female	Infanrix hexa, Synflorix	Infanrix hexa, Synflorix	1 Days	Urticaria	Germany	
D0069379A	09-Nov-10	Resolved	9 Weeks	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK), Rotavirus vaccine (Non-GSK)		20 Hours	Urticaria, Swelling, Erythema, Feeling hot	Germany	
D0069457A	17-Nov-10	Resolved	27 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Urticaria	Germany	Multiple allergies

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0069610A	02-Dec-10	Unresolved	1 Years	Female	Infanrix hexa, Vaccine		0 Years	Urticaria, Granuloma, Injection site swelling, Injection site erythema, Injection site induration, Pyrexia	Germany	
D0070154A	01-Feb-11	Unknown		Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Unknown	Urticaria	Germany	
D0070854A	31-Mar-11	Resolved	3 Months	Male	Infanrix hexa		8 Hours	Urticaria	Germany	Familial risk factor, Dermatitis atopic
D0070920A	06-Apr-11	Resolved	3 Months	Male	Infanrix hexa, Synflorix		1 Days	Urticaria	Germany	
D0071119A	20-Apr-11	Unknown		Unknown	Infanrix hexa		4 Hours	Urticaria	Germany	
D0071406A	17-May-11	Resolved	6 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Ergocalciferol	1 Hours	Urticaria, Rash, Rash erythematous, Blister, Restlessness, Cough, Skin reaction	Germany	Patent ductus arteriosus, Pneumonia respiratory syncytial viral
D0071462A	20-May-11	Resolved	10 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		2 Days	Urticaria	Germany	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0072500A	25-Aug-11	Unknown	13 Weeks	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK), Sodium Fluoride	5 Minutes	Anaphylactoid reaction, Hypersensitivity, Product quality issue, Urticaria, Rash, Apathy, Anaphylactic reaction, Erythema, Petechiae, Injection site erythema	Germany	Hyperbilirubinaemia, Phototherapy, Rhinitis
D0072586A	02-Sep-11	Unresolved		Male	Infanrix hexa		34 Days	Urticaria thermal	Germany	
D0072847A	26-Sep-11	Resolved	2 Months	Male	Infanrix hexa, Rotavirus vaccine (Non-GSK)		0 Days	Erythema multiforme, Urticaria, Arthropod bite, Swelling, Erythema, Pyrexia, Hypertonia, Herpes simplex, Rash, General physical health deterioration	Germany	

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6.5.2.12. Vascular disorders

6.5.2.12.1. Circulatory collapse

Seven (7) cases of Circulatory collapse were receved during the period:

- **B0698663A (Italy): Anaphylactic reaction, Circulatory collapse, Slow response to stimuli, Cyanosis, Hypotonia, Hypothermia, Pallor, Bradycardia, Oxygen saturation decreased, Pyrexia.**

  See Section 6.5.2.6.2 Anaphylactic/Anaphylactoid reaction and Drug hypersensitivity.

- **B0713106A (Netherlands): Circulatory collapse, Cyanosis, Pallor**

  This case was reported by a regulatory authority (NL-College ter Beoordeling van Geneesmiddelen # NL-LRB-116677) and described the occurrence of circulatory collapse in a 12-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevenar) for prophylaxis. No concomitant medication was reported. The subject had no known past drug therapy and had no known medical history. On 4 November 2010 the subject received unspecified dose of Infanrix hexa (intramuscular, unknown site of injection, batch number not provided) and unspecified dose of Prevenar (intramuscular, unknown site of injection, batch number not provided). On 4 November 2010, 22 hours after vaccination with Infanrix hexa and Prevenar, the subject experienced circulatory collapse with blue lips and pallor. When the subject was taken out of the bed, he recovered rapidly. This case was assessed as medically serious by GSK. The regulatory authority reported that the events were probably related to vaccination with Infanrix hexa and Prevenar. Further details will be provided by the Reporting Authority whenever available.

  Company comment: Case of near SUDI in a 12-month-old male subject 22 hours after combined vaccination with Infanrix hexa and Prevenar. The event resolved after stimulation.

- **D0069341A (Germany):Circulatory collapse, Apnoea, Loss of consciousness, Pallor, Bradycardia, Salivary hypersecretion, Cyanosis, Epilepsy, Partial seizures, Foaming at mouth, Hypotonia, Cardiac arrest, Vomiting, Dyskinesia, Eye movement disorder, Productive cough, Depressed level of consciousness, Hypokinesia, Bronchitis**

  See Section 6.5.2.2.2 Cardiac arrest.

- **D0069460A (Germany): Circulatory collapse, Apathy, Pallor, Asthenia, Heart rate decreased, Screaming, Staring**

  This case was reported by a physician, via a sales representative, and described the occurrence of apathy in a 3-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated

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poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Co-suspect vaccination included pneumococcal vaccines (Prevenar 13, Pfizer). On 14 October 2010 the subject received 1st dose of Infanrix hexa (unknown route and injection site) and contralaterally Prevenar 13 (unknown route and injection site). Minutes after vaccination, after the child screamed shortly, he experienced fixed gaze, and was weak and very pale (grey face colour). The subject was breathing spontaneously. Oxygen was administered. The emergency physician admitted the subject to the hospital. The subject was observed for 24 hours with no new findings. After that the subject was feeling well. Concurrent medications included Ergocalciferol (Vigantoletten). There were no concurrent medical conditions or any other risk factors. The next vaccination with Infanrix hexa and Prevenar 13 took place in hospital with monitoring of circulation. The events did not recur. The physician considered the events were probably related to vaccination with Infanrix hexa. All events were resolved.

Company comment: Case of circulatory collapse in a 3-month-old male subject minutes after 1st vaccination with Infanrix hexa and Prevenar. The event resolved after oxygen therapy. No new event after monitored 2nd vaccination.

- **D0070901A (Germany):Circulatory collapse, Respiratory arrest, Cyanosis, Hypotonic-hyporesponsive episode, Screaming, Agitation, Hypotonia, Peripheral coldness, Ill-defined disorder, Fatigue, Pyrexia**

  See Section 6.5.2.10.3 Respiratory arrest.

- **D0071446A (Germany): Hypotonic-hyporesponsive episode, Circulatory collapse, Apathy, Pallor**

  This case was reported by a physician and described the occurrence of hypotonic-hyporesponsive episode in an 8-week-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) and pneumococcal vaccine (non-gsk, Prevenar) for prophylaxis. On 15 April 2011 the subject received the first dose of Infanrix hexa ((batch number A21CB071A, unknown thigh) together with the first dose of Prevenar (other thigh). Six hours after vaccination, the subject fell pale, collapsed and became apathic. The subject was hospitalised. The patient had completely recovered at the time of reporting Follow-up information was received on 27 May 2011 via another manufacturer (PFIZER-INC, DE-PFIZER-INC-2011108012). The following narrative was provided: "The reporting physician was informed by the patient's mother that after vaccination the patient has collapsed. This collapse was described as follows: When the patient's father arrived at home he noticed that the patient was "snow-white". When he then picked up his child the patient's head fell to the side. The patient was still awake but seemed to be apathic. The parents immediately went to a local hospital. However, in hospital no physical examination was performed but the clinician only stated to the parents: "No wonder after receiving the vaccines".

  Company comment: Case of possible circulatory collapse in an 8-week-old male subject 6 hours after 1st combined vaccination with Infanrix hexa and Prevenar. The event was resolved after stimulation. No further examinations were performed.

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- **D0072852A (Germany): Circulatory collapse, Sepsis, Shock, Crying, Pallor**

  Ses Section 6.5.1 Cases with a fatal outcome.

6.5.2.12.2. Kawasaki's disease

Three (3) cases of Kawasaki's disease were reported during the period:

- **B0691861A (Italy): Kawasaki's disease, Rash maculo-papular, Diarrhoea, Pyrexia, Cheilitis, Skin exfoliation, Oedema peripheral, Erythema**

  This case was reported by a regulatory authority (IT-Agenzia Italiana del Farmaco # 130459) and described the occurrence of Kawasaki's disease in a 2-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevnar) for prophylaxis. Concurrent medical conditions included G6PD deficiency, conjunctivitis and upper respiratory tract infection. On 11 November 2010 the subject received unspecified dose of Infanrix hexa (intramuscular, unknown), unspecified dose of Prevnar (intramuscular, unknown). On 13 November 2010, 2 days after vaccination with Infanrix hexa and Prevnar, the subject experienced maculo-papular exanthema on trunk, spreading to the whole body and face, diarrhea and high fever. On 14 November 2010, the baby was hospitalised due to these symptoms. After 4 days of hospitalisation, the baby presented cheilitis, perianal desquamation, pedal edema and erythema of soles of feet with persisting fever. Kawasaki disease was suspected. Relevant test results included ECG (normal), chest X-ray on 16 November 2010 and 21November 2010 (both negative), echocardiogram (mild pericardial effusion), ultrasound of the abdomen (mild fluids below liver and behind bladder as well as troponin (normal). The subject was treated with antibiotics, anti-inflammatory (Antiinflammatory), IgG (IV, 20 unt/kg) and dipyridamole (Dipiridamol). At the time of reporting the outcome of the events was unspecified. The regulatory authority reported that the events were possibly related to vaccination with Infanrix hexa and Prevnar.

  Company comment: Kawasaki's disease in a 2-month-old male subject 2 days after combined vaccination with Infanrix Hexa and Prevenar.

- **D0070921A (Germany): Kawasaki's disease, Pyelonephritis, Pyrexia, Infection, Somnolence, Fluid intake reduced, General physical health deterioration, Pallor, Ill-defined disorder, Rash, Conjunctivitis, Erythema, Enanthema, Chapped lips, Hypertrophy of tongue papillae**

  This case was reported by a physician via regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2011009954) and described the occurrence of Kawasaki syndrome in a 2-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. According to completed questionnaire, signed on 23 March 2011, on 28 February 2011 the subject received 1st dose of Infanrix hexa (intramuscular, left thigh). On 03 March 2011, 3 days after vaccination with Infanrix hexa, the subject

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experienced Kawasaki's syndrome for several days. Diagnose was based on clinical symptoms and exclusion of other causes for fever after puncture of cerebrospinal fluid and urinary bladder. By differential diagnosis, sepsis, meningitis and urinary tract infection have been excluded. The subject was hospitalised and the reporter reported that the events were life threatening. In March 2011, the event was resolved. According to provided hospital report from paediatric unit, signed on 17 March 2011, the subject was hospitalised from 02 to 11 March 2011. Kawasaki's syndrome and haemangioma were diagnosed. The subject's medical history included premature baby (after 34th weeks of pregnancy). She was a twin. Postpartal the subject developed streptococcal infection, which was treated. Concurrent medical conditions included congenital hemangioma at back and forehead. There were no concurrent medical conditions, no continuous medications and no known allergies. On 28 February 2011 the subject received 1st dose of Infanrix hexa. On 28 February 2011 in the evening, the subject experienced fever with a body temperature up to 39.3 degC. The subject was treated with paracetamol on 28 February or 01 March 2011 in the evening and on 01 March or 02 March 2011 in the morning. Since 28 February 2011, the subject was sleeping a lot (sleepiness) and drinking less (fluid intake reduced). Blood examination showed increased value of C-reavtive protein (75 mg/L). By examination of urine via test strip, leucocytes were shown. The subject was hospitalised due to unclear highly febrile infection and suspected pyelonephritis. On admission examination, the subject was in reduced general condition. Skin coloration was mildly pale (paleness of skin). There were no signs for meningism. Values of inflammation were shown to be distinctly increased. Initially, urinary tract infection was suspected due to unusual urine test of urine bag. Puncture of bladder showed very low increased leukocyte count (15/mcl). Puncture of liquor showed also normal values. The subject was treated with cefotaxime (Cefotaxim) and mezlocillin. On the following day, the subject developed increasing exanthema on whole trunk and in further course non-purulent conjunctivitis, erythema at palmar and and plantar as well as a distinct enanthema with chapped lip and hypertrophy of tongue papillae. During treatment with antibiotics, fever remained. Due to clinical signs and fever, Kawasaki's syndrome was suspected. The subject was treated with normal immunoglobulin (Immunoglobulin) two times (2 g/kg body weight). Treatment with antibiotics was discontinued. Symptoms improved, fever resolved. By echocardiography, no coronary aneurism could be detected. The subjected was treated with aspirin (ASS, 3-5 mg/kg body weight/d) for prophylaxis. During hospitalisation, small haemangioma at forehead and a bigger one at back were treated with cryosurgery (Cryotherapy). Symptoms resolved and subject was discharged in good general condition.

Company comment: Kawasaki's disease in a 2-month-old female subject 3 days after 1st dose of Infanrix hexa. No cardiovascular findings were reported. The subject was hospitalized and the event resolved after treatment with immunoglobulins.

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- **D0071621A (Germany): Kawasaki's disease, Meningitis, Leukocytosis, Pericarditis, Mitral valve incompetence, Pyrexia, Fluid intake reduced, General physical health deterioration, Rash maculo-papular, Fungal skin infection, Cheilitis, Chapped lips, Palmar erythema, Lymphadenopa.**

  This case was reported by a regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2011017683) and described the occurrence of atypical kawasaki disease in an nearly 12-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Co-suspect vaccination included pneumococcal vaccines (non-gsk) (Prevenar 13, Pfizer). Previous vaccination included 1st dose of Infanrix hexa and Prevenar 13 (each unknown route and application site) given on 16 August 2011, which was well tolerated. On 2 November 2010 the subject received 2nd dose of Infanrix hexa and 2nd dose of Prevenar 13 (each unknown route and application site). At an unspecified after 2nd vaccination with Infanrix hexa and Prevenar 13, the subject experienced fever with a body temperature up to 38.2 degC. On 6 May 2011 the subject received 3rd dose of Infanrix hexa and 3rd dose of Prevenar 13 (each unknown route and application site). On 9 May 2011, 3 days after 3rd vaccination with Infanrix hexa and Prevenar 13, the subject experienced atypical Kawasaki disease. The subject developed fever with body temperatures up to 40 degC. On 11 May 2011, the subject developed exanthema on abdomen and back. Exanthema of mycotic cause was suspected. The subject was treated symptomatically with antipyretic (Antipyretics). On 12 May 2011, the subject's fluid intake was reduced. His general condition was reduced. The subject was treated with cefpodoxime. Symptoms did not improve. On 13 May 2011 the subject was hospitalised. Atypical Kawasaki syndrome, secondary meningitis and pericarditis were diagnosed. He showed maculo-papular exanthema at trunk, arms, legs and face. His lips and palms were reddened. Cervical lymph nodes were enlarged. His body temperature was up to 40.3 degC. Initially, there were clearly increased parameters for an infection (signs of infection) as well as distinct exanthema. Culture of blood and liquor were uneventfully. Due to abnormal midstream urine, the subject was treated with cefuroxime sodium (Cefuroxim). Fever did not resolve. On 18 May 2011, the subject still suffered from fever. He showed chapped lips, palmar erythema, leukocytosis and mild cervical lymphadenopathy. Kawasaki's disease was suspected. The subject was treated with normal immunoglobulin (Immunoglobulin) and aspirin (Acetylsalicylacid). Fever resolved and general condition improved. On 20 May 2011, echocardiography showed pericarditis and mitral insufficiency. On 24 May 2011, the subject was discharged from hospital after 12 days. At the time of reporting atypical Kawasaki disease was unresolved. The reporter reported that the events were life threatening. No further information will be available.

  Company comment: Kawasaki's disease in 12-month-old male subject 3 days after 3th dose of Infanrix hexa and 2nd dose of Prevenar. The subject was hospitalizend and the event resolved after treatment with immunoglogulins and aspirin.

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6.6. Follow-Up Data

Relevant follow-up information received during the period on fatal cases subsequent to their inclusion in PSUR 14 (B0580597A) and PSUR 15 (B0605003A and B0608494A) is mentioned in ***bold italic*** below. This information was taken into account for the observed-to-expected analysis of sudden deaths as provided in Section 9.3.1.1. CIOMS forms are presented in APPENDIX 5B.

- **B0580597A (Netherlands) Sudden infant death syndrome, Depressed level of consciousness, Hypotonia, Pallor**

  This case was reported by a healthcare professional and described the occurrence of death not otherwise specified in a 2-month-old female who was vaccinated with a 1st dose of Infanrix hexa and Prevenar. The subject had no medical history and no concomitant medication. One day after vaccination the subject was found in bed nonresponsive, floppy and pale. The subject died on 17 June 2009, cause of death was not reported. The autopsy report already received has confirmed SUDI. **The regulatory authority considered the events were unlikely to be related to vaccination with Infanrix hexa and Prevenar.**

- **B0605003A (Italy): *Sudden death*, Cardiac arrest, Convulsion, Hypokinesia.**

  This case was reported by the Italian regulatory authority and described the occurrence of cardiac arrest in a 2-month-old female who was vaccinated with an unspecified dose of Infanrix hexa on 10 August 2009. Less than one day after vaccination, the subject experienced convulsions. The subject was hospitalised from 14 August until 19 August 2009. At the time of reporting, the event was resolved with sequelae. Last convulsion episode was on 18 October 2009. The baby showed a regular growth but a light motor retardation in respect of the age. Her weight was 7.10 kg. Diagnostic tests as karyotype, ultrasonography, computerized axial tomography and nuclear magnetic resonance were negative. She was treated with Luminalette. The subject died due to a cardiac arrest ~~at an unspecified time after vaccination~~ ***on 5 March 2010. After autoptic exam, the physician reported that the convulsions and cardiac arrest were unrelated to vaccination with Infanrix hexa. The autopsy report confirmed that the event was a suddenly death with no specified cause.***

  Company comment: Case of Sudden Unexpected Death in Infancy (SUDI). The subject had a history of convulsions since 2-months of age, which started less than one day after vaccination with Infanrix hexa.

- **B0608494A (Netherlands): Sudden infant death syndrome, Depressed level of consciousness, Mouth haemorrhage, Nasopharyngitis**

  This case was reported by a healthcare professional and described the occurrence of cot death in a 14-week-old male who was vaccinated with the 2nd dose of Infanrix hexa and Prevenar on 12 November 2009. The child was born at term and weighed 4120 g. The child had a history of viral infection before vaccination with the 1st dose of Infanrix hexa and Prevenar. In the beginning of November, 2 weeks before death, the subject had a common cold. The subject did not experience any adverse events

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after vaccination. Four days after vaccination with Infanrix hexa and Prevenar, the subject was brought to day care centre. He had no fever.He burped well after being fed and was put into bed at 9:25 lying on the abdomen (with permission of the mother) and he was being checked every 20 minutes. At 12:00, the subject was nonresponsive and had blood in his mouth. Reanimation was started immediately and the the child was admitted to hospital. The child died on 16 November 2009 from sudden infant death syndrome. An autopsy was performed and did not reveal any cause of death found in autopsy or on toxicological investigation. ***Tryptase: 4.2 mcg/l blood from heart (normal: lower than 11.5 mcg/l for adults). No indication for anaphylactic reaction. In addition, time period of 4 days considered too long to suspect an anaphylactic reaction. No indications for a relation with vaccinations.***

Company comment: The subject had viral infections as medical history. No cause of death found in autopsy or toxicological investigation. Anaphylactic reaction was excluded.

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7. STUDIES

In line with the Addendum to ICH E2C [2], only studies with findings that have potential impact on product safety information are included in Sections 7.1, 7.3 and 7.4.

7.1. Newly-Analysed Studies

No study assessing Infanrix hexa was completed during the period. No change to the RSI is warranted.

7.2. Targeted Safety Studies

This section provides an update on any planned, ongoing or completed targeted safety studies involving Infanrix hexa in the reporting period. Targeted safety studies are those specifically planned or conducted to examine an actual or hypothetical safety concern (Vol 9A, Section 6.3.8.b) in a product marketed anywhere in the world. This includes any GSK-sponsored, and when applicable, GSK-supported pharmacoepidemiology study or clinical trial conducted anywhere in the world with the aim of identifying or quantifying a safety hazard. Although all clinical trials collect safety information as a matter of routine, only those initiated to examine a specific safety concern are considered a targeted safety study.

No targeted safety study was planned, ongoing or completed for Infanrix hexa.

7.3. Other Safety Studies

The following ongoing studies are not targeted safety studies but are also considered of interest as they may provide useful new information on the safety profile of Infanrix hexa:

- **103506 (DTPA-HBV-IPV-118 PRI)** A phase IV, non-randomised, open-label, multi centre study with two parallel groups to assess the immunogenicity and safety of GlaxoSmithKline (GSK) Biologicals combined DTPa-HBV-IPV/Hib vaccine administered as a three-dose primary vaccination course at 2, 4 and 6 months of age in healthy infants in Canada.
- **113948 (DTPA-HBV-IPV-124 PRI)** A phase II, double-blind, randomized, multicentre study to evaluate the safety and immunogenicity of new formulations of GlaxoSmithKline BiologicalsDTPa-HBV-IPV/Hib vaccine when administered to healthy toddlers as a booster dose at 12 to 15 months of age.
- **114843 (DTPA-HBV-IPV-125 BST:124)** A phase II, double-blind, randomized, multicentre study to evaluate the safety and immunogenicity of new formulations of GlaxoSmithKline BiologicalsDTPa-HBV-IPV/Hib vaccine when administered to healthy toddlers as a booster dose at 12 to 15 months of age.

7.4. Published Safety Studies

A full review of the literature was conducted during the reporting period. Useful information was published during the period concerning:

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a. safety and reactogenicity of Infanrix-IPV+Hib and Infanrix hexa (Lim, 2011). Both vaccines were well tolerated and substitution of DTPa-IPV/Hib with Infanrix hexa at Month 5 reduced the number of injections required at this age by one.

b. immunogenicity and safety of co-administration of Infanrix hexa with an investigational tetravalent meningococcal serogroups A, C, W-135 and Y-tetanus toxoid conjugate vaccine (ACWW-TT; Knuf, 2011). Pre-specified criteria for non-inferiority of immunogenicity following co-administration versus separate ACWY-TT and Infanrix hexa administration were reached, and the safety profile of co-administration was similar to that of Infanrix hexa alone.

These studies did not highlight any safety issue.

8. OTHER INFORMATION

8.1. Efficacy Related Information

Sixty two (62) cases suggesting potential lack of efficacy were received during the period and included at least one of the following MedDRA Preferred Terms: Pertussis (n=41), Bordetella test positive (n=2), Meningitis haemophilus (n=4), Haemophilus infection (3), Hepatitis B antibody negative (n=3), Therapeutic response decreased (n=1), Meningitis (3), Vaccination failure (n=48). These preferred terms were suggestive of lack of efficacy of the Pertussis, Hib and/or the Hepatitis B component.

8.1.1. Pertussis component

Forty-three (43) cases including the event Pertussis (n=41) or Bordetella test positive (n=2) were identified during the reporting period. Out of 41 cases including the event Pertussis, 34 were reported with a MedDRA Preferred Terms vaccination failure. These cases are summarized in Table 29.

Out of the 43 cases, there were 23 female subjects and 15 male subjects; in 5 cases gender was unknown. The age of the subjects ranged from 5 months to adult. There were 39 cases reported as serious and 4 as non-serious. In 9 cases the outcome of the event was reported as improved, resolved in 8 cases, unknown and unresolved at the time of report in 4 cases. Time to onset ranged between 5 months and 5 years.

In 27 of these cases, subjects had Pertussis diagnosis confirmed by laboratory test and 16 were not laboratory confirmed. Two of the 27 laboratory-confirmed cases were asymptomatic, and the 25 symptomatic and laboratory confirmed case all received a comlete vaccination schedule.

During the previous 1 year period, GSK received 13 potential lack of efficacy cases. The observed increase in the number of potential Pertussis component-related lack of efficacy reports is concurrent to the increase in number of cases received specifically from Germany (38 during the current period compared to 12 during the previous period).

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Table 29 Summary of cases of potential pertussis compononent-related lack of efficacy received during the period

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0682709A	29-Oct-10	Unknown	9 Years	Female	Infanrix hexa		Unknown	Pertussis, Vaccination failure, Bordetella test negative	Australia	
B0687509A	03-Dec-10	Unknown	5 Years	Female	Infanrix hexa		Unknown	Pertussis, Vaccination failure	Austria	
B0735430A	26-Jul-11	Unknown	18 Months	Female	Infanrix hexa		Unknown	Pertussis, Sneezing, Post-tussive vomiting, Rhinorrhoea, Respiratory syncytial virus infection, Pyrexia, Cough, Vaccination failure	South Africa	
B0737601A	05-Aug-11	Unknown	18 Months	Female	Infanrix hexa		Unknown	Pertussis	South Africa	
B0745561A	07-Sep-11	Improved	9 Months	Female	Infanrix hexa		77 Days	Pertussis, Cyanosis, Cough, Pyrexia, Vaccination failure	Switzerland	
D0069221A	22-Oct-10	Resolved	2 Years	Male	Infanrix hexa		21 Months	Pertussis, Vaccination failure	Germany	
D0069222A	22-Oct-10	Resolved	11 Months	Male	Infanrix hexa	Fluticasone propionate	8 Days	Pertussis	Germany	Angiopathy, Tracheal stenosis, Surgery
D0069277A	29-Oct-10	Resolved	5 Years	Female	Infanrix hexa	Varicella virus vaccine	3 Years	Pertussis, Vaccination failure, Cough, Vomiting, Rhinitis, Decreased appetite, Weight decreased	Germany	Neurodermatitis, Food allergy, Seasonal allergy
D0069673A	08-Dec-10	Improved	1 Years	Male	Infanrix hexa		0 Years	Pertussis, Vaccination failure	Germany	
D0069696A	08-Dec-10	Improved	12 Years	Male	Infanrix hexa, Boostrix		Unknown	Pertussis, Vaccination failure	Germany	
D0069697A	08-Dec-10	Improved	7 Years	Male	Infanrix hexa, Boostrix		Unknown	Pertussis, Vaccination failure	Germany	
D0069698A	09-Dec-10	Improved	Adult	Female	Infanrix hexa		Unknown	Pertussis, Vaccination failure	Germany	

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D0069825A	23-Dec-10	Resolved	3 Years	Female	Infanrix hexa		23 Months	Pertussis, Vaccination failure	Germany	Exposure to communicable disease
D0070091A	25-Jan-11	Resolved	11 Months	Female	Infanrix hexa		5 Months	Pertussis, Vaccination failure	Germany	
D0070092A	25-Jan-11	Resolved	5 Years	Unknown	Infanrix hexa		4 Years	Pertussis, Vaccination failure	Germany	
D0070099A	27-Jan-11	Unknown	9 Years	Female	Boostrix, Infanrix hexa		19 Months	Pertussis, Vaccination failure	Germany	
D0070108A	27-Jan-11	Unknown	4 Years	Male	Infanrix hexa		3 Years	Pertussis, Vaccination failure	Germany	
D0070132A	27-Jan-11	Unknown	4 Years	Male	Infanrix hexa		3 Years	Pertussis, Vaccination failure	Germany	
D0070133A	27-Jan-11	Unknown	4 Years	Female	Infanrix hexa		3 Years	Bordetella test positive, Vaccination failure	Germany	
D0070137A	27-Jan-11	Unknown	5 Years	Female	Infanrix hexa		4 Years	Bordetella test positive, Vaccination failure	Germany	
D0070138A	27-Jan-11	Unknown	5 Years	Female	Infanrix hexa		4 Years	Pertussis, Vaccination failure, Inappropriate schedule of drug administration	Germany	
D0070264A	09-Feb-11	Unknown	Child	Unknown	Infanrix hexa		Unknown	Pertussis, Vaccination failure	Germany	
D0070268A	09-Feb-11	Unknown	Child	Unknown	Infanrix hexa		Unknown	Pertussis, Vaccination failure	Germany	
D0070831A	28-Mar-11	Unknown	Child	Unknown	Infanrix hexa		Unknown	Pertussis	Germany	Cardiac operation, Mechanical ventilation
D0071587A	30-May-11	Unresolved	9 Months	Female	Infanrix hexa	Pneumococcal vaccines (Non-GSK), Rotavirus vaccine (Non-GSK)	5 Months	Pertussis, Vaccination failure	Germany	Exposure to communicable disease
D0071749A	17-Jun-11	Resolved	5 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Pertussis	Germany	
D0071806A	22-Jun-11	Resolved	8 Years	Female	Infanrix hexa, Boostrix		20 Months	Pertussis, Vaccination failure	Germany	

D0071888A	30-Jun-11	Resolved	4 Years	Male	Infanrix hexa		3 Years	Pertussis, Vaccination failure, Cough, Infection	Germany	
D0071988A	08-Jul-11	Improved	2 Years	Female	Infanrix hexa		12 Months	Pertussis, Cough, Vaccination failure	Germany	
D0072007A	08-Jul-11	Unknown	6 Months	Female	Infanrix hexa		29 Days	Pertussis, Pyrexia, Cough, Rhinitis, Lymphadenopathy	Germany	
D0072008A	08-Jul-11	Improved	8 Years	Female	Infanrix hexa, Boostrix		2 Years	Pertussis, Cough, Vaccination failure	Germany	
D0072016A	12-Jul-11	Unknown	31 Months	Female	Infanrix hexa		17 Months	Pertussis, Vomiting, Rhinitis, Vaccination failure	Germany	
D0072212A	28-Jul-11	Improved	6 Years	Male	Infanrix hexa, DTPa-HepB-IPV-HIB (Non-GSK)		5 Years	Pertussis, Cough, Vaccination failure	Germany	Lactose intolerance
D0072273A	02-Aug-11	Unresolved	5 Months	Male	Infanrix hexa		12 Days	Pertussis, Choking, Cyanosis, Apnoea, Bronchopneumonia, Cough, Vomiting	Germany	
D0072725A	13-Sep-11	Improved	6 Months	Male	Infanrix hexa		35 Days	Pertussis, Cough, Vomiting, Vaccination failure	Germany	Gastroenteritis norovirus
D0072784A	19-Sep-11	Resolved	5 Years	Female	Infanrix hexa	DTPa-IPV (Non-GSK)	Unknown	Pertussis, Vaccination failure	Germany	
D0072839A	23-Sep-11	Unknown	Child	Male	Infanrix hexa		3 Years	Pertussis, Vaccination failure	Germany	
D0072909A	30-Sep-11	Unknown	4 Years	Unknown	Infanrix hexa		Unknown	Pertussis	Germany	
D0072947A	28-Sep-11	Unknown	3 Years	Male	Infanrix hexa		2 Years	Pertussis, Cough, Vaccination failure	Germany	
D0072968A	07-Oct-11	Unknown	5 Months	Male	Infanrix hexa		57 Days	Pertussis, Vaccination failure	Germany	
D0073001A	12-Oct-11	Unknown	6 Years	Male	Infanrix hexa		5 Years	Pertussis, Vaccination failure	Germany	
D0073013A	12-Oct-11	Unresolved	5 Years	Female	Infanrix hexa		4 Years	Pertussis, Vaccination failure	Germany	
D0073015A	12-Oct-11	Unresolved	27 Months	Female	Infanrix hexa, Pertussis vaccine		15 Months	Pertussis, Vaccination failure	Germany	

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8.1.2. *Haemophilus influenza* type b component

Seven (7) cases including the preffered terms Meningitis haemophilus (4) or Haemophilus infection (3) were received during the period. Four were reported from Australia. All were serious. The preferred term Vaccination failure was reported in all cases. These cases are summarized in Table 30.

Table 30 Summary of cases of potential Hib compononent-related lack of efficacy received during the period

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0685610A	19-Nov-10	Resolved	10 Months	Male	Infanrix hexa, Infanrix-polio-HIB		5 Months	Meningitis haemophilus, Vaccination failure	Andorra	
B0711853A	05-Apr-11	Resolved	11 Months	Male	Infanrix hexa		4 Months	Meningitis haemophilus, Bacteraemia, Vaccination failure	Australia	
B0711894A	05-Apr-11	Resolved	28 Months	Male	Infanrix hexa		16 Months	Haemophilus infection, Bacteraemia, Pharyngitis, Lethargy, Pyrexia, Dyspnoea, Vaccination failure	Australia	
B0727262A	17-Jun-11	Resolved	11 Months	Female	Infanrix hexa		4 Months	Meningitis haemophilus, Pyrexia, Headache, Lethargy, Decreased appetite, Vomiting, Vaccination failure	Australia	
B0727263A	17-Jun-11	Resolved	10 Months	Male	Infanrix hexa	Infanrix hexa	5 Months	Haemophilus infection, Irritability, Pyrexia, Abasia	Australia	
B0735156A	26-Jul-11	Resolved	3 Years	Female	Infanrix hexa		2 Years	Meningitis haemophilus, Vaccination failure	South Africa	
D0070187A	03-Feb-11	Unresolved	25 Months	Male	Infanrix hexa		7 Months	Tympanic membrane perforation, Haemophilus infection, Vaccination failure	Germany	

8.1.3. Hepatitis B

Three (3) non-serious cases of Hepatitis B antibody negative were reported over the period. These cases are summarized in Table 31.

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Table 31 Summary of cases of potential Hepatits B compononent-related lack of efficacy received during the period

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0728114A	22-Jun-11	Not Applicable	Child	Female	Infanrix hexa		Unknown	Hepatitis B antibody negative	France	
B0731677A	20-Jun-11	Not Applicable	4 Years	Male	Infanrix hexa		See text	Corynebacterium test negative, Clostridium test negative, Hepatitis B antibody negative	Austria	
D0072530A	29-Aug-11	Not Applicable		Unknown	Infanrix hexa		1 Year	Hepatitis B antibody negative	Germany	

8.1.4. Conclusion of cases of potential lack of efficacy

During the period of this PSUR, 62 cases were identified where the MedDRA Preferred Terms could potentially correspond to a lack of effect of the Hib, pertussis or hepatitis B component.

Table 32 shows the number of cases and respective reporting frequencies as reported during this PSUR and the previous PSUR periods.

Table 32 Reporting rate of potential lack of efficacy cases

	PSUR #15		PSUR#16	
	Number of cases	Reporting rate per 100 000 doses distributed	Number of cases	Reporting rate per 100 000 doses distributed
Pertussis	21	0.18	43	0.35
Hib	6	0.05	7	0.06
Hepatitis B	1	0.01	3	0.02

There has been no unusual level of reports of lack of efficacy regarding the Hib and Hepatits B components. The reporting rate for potential Pertussis componenent related lack of efficacy has increased by 94%.

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8.2. Late-breaking information

One new fatal case (B0762668A) was received after the data lock point as well as new follow-up data for one of the fatal cases described in Section 6.5.1 (D0072852A). The latest CIOMS forms for these cases are attached in APPENDIX 5C.

- **B0762668A (Belgium) Sepsis, Pyrexia, Diarrhoea**

  This case was reported by a pharmacist and by another health professional and described the occurrence of septicemia in a 3-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), live attenuated human rotavirus vaccine (Rotarix) and pneumococcal vaccines (non-gsk) (Prevenar) for prophylaxis. The subject was a premature baby. Concurrent medical conditions included cold. On 13 October 2011, the subject received 1st dose of Infanrix hexa (route and injection site unknown, batch number not provided), 1st dose of Rotarix (route unknown, batch number not provided) and 1st dose of Prevenar (route and injection site unknown, batch number not provided). On 21 October 2011, 8 days after vaccination with Infanrix hexa, Prevenar and Rotarix, the subject experienced fever and diarrhea. The subject was hospitalised. The subject died in the night 21 and 22 October 2011 from septicemia. It was unknown whether an autopsy was performed. The subject's twin sister had received the same vaccination without problem. Information inadvertently not recorded in the initial report: The event septicemia was added. Follow-up information received on 30 November 2011 and 2 December 2011 from 2 newspapers and from a consumer via a web forum: The mother's medical history included allergy and the family history included baby sudden death. The organisation who administered the vaccines was not aware that the subject had a cold. When the subject developed fever (39.9 deg.C) on 21 October 2011, the subject was treated by her parents with an antipyretic drug (suppository) and was taken to the hospital. At the hospital, gastroenteritis was firstly diagnosed, and after this diagnosis was changed to a pulmonary infection. The subject was treated with an antibiotic. But at 11 pm, her body was covered with purpura. The subject died at about 3 o'clock in the morning on 22 October 2011, 9 hours after she arrived at the hospital. Her body was covered with blue plaques. The diagnosis of purpura fulminans reported. The consumer also reported that rapid meningococcal meningitidis was mentioned, but no lumbar puncture and no hemoculture were performed therefore they could not conclude to this diagnosis. The subject's parents lodged a complaint against "X" because of the lack of information provided before the vaccination about the risks and the lack of precaution taken regarding the family history. The subject's twin sister of this case also experienced an adverse event after vaccination with same vaccines. Please see case B0767303A for details about the subject's twin sister.

  Company comment: Death of a 3-month-old female subject due to septicaemia 8 days after combined 1st vaccination with Infanrix hexa, Rotarix and Prevenar. The subject's twin sister had received the same vaccination without problem. It is unknown whether an autopsy was performed.

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- **D0072852A (Germany) Circulatory collapse, Sepsis, Shock, Crying, Pallor**

  Data received after the data lock point: An autopsy was performed on 23 September 2011. Death was identified as respiratory failure with protracted shock due to interstitial pneumonia, probably of viral origin. Pathogenic microorganisms were not detected. There was no reaction at the injection site. Follow-up received on 12 December 2011 included a complete hospital report. The subject was hospitalized on 21 September 2011 at 09:30. In hospital the subject was diagnosed with death after ventricular tachycardia with hyperkaliemia and acute circulatory shock of unclear genesis with anuria and hyperkaliemia. Childhood examination U4 (performed in 3rd to 4th month of life) showed anemia (hemoglobin 8.5 g/dl). The subject's mother had arterial hypertension and received bisoprolol. She formerly underwent surgery because of wrong lung vein ostium. After the subject had received the vaccinations, there was nothing abnormal during the day. In the night, around 01:00 o'clock the subject had been drinking about 200 ml. At 03:00 the subject started crying, which increased despite treatment with simethicone (Sab). He was vomiting twice. There was a transient improvement after receiving caraway suppository at 05:00. In the morning the subject became pale with strange breathing. When hospitalized, the subject was in bad condition, with circulatory depression, tachycardia with heart rate over 210 per min, pallor, muscle hypotonia, high irritability, moaning breathing. Green stool was excreted once. Supraventricular tachycardia could be excluded by electrocardiogram (ECG), which showed sinus tachycardia. Blood gas analysis showed acidosis with increased lactate and potassium. The subject received volume bolus via infusion on the head. After sudden worsening of condition with fall in oxygen saturation the subject received ketamine and diazepam. There was a short phase of bradycardia with the need for cardiac massage. The subject received further volume via intra-osseous access, as well as dobutamine, adrenaline (Adrenalin), claforan for suspected sepsis and hydrocortisone for circulatory support. Echocardiogram excluded dilated cardiomyopathy, but showed reduced pump function of heart. Sonogram of head excluded acute bleeding. Abdominal sonogram was normal. The subject's body temperature had decreased to 33.1 degC rectal and exogenous warmth treatment was started. Blood test results challenged the diagnosis of sepsis, without fever and with no relevant inflammatory signs. Ammonia was increased, which was considered a possible sign for metabolic disorder. The subject received central vein catheter in V. jugularis interna and arterial catheter in V. femoralis at the right, but no stabilization could be achieved. Katecholamines were increased. The subject still had no diuresis and was treated with frusemide (Lasix). In further course the subject developed increasing potassium values, T-wave elevation, ventricular tachycardia, anuria and no improvement of the situation. Further treatment was without success. At 16:20 further cardiac problems developed, but because of the bad situation no defibrillation was started. The subject died at 16:21 in the parent's presence. The hospital physician stated that after exclusion of cardiac, cerebral and abdominal causes, the event was most likely an atypical sepsis without fever and inflammatory signs. However, postmortal cultures of blood and cerebrospinal fluid also showed no germs. Despite of the autopsy results, the cause of death still kept unclear for the hospital physician. He stated that there were no radiologic signs for pneumonia and artificial respiration had been successful, with normalization of blood gas values. A metabolic disorder was considered possible, but

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it was more likely that lactic acidosis and hyperammonia were a secondary effect of shock.

Company comment: Death was identified in the autopsy as respiratory failure with protracted shock due to interstitial pneumonia, probably of viral origin. The cause of death in the autopsy and the hospital report were not congruent.

8.3. EU Risk Management Plan

There is no specific risk management plan in place for Infanrix hexa

8.4. Benefit Risk Analysis

During the PSUR reporting period, no separate risk-benefit analysis has been conducted.

9. OVERALL SAFETY EVALUATION

9.1. Signal Management

GSK employs a routine, pro-active process for identifying safety signals[2] with three main components:

1. Ongoing awareness and review of important individual cases, including all reports with a fatal outcome.
2. Systematic, regular and proactive review of aggregate safety data. This includes trend analysis to detect increased frequency of reporting and quantitative methodologies to detect signals.
3. Systematic, regular review of the literature.

A holistic approach is used so that all relevant data sources are interrogated when evaluating safety signals e.g. external sources, clinical studies, epidemiological studies, pre-clinical information.

All signals identified are evaluated; however, priority is given for serious events, particularly events reported with disproportionately high frequency, DMEs[3], and events that if found to be causally related to the vaccine could significantly affect the benefit-risk profile.

Following evaluation of the signal, appropriate action is agreed. The options include continuing routine proactive pharmacovigilance, defining further work to better understand the risk, or recommendation of a label change and/or amendment to the Risk Management Plan (RMP).

[2] A safety signal is defined as a report or reports of an event with an unknown causal relationship to vaccination that is recognised as worthy of further exploration and continued surveillance (CIOMS VI).

[3] Designated Medical Events: medically important events that are generally associated with drug toxicity.

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GSK is able to detect issues of potential concern promptly and, where appropriate, communicate them expeditiously to regulators outside the PSUR process. Actions taken on these issues are then reflected in the PSUR to ensure information is communicated appropriately to all regulatory authorities.

Table 33 presents the reporting frequency of the 10 most frequently reported events for Infanrix hexa arising from spontaneous reporting including regulatory and consumer reports. For this analysis both serious and non-serious events reported were taken into account, from launch (23 October 2000) up to the data lock point of this safety update report. Listed events (according to RSI version 10) are in bold.

Table 33 Overview of the 10 most frequently spontaneously reported events for Infanrix hexa.

Event SOC	Event PT	Number Of Events[1]	Reporting frequency per 100,000 doses distributed
General disorders and administration site conditions	**Pyrexia**	4207	5.77
Nervous system disorders	**Crying**	1300	1.78
General disorders and administration site conditions	**Injection site erythema**	1124	1.54
General disorders and administration site conditions	**Injection site swelling**	921	1.26
Nervous system disorders	**Hypotonia**	617	0.85
Vascular disorders	Pallor	558	0.77
Skin and subcutaneous tissue disorders	Erythema	546	0.75
General disorders and administration site conditions	**Injection site induration**	480	0.66
Skin and subcutaneous tissue disorders	**Urticaria**	471	0.65
Skin and subcutaneous tissue disorders	**Rash**	468	0.64

1. Including regulatory non-serious and consumer reports, but excluding clinical trial cases.

All these events were reported with a frequency between 0.64 to 5.77 per 100 000 doses distributed.

Since the last PSUR the top 10 events has not significantly changed in the reporting frequency except for 'Inappropriate schedule of drug administration', which is no longer part of the top 10 events. Conversely, Urticaria and Rash, which are already quoted in the GDS/RSI, appear with a relative reportive frequency of 0.65 per 100 000 doses distributed.

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9.2. Summary of Evaluations

No new safety signals were identified and/or evaluated during the reporting period.

9.3. Adverse events of interest

The cumulative count of an event since launch if provided in the following sections is based on the count of MedDRA PTs from cases originating from spontaneous reporting (including non-medically verified and regulatory non-serious cases).

9.3.1. Cases with a fatal outcome

During the period covered by this report 13 fatal cases were identified.

Ten cases suggestive of sudden deaths (sudden infant death syndrome: SIDS and sudden unexpected death in infancy: SUDI) were identified during the period covered by this PSUR. Cases remained poorly documented in the following suspected SUDI (B0706503A, B0727175A, and B0735723A) or without rationale explanation other than otitis media (D0071496A). SIDS was assessed in all other cases and autopsy confirmed the absence of causes (D0072663A, B0688734A, B0705290A, B0716780A, and D0070324A). A possible circulatory or septic shock was assessed for the last case but autopsy is still expected *(*D0072852A).

Death occurred in a context of Viral Meningitis (B0683335A); during multi organ failure contemporary of acute meningitis (possible pneumococcus) (B0700040A), death in a context of severe hypoxic-ischemic encephalopathy (B0712016A).

As shown in Table 34, 74 cases suggestive of sudden deaths have been received since launch, corresponding to a reporting frequency of 0.10 per 100 000 doses distributed (frequency of 0.08 per 100,000 doses distributed over the last one-year period).

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Table 34 Reporting rate of sudden death since launch per PSUR period

PSUR #	Period	Time period	Number of doses sold doses	Number of SD as reported in the different PSURs	reporting rate per 100,000 doses distributed
16	23oct10-22oct11	1Y	12301693	10	0.08
15	23oct09-22oct10	1Y	11981722	10	0.08
14	23oct08-22oct09	1Y	11496552	11	0.09
13	23oct07-22oct08	1Y	10067611	7	0.07
12	23oct06-22oct07	1Y	8621066	6	0.07
11	23oct05-22oct06	1Y	7166964	9	0.13
10	23apr05-22oct05	6M	2282686	2	0.09
9	23oct00-22apr05	4 1/2Y	9681894	18	0.19
8	23apr04-22oct04	6M	1386298	1	0.07
7	23oct03-22apr04	6M	1246906	5	0.40
6	23apr03-22oct03	6M	1247422	4	0.32
5	23oct02-22apr03	6M	1041975	1	0.10
4	23apr02-22oct02	6M	998814	0	0.00
3	23oct01-22apr02	6M	772137	1	0.13
2	23apr01-22oct01	6M	1050000	1	0.10
1	23oct00-22apr01	6M	430000	0	0.00

A cumulative review of Sudden Death since launch has been performed. Follow-up information was taken into account.

9.3.1.1. Cases of Sudden death

9.3.1.1.1. Introduction

In the assessment report (dated 3 March 2010) of PSUR 14, EMA request that "*The MAH should try to collect relevant and recent data of background incidence rates of sudden death in other European countries. An observed/expected analysis of sudden death should be performed in the next PSUR as well.*"

9.3.1.1.2. Methods

- **Literature search**

In order to collect relevant and recent data, a literature review of sudden infant death was performed for Europe. The search of the literature was made in PubMed and Embase using simultaneously the key words "sudden infant death" or "sudden death", "incidence rate" and "Europe"; only publications after 1990 were selected due to the effect of the "Back to Sleep" campaign performed in several European countries. Publications were limited to those published in French and English languages. The bibliographies of identified studies and reviews were searched to identify additional studies of interest. The German Federal Statistical Office was also consulted on line.

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- **Observed to Expected Analysis**

To estimate the expected numbers, the incidence rate of SID was considered homogenous within each age (i.e. over 1st or 2d year of life); therefore the expected number over any day was linearly extrapolated (i.e. 1/365) from the prevalence per birth cohort. The number of cases expected to occur within a predetermined risk period following vaccination (Ne) for children under 1 year of age and those between 1 and 2 years of age is derived from the following formula:

$$Ne = Inc \times Nbc \times RiskPeriod \times \alpha$$

where
Inc = the incidence of the disease in the first or second year of life
0.454 per 1,000 live births for < 1 year olds
0.062 per 1,000 live births for 1 < 2 year olds
Nbc = the number of doses of vaccine sold since launch (assumption: proportion of adverse events by age is representative for the actual age distribution at vaccination).
Risk Period = adjustement from a predetermined risk period (Days/365)
α = healthy vaccinee correction factor (taken here to be 0.8 based on various case-control studies of SIDS or SUID).

9.3.1.1.3. Results

Table 35 present the background incidence rate of Sudden Infant Death in Europe from the selected publications.

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Table 35 Incidence rate of Sudden Infant Death (<1 year of age) per 1,000 live births

Country/Population	Time period	Incidence Rate (/1 000 live birth)	Source
Data from the European Concerted Action on Sids. Case-control studies of SIDS done in 20 regions in Europe.	1992-1996	European range: 0.17 – 1.3 (median: 0.6)	Carpenter, 2004
Ireland. Data from National Sudden Infant Death Register.	1993-1997	0.80	Mehanni, 2000
Austria. Prospective study. Data from autopsy records in the Tyrol.	1994-1998	0.4	Kiechl-Kohlendorfer, 2001
Italy. Data from mortality registry of the 15 health districts in the Lombardy region.	1990-2000	0.13-0.54	Montomoli, 2004
Sweden. Data from the Medical Birth Registry of Sweden.	1999	0.30	Alm, 2001
Sweden. Literature review of Scandinavian studies.	2004	0.2-0.3	Wennergren, 2004
Sweden. Data from the Medical Birth Register of Sweden from 1997-2005.	2005	0.23	Mollborg, 2010
France. National statistics from CepiDc- Inserm	2005	0.32	Aouba, 2008
Germany. Data extracted from the Federal Health Monitoring of Germany (ICD code R95).	2005 2007	0.43 0.33	Nennstiel-Ratzel, 2010
Germany. Data from the German Federal Statistical Office (ICD code R95-R99).	2007 2008	0.44 0.45	German Federal Statistical Office, 2010

- **Observed/Expected Analysis of Sudden Deaths (SD)**

Given the attention that has been given to the occurrence of sudden deaths in children in the second year of life within 14 days of the administration of hexavalent vaccines, the Company evaluated whether the number of sudden deaths reported in this age group exceeded the number one could expect to occur by coincidence, i.e. from the natural background incidence of sudden deaths.

Since the distribution of the age at which subjects are vaccinated is unknown, the Company assumed that the proportion of adverse events by age is representative for the actual age distribution at vaccination. It can thus be estimated that 75% of all recipients of Infanrix hexa were in their first year of life, and 20% were in their second year of life (5% were not attributable because the age at vaccination was unknown). Therefore the number of doses (since launch) was estimated to be 54,7 and 14,6 millions respectively. Given that Germany is the main country where Infanrix hexa doses are distributed (close to 30% only in Germany), it was assumed that the incidence of sudden death observed in Germany is representative for the entire population of Infanrix hexa recipients (German Federal Bureau of Statistics, Statistisches Bundesamt; incidence rate in 1st year of life: 0.454/1,000 live births; second year: 0.062/1,000 live births, data 2008). These rates are in line with the other rates described above. A healthy vaccinee correction factor (taken here to be 0.8 based on various case-control studies of SIDS or SUID) was applied. The results of this analysis are present in Table 36 which shows the number of sudden deaths that could be expected to occur by chance within a range of days post vaccination.

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Table 36 Cumulative number of observed and expected cases of SD following Infanrix hexa in children in their first or second year of life

Time since vaccination (days)	Observed (1st year)	Expected	Observed (2d year)	Expected
0	16	54.4	2	1.98
1	29	108.8	5	3.96
2	42	163.2	6	5.94
3	50	217.6	6	7.92
4	57	272	6	9.9
5	60	326.4	7	11.88
6	60	380.8	7	13.86
7	62	435.2	7	15.84
8	63	489.6	7	17.82
9	65	544	7	19.8
10	65	598.4	7	21.78
11	65	652.8	7	23.76
12	65	707.2	7	25.74
13	65	761.6	8	27.72
14	65	816	8	29.7
15	66	870.4	8	31.68
16	67	924.8	8	33.66
17	67	979.2	8	35.64
18	67	1033.6	8	37.62
19	67	1088	8	39.6

This analysis shows that the number of sudden death cases reported after vaccination with Infanrix hexa is below the number of cases expected in children in their 1st year of life; it is equal or below the number of cases expected in children between in their 2d year of life.

The Company monitors these cases and their reporting frequencies on an ongoing basis.

9.3.1.1.4. Limitations

There are several limitations for Observed/Expected analyses, and several levels of uncertainty. The major factors affecting O/E analyses are related to:

- Underreporting, reporting biases, and incomplete case details.
- Uncertainty on the number of subjects actually vaccinated.
- No age stratification within the two age groups.

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9.3.2. Other adverse events of interest

9.3.2.1. Blood and lymphatic system disorders

9.3.2.1.1. Anaemia haemolytic autoimmune, Haemolytic anemia and Haemorrhagic diathesis

One (1) case of Anaemia haemolytic autoimmune, no (0) case of Haemolytic anaemia and two (2) cases of Haemorrhagic diathesis were reported during the period (see Section 6.5.2.1).

D0072751A described a 7-month-old male subject who experienced anemia haemolytic autoimmune within 28 days of Infanrix hexa vaccination. B0737478A described a 4-month-old male subject who experienced haemorrhagic diathesis 8 hours after second dose of Infanrix hexa and first dose of Prevenar. D0070397A described a 3-month-old male subject who experienced haemorrhagic diathesis in the context of an upper respiratory tract infection within 24 hours of receiving the first dose of Infanrix hexa, Prevenar and Rotarix.

These three cases represent a reporting frequency of **0.02** cases per 100 000 doses distributed during the period. Since launch, 10 spontaneous cases of Anaemia haemolytic autoimmune/Haemolytic anemia/Haemorrhagic diathesis were received, corresponding to a reporting frequency of **0.01** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal. The Company closely monitors cases of Anaemia haemolytic autoimmune and Haemolytic anemia.

9.3.2.1.2. Autoimmune thrombocytopenia, Idiopathic thrombocytopenic purpura, Thrombocytopenic purpura and Thrombocytopenia

No (0) case of Autoimmune thrombocytopenia, five (5) cases of Idiopathic thrombocytopenic purpura, four (4) cases of Thrombocytopenic purpura and nine (9) cases of Thrombocytopenia were reported during the period (see Section 6.5.2.1). Autoimmune thrombocytopenia was confirmed by positive antiplatelet antibodies in only one case (D0071125A).

These 15 cases represent a reporting frequency of **0.12** cases per 100 000 doses distributed during the period. Since launch, 78 spontaneous cases of Autoimmune thrombocytopenia/Idiopathic thrombocytopenic purpura/Thrombocytopenic purpura, Thrombocytopenia were received, corresponding to a reporting frequency of **0.11** per 100 000 doses distributed.

Thrombocytopenia is a listed event.

The information received with these cases does not provide evidence of a specific safety signal. The Company closely monitors Autoimmune thrombocytopenia, Idiopathic thrombocytopenic purpura, Thrombocytopenic purpura and Thrombocytopenia.

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9.3.2.1.3. Thrombocytosis

Two (2) cases of Thrombocytosis were reported during the period (see Section 6.5.2.1.8). Out of these, one was associated with a pemphigoid (B0729166A). It remains difficult to determine a causal relationship between vaccination and the bullous pemphigoid.

These 2 cases represent a reporting frequency of **0.02** cases per 100 000 doses distributed during the period. Since launch, 10 spontaneous cases of Thrombocytosis were received, corresponding to a reporting frequency of **0.01** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.2. Cardiac disorders

9.3.2.2.1. Bradycardia

Eleven (11) cases including the event Bradycardia were reported over the period (see Section 6.5.2.2.1).

These 11 cases represent a reporting frequency of **0.09** cases per 100 000 doses distributed during the period. Since launch, 44 spontaneous cases of Bradycardia were received, corresponding to a reporting frequency of **0.06** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.2.2. Cardiac arrest

Three (3) cases including the PT Cardiac arrest were reported during the period (see Section 6.5.2.2.2). Cases B0706503A and B0716780A are discussed in Section 9.3.1 Cases with a fatal outcome. Case D0069341A described a 3-month-old female who experienced an unspecified collapse less than 1 hour after Infanrix hexa vaccination. Possible epilepsy was suspected without conclusive investigations.

These 3 cases represent a reporting frequency of **0.02** cases per 100 000 doses distributed during the period. Since launch, 11 spontaneous cases of Cardiac arrest were received, corresponding to a reporting frequency of **0.02** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.2.3. Cardio-respiratory arrest

One (1) case including the PT Cardio-respiratory arrest was received during the period (B0705290A) and is discussed in Section 9.3.1 Cases with a fatal outcome.

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9.3.2.2.4. Cardiogenic shock

One (1) case including the PT Cardiogenic shock was reported during the period (see Section 6.5.2.2.4) and described a 3-month-old male who experienced cardiogenic shock 12 days after Infanrix hexa vaccination combined with Rotarix and Prevenar. Diagnosis of pre-existing focal atrial tachycardia and heart insufficiency recovered with anti-arritmica.

This case represents a reporting frequency of **0.01** cases per 100 000 doses distributed during the period. Itis the first spontaneous cases of Cardiogenic shock since launch.

The information received with this case does not provide evidence of a specific safety signal.

9.3.2.2.5. Cyanosis

Fifty eight (58) cases including the preferred term Cyanosis were identified during the period (see Section 6.5.2.2.5). Most were reported in association with a concurrent causal disease.

These 58 cases represent a reporting frequency of **0.47** cases per 100 000 doses distributed during the period. Since launch, 284 spontaneous cases of Cyanosis were received, corresponding to a reporting frequency of **0.39** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal. The Company closely monitors Cyanosis.

9.3.2.3. Eye disorders

9.3.2.3.1. Gaze palsy

Eighteen (18) cases including the event Gaze palsy were identified during the period. In two-third of cases the event was associated to a reported convulsion. The outcomes resolved spontaneously in half of the cases.

These 18 cases represent a reporting frequency of **0.18** cases per 100 000 doses distributed during the period. Since launch, 70 spontaneous cases of Gaze palsy were received, corresponding to a reporting frequency of **0.10** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.4. Gastrointestinal disorders

9.3.2.4.1. Diarrhoea haemorrhagic, Haematochezia, Intussusception, Rectal haemorrhage

Six (6) cases of Diarrhoea haemorrhagic/Haematochezia/Intussusception/Rectal haemorrhage were identified during the period (see Section 6.5.2.4).

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These 6 cases represent a reporting frequency of **0.05** cases per 100 000 doses distributed during the period. Since launch, 41 spontaneous cases of Diarrhoea haemorrhagic/ Haematochezia/Intussusception/Rectal haemorrhage were received, corresponding to a reporting frequency of **0.06** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal. The Company closely monitors cases of Haematochezia.

9.3.2.5. General disorders and administration site conditions

9.3.2.5.1. Abscess sterile, Injection site abscess sterile

Seven (7) cases of Abscess sterile/Injection site abscess sterile were received during the period (see Section 6.5.2.5.1).

These 7 cases represent a reporting frequency of **0.06** cases per 100 000 doses distributed during the period. Since launch, 38 spontaneous cases of Abscess sterile/Injection site abscess sterile were received, corresponding to a reporting frequency of **0.05** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.5.2. Extensive swelling of vaccinated limb

Twenty-eight (28) cases of Extensive swelling of vaccinated limb (see Section 6.5.2.5.2), out of which 5 were quoted as serious, were received during the period. The reported outcomes resolved in 80% of cases and improved in the others.

These 28 cases represent a reporting frequency of **0.23** cases per 100 000 doses distributed during the period. Since launch, 65 spontaneous cases of Extensive swelling of vaccinated limb were received, corresponding to a reporting frequency of **0.09** per 100 000 doses distributed.

Extensive swelling reactions and swelling of the entire vaccinated limb is included in the current Reference Safety Information of Infanrix hexa.The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.5.3. Gait disturbance

During the period, 19 cases of Gait disturbance were received (see Section 6.5.2.5.3). Out of these, 18 cases were associated with at least one other class event (pyrexia and/or nervous system). The outcome was resolved in 75% of the serious cases.

These 19 cases represent a reporting frequency of **0.15** cases per 100 000 doses distributed during the period. Since launch, 71 spontaneous cases of Gait disturbance were received, corresponding to a reporting frequency of **0.10** per 100 000 doses distributed.

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The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.5.4. Injection site urticaria

See Section 9.3.2.11.5 Urticaria, Urticaria popular and Urticaria thermal.

9.3.2.5.5. Nodule, Injection site nodule and Subcutaneous nodule

Twenty seven (27) cases of Nodule/Injection site nodule/Subcutaneous nodule were received during the period (see Sections 6.5.2.5.4, 6.5.2.5.6 and 6.5.2.11.6).

These 26 cases represent a reporting frequency of **0.21** cases per 100 000 doses distributed during the period. Since launch, 178 spontaneous cases of Nodule/Injection site nodule/Subcutaneous nodule were received, corresponding to a reporting frequency of **0.24** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal. The Company closely monitors Injection site nodule.

9.3.2.6. Immune system disorders

9.3.2.6.1. Anaphylactic shock, Anaphylactic reaction, Anaphylactoid reaction and Drug hypersensitivity

Seven (7) cases of Anaphylactic shock/Anaphylactic reaction/Anaphylactoid reaction/Drug hypersensitivity were received during the period (see Section 6.5.2.6).

The individual reports were reviewed following the case definition and diagnostic levels of certainty developed by The Brighton Collaboration Anaphylaxis Working Group. Three (3) cases of Anaphylactic shock were reported over the period. B0680987A and B0741646A were classified as Level 2 and 3 of diagnostic certainty, respectively. Case D0071107A was classified as Level 4 of diagnostic certainty.

Four (4) additional cases of anaphylactic reaction and hypersensitivity were reported over the period. B0698663A was classified as Level 2 and D0072050A as Level 5 of diagnostic certainty. In case D0072500A, the subject did not experience anaphylaxis (Level 5 of diagnostic certainty). The case was also received as pharmaceutical product complaint and it was concluded that there was no evidence for a specific safety signal for the used lot of Infanrix hexa. Case B0712429A was a generalised allergic reaction (exanthema) where a Salmonella sepsis could have played a trigger role in drug hypersensitivity (Level 5 of diagnostic certainty).

The 4 cases that were Level 2, 3 or 4 represent a reporting frequency of **0.03** cases per 100 000 doses distributed during the period. Since launch, 29 spontaneous cases of Anaphylactic shock/ Anaphylactic reaction/Anaphylactoid reaction/Drug hypersensitivity were received (regardless of Brighton certainty level), corresponding to a reporting frequency of **0.04** per 100 000 doses distributed.

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The information received with these cases does not provide evidence of a specific safety signal. The Company closely monitors allergic reactions (including Anaphylactic reaction and Anaphylactoid reaction).

9.3.2.7. Infections and infestations

9.3.2.7.1. Abscess, Abscess limb, Incision site abscess, Injection site abscess Injection site infection, Streptococcal abscess

During the reporting period, 25 cases were received including one of the following MedDRA Preferred Terms: Abscess (n=10), Abscess limb (n=1), Incision site abscess (n=2), Injection site abscess (n=12), Injection site infection (n=2), Streptococcal abscess (n=2) (see Section 6.5.2.7.1). There was no clustering of these cases by batch, supportive of a manufacturing issue.

These 25cases represent a reporting frequency of **0.20** cases per 100 000 doses distributed during the period. Since launch, 144 spontaneous cases of Abscess/Abscess limb/Incision site abscess/Injection site abscess/Injection site infection/Streptococcal abscess were received, corresponding to a reporting frequency of **0.20** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal. The Company closely monitors Abscess and Injection site abscess.

9.3.2.7.2. Cellulitis and Injection site cellulitis

Four (4) cases of Cellulitis/Injection site cellulitis were received during the period (see Sections 6.5.2.7.2 and 6.5.2.7.4).

These 4 cases represent a reporting frequency of **0.03** cases per 100 000 doses distributed during the period. Since launch, 39 spontaneous cases of Cellulitis/Injection site cellulitis were received, corresponding to a reporting frequency of **0.05** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.7.3. Encephalic infection

See Section 9.3.2.9.5 Encephalitis, Encephalopathy and Encephalic infection.

9.3.2.7.4. Meningitis aseptic, Meningitis pneumococcal, Meningitis viral

Four (4) cases of Meningitis aseptic/Meningitis pneumococcal/Meningitis viral were received during the period (see Sections 6.5.2.7.5, 6.5.2.7.6 and 6.5.2.7.7).

These 4 cases represent a reporting frequency of **0.03** cases per 100 000 doses distributed during the period. Since launch, 12 spontaneous cases of Meningitis aseptic/Meningitis pneumococcal/Meningitis viral were received, corresponding to a reporting frequency of **0.02** per 100 000 doses distributed.

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The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.7.5. Osteomyelitis

One (1) case (D0069814A) diagnosed with Osteomyelitis at tibia metaphysic left medial with periosteal abscess (bone abscess) and treated surgically was received during the period (see Section 6.5.2.7.8).

This case represents a reporting frequency of **0.01** cases per 100 000 doses distributed during the period. Since launch, 4 spontaneous cases of Osteomyelytis were received, corresponding to a reporting frequency of **0.01** per 100 000 doses distributed.

The information received with this case does not provide evidence of a specific safety signal.

9.3.2.7.6. Pneumococcal sepsis, Salmonella sepsis, Sepsis, Septic shock

Six (6) cases of Pneumococcal sepsis/Salmonella sepsis/Sepsis/Septic shock were received during the period (see Sections 6.5.2.7.9, 6.5.2.7.10, 6.5.2.7.11 and 6.5.2.7.12).

These 6 cases represent a reporting frequency of **0.05** cases per 100 000 doses distributed during the period. Since launch, 35 spontaneous cases of Pneumococcal sepsis/ Salmonella sepsis/Sepsis/Septic shock were received, corresponding to a reporting frequency of **0.05** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.8. Musculoskeletal and connective tissue disorders

9.3.2.8.1. Muscle spasms

Seventeen (17) cases of Muscle spasms were reported during the period (see Section 6.5.2.8.1). These were associated with other neurologic signs such as convulsion (n=8).

These 17 cases represent a reporting frequency of **0.14** cases per 100 000 doses distributed during the period. Since launch, 53 spontaneous cases of Muscle spasms were received, corresponding to a reporting frequency of **0.07** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.8.2. Soft tissue necrosis

One (1) case of Soft tissue necrosis was reported during the period (see Section 6.5.2.8.2).

This case represents a reporting frequency of **0.01** cases per 100 000 doses distributed during the period. This is the second Soft tissue necrosis case received since launch.

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The information received with this case does not provide evidence of a specific safety signal.

9.3.2.9. Nervous system disorders

9.3.2.9.1. Cerebral atrophy and Cerebral ischemia

Three (3) cases of Cerebral atrophy/Cerebral ischemia were reported during the period (see Section 6.5.2.9.1). Case B0716780A (Cerebral atrophy) is discussed in Section 9.3.1.1 Cases of Sudden death. Death occurred through multi organ failure.

These 3 cases represent a reporting frequency of **0.02** cases per 100 000 doses distributed during the period. Since launch, 11 spontaneous cases of Cerebral atrophy/Cerebral ischemia were received, corresponding to a reporting frequency of **0.02** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.9.2. Seizures and Epilepsy

During the period, 118 cases of Clonic convulsion/Clonus/Convulsion/Febrile convulsion/Grand mal convulsion/Myoclonus/Partial seizures/Seizure like phenomena/Tonic clonic movements/Tonic convulsion were received, as well as, 19 cases of Complex partial seizures/Epilepsy/Infantile spasms/Petit Mal Epilepsy/Status epilepticus (see Section 6.5.2.9.2).

These 118 and 19 cases represent a reporting frequency of **0.96** and **0.15** cases per 100 000 doses distributed during the period, respectively. Since launch, 761 spontaneous cases of Convulsions (any kind of convulsion) were received, corresponding to a reporting frequency of **1.04** per 100 000 doses distributed.

Convulsions (with or without fever) is included in the current Core Safety Information for Infanrix hexa.

The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.9.3. Demyelination and Demyelinating polyneuropathy

Two (2) cases of Demyelination/Demyelinating polyneuropathy were received during the period (see Section 6.5.2.9.3).

These 2 cases represent a reporting frequency of **0.02** cases per 100 000 doses distributed during the period. Since launch, 6 spontaneous cases of Demyelination/Demyelinating polyneuropathy were received, corresponding to a reporting frequency of **0.01** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

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9.3.2.9.4. Depressed level of consciousness and Loss of consciousness

Fifity four (54) cases of Depressed level of consciousness/Loss of consciousness were reported during the period (see Section 6.5.2.9.4).

These 54 cases represent a reporting frequency of **0.44** cases per 100 000 doses distributed during the period. Since launch, 280 spontaneous cases of Depressed level of consciousness/Loss of consciousness were received, corresponding to a reporting frequency of **0.38** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.9.5. Encephalitis, Encephalopathy and Encephalic infection

Five (5) cases of Encephalitis/Encephalopathy/Encephalic infection were received during the period (see Section 6.5.2.9.5). Postvaccinal cerebellitis was compatible with the time sequence (D0070015A). A causal relationship between Infanrix hexa and Prevenar was reported but the relationship remained dubious in two other cases (D0071549A, B0692285A). Case B0686208A lacked data on subject medical and results of investigation.

These 5 cases represent a reporting frequency of **0.04** cases per 100 000 doses distributed during the period. Since launch, 34 spontaneous cases of Encephalitis/Encephalopathy/ Encephalic infection were received, corresponding to a reporting frequency of **0.05** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal. The company closely monitors important neurological events (including Encephalitis and Encephalopathy).

9.3.2.9.6. Guillain-Barre syndrome

Two (2) cases of Guillain-Barré syndrome were reported over the period from Italy (1) and Germany (1) (see Section 6.5.2.9.6). The individual reports were reviewed following the case definition and diagnostic levels of certainty developed by The Brighton Collaboration Guillain-Barré Syndrome Working Group (Sejvar, 2011). The reports were classified to Level 4 of diagnostic certainty as the information provided was insufficient to meet the case definition of GBS according to Brighton Collaboration criteria.

These 2 cases represent a reporting frequency of **0.02** cases per 100 000 doses distributed during the period. Since launch, 5 spontaneous cases of Guillain-Barré syndrome were received, corresponding to a reporting frequency of **0.01** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

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9.3.2.9.7. Hemiparesis

One (1) case of Hemiparesis was received during the period (see Section 6.5.2.9.7) and is discussed in Section 9.3.2.9.11 Thalamus haemorrhage.

9.3.2.9.8. Lennox Gastaut syndrome

One (1) case of Lennox-Gastaut syndrome was received during the period (see Section 6.5.2.9.5 Encephalitis, Encephalopathy and Encephalic infection).

This case represents a reporting frequency of 0.01 cases per 100 000 doses distributed during the period. This is the first Lennox-Gastaut syndrome case received since launch.

The information received with this case does not provide evidence of a specific safety signal.

9.3.2.9.9. Somnolence

Over the period 59 cases of Somnolence were reported, out of which 19 were non-serious (see Section 6.5.2.9.10).

These 59 cases represent a reporting frequency of **0.48** cases per 100 000 doses distributed during the period. Since launch, 288 spontaneous cases of Somnolence were received, corresponding to a reporting frequency of **0.39** per 100 000 doses distributed.

Figure 1 shows the yearly reporting rate since launch. Note that the number of Somnolence cases displayed for 2011 differs from the one in this PSUR (i.e. 39 cases in Figure 1 and 59 cases in this PSUR) for the following reasons:

- The reporting rate in Figure 1 is plotted by calendar year and not by PSUR period
- Vaccination date was not provided for all somnolence cases.
- The date used to plot each case is the vaccination date, not the date at which the case was received by GSK Biologicals Clinical Safety and Pharmacovigilance department

The rationale for having chosen to plot the vaccination date instead of the reporting date is that many of these cases were reported with a delay of approximately 100 days after event onset, which contributed to the increase in the reporting rate observed during this period.

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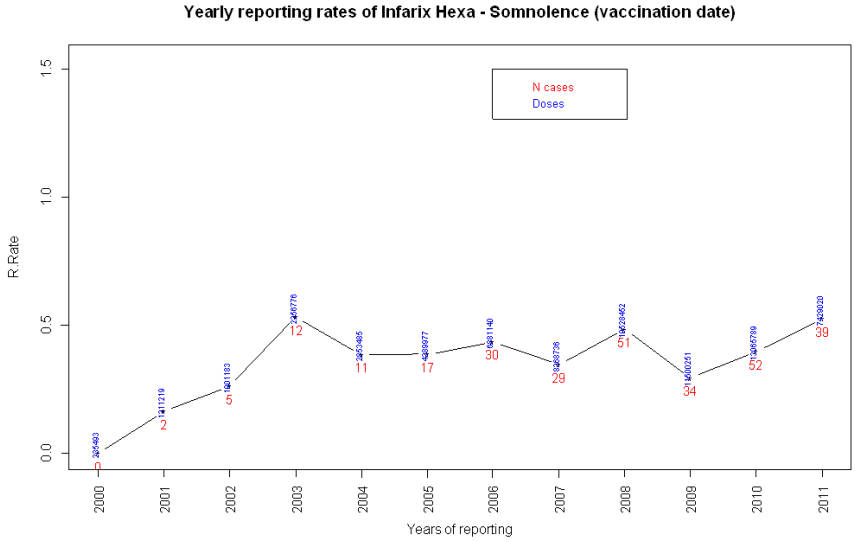
Figure 1 Reporting rate of Somnolence cases per 100 000 doses distributed and per calendar year



The information received with these cases, as well as the data in Figure 1, do not provide evidence of a specific safety signal.

9.3.2.9.10. Syncope and Presyncope

Fifteen (15) cases of Syncope/Presyncope were received during the period (see Section 6.5.2.9.11).

These 15 cases represent a reporting frequency of **0.12** cases per 100 000 doses distributed during the period. Since launch, 68 spontaneous cases of Syncope/Presyncope were received, corresponding to a reporting frequency of **0.09** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.9.11. Thalamus haemorrhage

One (1) case of Thalamus haemorrhage was received during the period (see Section 6.5.2.9.12).

This case represents a reporting frequency of 0.01 cases per 100 000 doses distributed during the period. This is the first Thalamus haemorrhage case received since launch.

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The information received with this case does not provide evidence of a specific safety signal.

9.3.2.9.12. VIth nerve paralysis and VIIth nerve paralysis

Three (3) cases of VIth nerve paralysis/VIIth nerve paralysis were received during the period (see Sections 6.5.2.9.13 and 6.5.2.9.14).

These 3 cases represent a reporting frequency of **0.12** cases per 100 000 doses distributed during the period. Since launch, 7 spontaneous cases of VIth nerve paralysis/VIIth nerve paralysis were received, corresponding to a reporting frequency of **0.01** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.10. Respiratory, thoracic and mediastinal disorders

9.3.2.10.1. Apparent life threatening event

Four (4) cases of Apparent life threatening event were received during the period (see Section 6.5.2.10.1).

These 4 cases represent a reporting frequency of **0.03** cases per 100 000 doses distributed during the period. Since launch, 33 spontaneous cases of Apparent life threatening event were received, corresponding to a reporting frequency of **0.05** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.10.2. Asphyxia

One (1) case of Asphyxia was reported during the period (see Section 6.5.2.10.2) and is discussed in Section 9.3.1 Cases with a fatal outcome.

9.3.2.10.3. Respiratory arrest

Seven (7) cases of Respiratory arrest were received during the period (see Section 6.5.2.10.3).

These 7 cases represent a reporting frequency of **0.06** cases per 100 000 doses distributed during the period. Since launch, 36 spontaneous cases of Respiratory arrest were received, corresponding to a reporting frequency of **0.05** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

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9.3.2.11. Skin and subcutaneous tissue disorders

9.3.2.11.1. Angioedema

Four (4) cases of Angioedema were reported over the period (see Section 6.5.2.11.1). All cases lacked data on the subject's medical history and other possible diagnosis to provide a precise overall assessment.

These 4 cases represent a reporting frequency of **0.03** cases per 100 000 doses distributed during the period. Since launch, 34 spontaneous cases of Angioedema were received, corresponding to a reporting frequency of **0.05** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.11.2. Erythema multiforme

Two (2) cases of Erythema multiforme were reported during the period (see Section 6.5.2.11.2).

These 2 cases represent a reporting frequency of **0.02** cases per 100 000 doses distributed during the period. Since launch, 15 spontaneous cases of Erythema multiforme were received, corresponding to a reporting frequency of **0.02** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.11.3. Henoch Schonlein Purpura and Purpura

Five (5) cases of Henoch-Schonlein purpura/Purpura were received during the period (see Sections 6.5.2.11.3 and 6.5.2.11.5).

These 5 cases represent a reporting frequency of **0.04** cases per 100 000 doses distributed during the period. Since launch, 38 spontaneous cases of Henoch-Schonlein purpura/ Purpura were received, corresponding to a reporting frequency of **0.05** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal. The Company closely monitors cases of Purpura and Henoch-Schonlein purpura.

9.3.2.11.4. Petechiae

Twenty nine (29) cases of Petechiae were reported during the period (see Section 6.5.2.11.4). In the majority of serious cases, haematologic disorders were associated: idiopathic / non-specified thrombocytic purpura or thrombocytopenia.

These 29 cases represent a reporting frequency of **0.24** cases per 100 000 doses distributed during the period. Since launch, 161 spontaneous cases of Petechiae were received, corresponding to a reporting frequency of **0.22** per 100 000 doses distributed.

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The information received with these cases does not provide evidence of a specific safety signal. The Company closely monitors cases of Petechiae.

9.3.2.11.5. Urticaria, Urticaria popular and Urticaria thermal

Sixty seven (67) cases of Urticaria/Urticaria papular/Urticaria thermal were received during the period (plus one received during a previous period but not included in a previous PSUR), out of which most resolved spontaneously (see Section 6.5.2.11.7).

These 68 cases represent a reporting frequency of **0.55** cases per 100 000 doses distributed during the period. Since launch, 432 spontaneous cases of Urticaria/Urticaria papular/Urticaria thermal were received, corresponding to a reporting frequency of **0.59** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.11.6. Subcutaneous nodule

Discussed in Section 9.3.2.5.5 Nodule, Injection site nodule and Subcutaneous nodule.

9.3.2.12. Vascular disorders

9.3.2.12.1. Circulatory collapse

Seven (7) cases of Circulatory collapse were receved during the period (see Section 6.5.2.12.1).

These 7 cases represent a reporting frequency of **0.06** cases per 100 000 doses distributed during the period. Since launch, 38 spontaneous cases of Circulatory collapse were received, corresponding to a reporting frequency of **0.05** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal.

9.3.2.12.2. Kawasaki's disease

Three (3) cases of Kawasaki's disease were reported during the period (see Section 6.5.2.12.2). In 2 out of these 3 cases, the reported information is compatible with the typical symptomatology of Kawasaki's disease and subjects were treated with immunoglobulins. One of the subjects developed pericarditis. The etiology of Kawasaki's disease remains unknown although in 2 of the cases the clinical history suggests an infectious disease.

These 3 cases represent a reporting frequency of **0.02** cases per 100 000 doses distributed during the period. Since launch, 21 spontaneous cases of Kawasaki's disease were received, corresponding to a reporting frequency of **0.03** per 100 000 doses distributed.

The information received with these cases does not provide evidence of a specific safety signal. The Company closely monitors cases of Kawasaki's disease.

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9.4. Areas of Regulatory Interest

Areas of regulatory interest (specifically Drug Interactions, Overdose and Medication Errors, Abuse Potential, Pregnancy and Lactation, Use in Children) routinely monitored throughout the product lifecycle and during the period of the PSUR are presented below. Note that non-medically verified reports and non-serious reports received from regulatory authorities are included in these analyses.

9.4.1. Drug interactions

No cases of potential drug interactions have been received during the period.

Most spontaneous cases reported during the period included coadministration(s) with other vaccines (mostly pneumococcal vaccines). Vaccination with pneumococcal vaccines is standard practice in the countries where most reports originated from (Germany and Italy).

No relevant findings were noticed as regarding the co-administration profile of the vaccine. No cluster of events suggestive of potential interaction was found.

No new important safety information regarding drug interactions has been identified in the time period.

9.4.2. Overdose and Medication Errors

There were 319 cases of potential overdose and/or reports of medication error have been received during the reporting period. Non-medically verified and regulatory non-serious cases are included in this analysis.

In addition to cases of overdoses, an inappropriate drug use event has been reported 249 times over the period. An overview per category of maladministration is presented in the below table. Note that a case can contain more than one PT related to maladministration.

In view of the varying ways in which reports of overdose and medication error are described and coded, there is often much overlap between these concepts.

9.4.2.1. Overdose

“Overdose” is defined as more than the recommended dose of vaccine administered at the same occasion (either two vaccine doses administered too soon one after each other or two vaccines with overlapping components accidentally co-administered.)

A total of 30 Overdose/Accidental overdose cases were received during the period. Out of these 30, adverse events were reported in 8 cases, including two serious. These cases are listed in Table 37.

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Table 37 Overdose cases reported with adverse events during the period

Case ID	Seriousness	Events PT Comma Sep
B0683346A	Not serious	Wrong drug administered, Overdose, Somnolence, Irritability
B0685920A	Not serious	Irritability, Overdose, Wrong technique in drug usage process
B0708048A	Not serious	Pyrexia, Overdose, Wrong drug administered
B0736206A	Not serious	Pyrexia, Decreased appetite, Wrong drug administered, Overdose
B0738500A	Serious	Injection site induration, Pyrexia, Wrong technique in drug usage process, Overdose
B0741664A	Not serious	Accidental overdose, Pyrexia
B0743545A	Serious	Injection site reaction, Wrong technique in drug usage process, Medication error, Overdose, Injection site induration, Pyrexia
D0070270A	Not serious	Pyrexia, Restlessness, Accidental overdose

The two serious Overdose cases are described below:

- **Case B0738500A (France): Injection site induration, Pyrexia, Wrong technique in drug usage process, Overdose.**

  This case described an inappropriate preparation of medication in a 4-month-old infant who was vaccinated with Infanrix hexa. In August 2011, the subject received a second dose of Infanrix hexa without the Hib component (inappropriate preparation of medication). A third dose of Infanrix hexa was administered immediately (overdose). At an unspecified time after vaccination, the subject presented with mild fever and induration at injection site on 2 cm of diameter.

- **Case B0743545A (France): Injection site reaction, Wrong technique in drug usage process, Medication error, Overdose, Injection site induration, Pyrexia**

  This case described the occurrence of local reaction at injection site in a 4-month-old female who was vaccinated with Infanrix hexa. On 09 August 2011 the subject received a first dose of Infanrix hexa. The vaccine used had not been properly reconstituted (wrong injection technique, medication error). As the physician thought he had only administered the solution for reconstitution of the vaccine, the physician administered on that same date an additional dose of reconstituted Infanrix hexa. The subject subsequently received two doses of diphtheria, tetanus-acellular pertussis, hepatitis B vaccine (overdose). Medication error was reported. One day after the vaccination, the subject experienced induration at injection site of 2 cm which lasted 8 days and mild febricula during 24 hours. At the time of reporting, the events were resolved without sequelae.

The information received with these cases does not provide evidence of a specific safety signal.

9.4.2.2. Medication Errors

In addition to Overdose and Accidental overdose cases, 301 cases involving medication errors were received during period. Out of these, 250 were reported with no adverse events and 51 with at least one adverse event. An overview per category of maladministration is presented in Table 38. Note that a case can contain more than one PT related to maladministration.

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Table 38 Overview of medication errors by category of maladministration

Event PT	Number Of Events
Wrong technique in drug usage process	88
Incorrect product storage	47
Wrong drug administered	30
Inappropriate schedule of drug administration	28
Drug administration error	23
Incorrect dose administered	23
Underdose	20
Incorrect route of drug administration	18
Incorrect storage of drug	18
Off label use	13
Expired drug administered	10
Drug administered to patient of inappropriate age	7
Drug prescribing error	1
Medication error	1
Accidental exposure	1

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Table 39 Cases of maladministration identified during the reporting period

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
A0901400A	23-Dec-10	Improved	67 Days	Female	Infanrix hexa	Tri-Vi-Sol, Ferrous sulfate	Hours	Apnoea, Bradycardia, Oxygen saturation decreased, Wrong technique in drug usage process	Canada	Anaemia neonatal, Bronchopulmonary dysplasia, Premature baby, Apnoea, Bradycardia, Oxygen saturation decreased
B0683007A	04-Nov-10	Unresolved	5 Months	Female	Infanrix hexa, Priorix	Pneumococcal vaccines (Non-GSK), Infanrix hexa	0 Months	Injection site nodule, Injection site pruritus, Hypertrichosis, Injection site discolouration, Injection site inflammation, Papule, Wrong drug administered	France	Gastrooesophageal reflux disease, Haemangioma, Varicella, Nasopharyngitis, Salmonellosis, Otitis media acute, Sarcoidosis
B0683346A	05-Nov-10	Unknown	4 Months	Male	Boostrix, Infanrix hexa	Oral fluid	24 Hours	Wrong drug administered, Overdose, Somnolence, Irritability	Australia	
B0684559A	15-Nov-10	Resolved	2 Months	Unknown	Infanrix hexa		Same day	Pyrexia, Incorrect product storage	France	
B0685920A	24-Nov-10	Resolved	4 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		See text	Irritability, Overdose, Wrong technique in drug usage process	France	
B0686436A	25-Nov-10	Not Applicable	20 Months	Female	Infanrix hexa		See text	Therapeutic response decreased, Incorrect product storage	France	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0686753A	01-Dec-10	Improved	11 Months	Female	Infanrix hexa		0 Days	Pyrexia, Wrong technique in drug usage process	Italy	
B0692240A	05-Jan-11	Unknown	3 Years	Male	Infanrix hexa, MMR vaccine, strain not specified		1 Years	No therapeutic response, Expired drug administered	Belgium	
B0692241A	05-Jan-11	Not Applicable	6 Years	Female	Infanrix hexa, MMR vaccine, strain not specified		3 Years	No therapeutic response, Expired drug administered	Belgium	
B0695084A	20-Jan-11	Resolved	2 Years	Female	Infanrix hexa, Priorix		0 Days	Thrombocytopenia, Anaemia, Haematoma, Pyrexia, Gingival bleeding, Fall, Epistaxis, Blood lactate dehydrogenase increased, Incorrect route of drug administration	France	
B0695165A	20-Jan-11	Not Applicable	2 Months	Female	Infanrix hexa, Hepatitis B vaccine		See text	No therapeutic response, Incorrect dose administered	France	Viral hepatitis carrier
B0695865A	25-Jan-11	Unknown	3 Months	Male	Infanrix hexa		0 Days	Pyrexia, Wrong technique in drug usage process	Italy	
B0697679A	01-Feb-11	Unknown		Female	Infanrix hexa		Unknown	Erythema, Injection site swelling, Wrong technique in drug usage process	Italy	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0697688A	01-Feb-11	Improved		Male	Infanrix hexa		Unknown	Rash morbilliform, Injection site erythema, Injection site oedema, Wrong technique in drug usage process	Italy	
B0701338A	21-Feb-11	Resolved	4 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		See text	Irritability, Sleep disorder, Pyrexia, Injection site induration, Nodule, Incorrect product storage	France	
B0702562A	25-Feb-11	Resolved	10 Weeks	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK), Rotavirus vaccine (Non-GSK)		18 Hours	Hypotonic-hyporesponsive episode, Somnolence, Pallor, Incorrect route of drug administration, Neurological examination abnormal	France	Anaemia
B0702721A	28-Feb-11	Resolved	7 Weeks	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Tonic convulsion, Apnoeic attack, Pyrexia, Hypertonia, Pallor, Hypotonia, Staring, Opisthotonus, Drug administration error	France	Breast feeding
B0703591A	03-Mar-11	Resolved	20 Months	Male	Infanrix-polio-HIB, Infanrix hexa	Infanrix hexa	2 Days	Extensive swelling of vaccinated limb, Injection site erythema, Injection site warmth, Injection site oedema, Pyrexia, Wrong drug administered	France	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0705706A	14-Mar-11	Resolved	18 Months	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		Same day	Arthralgia, Injection site oedema, Pain, Injected limb mobility decreased, Incorrect route of drug administration	France	Premature baby, Hernia, Exanthema subitum, Tonsillitis, Pharyngitis
B0705783A	14-Mar-11	Resolved	6 Months	Male	Infanrix hexa, Infanrix-polio-HIB, Priorix, Pneumococcal vaccines (Non-GSK), Seasonal influenza vaccine (Non-GSK)		6 Hours	Pyrexia, Diarrhoea, Nausea, Vomiting, Inappropriate schedule of drug administration	France	Glycogen storage disease type I, Gastrointestinal tube insertion, Hypoglycaemia
B0707392A	21-Mar-11	Unknown	2 Months	Female	Infanrix hexa	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	See text	Inappropriate schedule of drug administration, Decreased appetite, Weight decreased	France	
B0708048A	23-Mar-11	Resolved	4 Months	Male	Infanrix-polio-HIB, Infanrix hexa		Same day	Pyrexia, Overdose, Wrong drug administered	France	
B0711364A	06-Apr-11	Improved	2 Years	Female	Infanrix hexa		2 Days	Extensive swelling of vaccinated limb, Injection site warmth, Injection site inflammation, Injection site erythema, Incorrect route of drug administration	France	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0716297A	29-Apr-11	Resolved	2 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK), Rotavirus vaccine (Non-GSK)		1 Days	Hypotonia, Slow response to stimuli, Pallor, Incorrect route of drug administration	France	Haemoglobin decreased
B0718002A	06-May-11	Not Applicable	4 Months	Unknown	Infanrix hexa, Infanrix-polio-HIB		See text	Clostridium test negative, Underdose	France	
B0722680A	26-May-11	Resolved	2 Months	Female	Infanrix hexa		12 Hours	Pyrexia, Incorrect product storage	France	
B0727081A	17-Jun-11	Resolved	16 Months	Female	Infanrix hexa, Infanrix-polio-HIB	Infanrix-polio-HIB, DTPa-Polio-HIB (Non-GSK)	0 Months	Injection site swelling, Injection site erythema, Incorrect dose administered	France	
B0729547A	27-Jun-11	Resolved	26 Months	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		See text	Pyrexia, Expired drug administered	France	
B0733404A	14-Jul-11	Resolved	18 Months	Male	Infanrix hexa		During	Wrong technique in drug usage process, Oedema peripheral, Insomnia, Anxiety, Erythema	Poland	
B0733788A	15-Jul-11	Unknown	1 Years	Male	Infanrix hexa		During	Incorrect route of drug administration, Dyskinesia, Underdose, Injection site erythema, Injection site swelling, Injection site mass	Sweden	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0736206A	26-Jul-11	Unknown	2 Months	Male	Infanrix hexa, Infanrix-polio		Hours	Pyrexia, Decreased appetite, Wrong drug administered, Overdose	Netherlands	
B0738500A	09-Aug-11	Unknown	4 Months	Unknown	Infanrix hexa	Infanrix-polio-HIB	See text	Injection site induration, Pyrexia, Wrong technique in drug usage process, Overdose	France	
B0742113A	25-Aug-11	Resolved	6 Months	Unknown	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		During	Incorrect route of drug administration, Injection site haematoma, Injection site swelling, Injection site pain, Injection site erythema	Australia	
B0743545A	31-Aug-11	Resolved	4 Months	Female	Infanrix hexa		1 Days	Injection site reaction, Wrong technique in drug usage process, Medication error, Overdose, Injection site induration, Pyrexia	France	
B0744411A	02-Sep-11	Resolved	2 Months	Female	Priorix, Infanrix hexa		5 Days	Oedema, Diarrhoea, Vomiting, Urticaria, Transaminases increased, Drug administered to patient of inappropriate age, Papule, Crying, Pain	France	
B0745305A	06-Sep-11	Resolved	3 Months	Unknown	Infanrix hexa	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Unknown	Pyrexia, Erythema, Diarrhoea, Acne, Wrong drug administered	France	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
B0747196A	12-Sep-11	Unknown	70 Years	Male	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Candesartan cilexetil + hydrochlorothiazide, Clonidine hydrochloride, Torasemide, Tamsulosin hydrochloride, Pantoprazole, Simvastatin, Ticlopidine	1 Days	Asthenia, Pyrexia, Drug administered to patient of inappropriate age	Italy	Polycythaemia vera
B0747469A	14-Sep-11	Unknown	2 Months	Female	Infanrix hexa	Pneumococcal vaccines (Non-GSK)	Same day	Injection site erythema, Incorrect product storage, Incorrect route of drug administration	France	
B0747719A	14-Sep-11	Resolved	5 Months	Male	Infanrix hexa	Infanrix hexa, Pneumococcal vaccines (Non-GSK), Rotavirus vaccine (Non-GSK)	See text	Incorrect storage of drug, Pyrexia, Irritability, Diarrhoea, Abdominal pain	Belgium	
B0747819A	16-Sep-11	Resolved	7 Weeks	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Hypotonia, Hypersomnia, Feeding disorder neonatal, Drug administration error	France	Premature baby, Infection
B0753926A	03-Oct-11	Resolved	3 Months	Male	Infanrix hexa	Infanrix hexa	See text	Crying, Inappropriate schedule of drug administration	France	
D0069239A	27-Oct-10	Resolved	1 Years	Male	Infanrix hexa		During	Soft tissue necrosis, Debridement, Incorrect route of drug administration	Germany	

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Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0069721A	13-Dec-10	Unknown	18 Months	Female	Infanrix hexa	Infanrix hexa	0 Days	Tonsillitis, Pyrexia, Incorrect dose administered	Germany	
D0070074A	25-Jan-11	Unknown	15 Months	Male	Infanrix hexa		0 Days	Injection site irritation, Underdose	Germany	
D0070138A	27-Jan-11	Unknown	5 Years	Female	Infanrix hexa		5 Years	Pertussis, Vaccination failure, Inappropriate schedule of drug administration	Germany	
D0070791A	23-Mar-11	Resolved	12 Months	Female	Infanrix hexa, Priorix Tetra		During	Injection site erythema, Injection site swelling, Wrong technique in drug usage process	Germany	
D0070922A	07-Apr-11	Unknown	16 Months	Female	Priorix Tetra, Infanrix hexa		0 Days	Pyrexia, Ear infection, Bronchitis, Wrong technique in drug usage process, Incorrect route of drug administration	Germany	
D0070972A	11-Apr-11	Unknown	2 Months	Female	Infanrix hexa		0 Days	Muscle spasms, Underdose	Germany	
D0071405A	17-May-11	Resolved	3 Months	Female	Rotavirus vaccine, Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Minutes	Vomiting, Underdose	Germany	
D0071543A	26-May-11	Resolved	4 Years	Female	Infanrix hexa		0 Days	Injection site erythema, Injection site swelling, Incorrect route of drug administration, Off label use	Germany	

Case ID	Initial Date Received By Dept	Case Outcome	Age	Gender	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Events PT Comma Sep	Country Of Reporter	Medical Conditions PT Comma
D0072541A	30-Aug-11	Unknown	40 Years	Female	Infanrix hexa		0 Days	Injection site pain, Wrong drug administered	Germany	

No new important safety information regarding medication errors has been identified during the time period.

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9.4.3. Abuse or misuse

Not applicable to vaccines.

9.4.4. Pregnancy and Lactation

9.4.4.1. Pregnancy

All cases involving a pregnant patient are included. In addition, the search strategy includes a broad selection of MedDRA PTs suggesting exposure *in utero* or via breast feeding or indicative of birth defects (e.g. congenital or hereditary disorders). Thus the search retrieves cases where pregnancy outcome is abnormal, normal or unknown. Cases involving females over 60 years of age and adult males (where the case was not reported as a partner pregnancy) have been excluded. Note that this search does not include the entire SMQ for 'Adverse Pregnancy Outcome/Reproductive Toxicity (incl neonatal disorders)'; furthermore, it includes some terms that are not in the SMQ.

One (1) case possibly related to administration during pregnancy or lactation was received during the reporting period:

- **B0681410A (France): Maternal exposure during pregnancy, Off label use**

This prospective case of pregnancy was reported by a gynecologist and described a vaccine exposure during pregnancy in a female subject aged between 20 and 29 years old who was vaccinated with Infanrix hexa and meningococcal polysaccharide vaccine group C (Meningitec, non-GSK) during pregnancy (3 weeks of amenorrhea). The subject's medical history included a previous pregnancy with a delivery in July 2010. She had no concurrent pathology and took no concurrent long time treatment. Estimated date of delivery was June 2011. On 30 September 2011n the subject was lost to follow-up. No response to letters. Outcome of pregnancy was unknown.

Pregnancy outcomes for the current reporting period and cumulative totals are summarised in Table 40. Changes in the numbers of the cumulative outcomes since the previous safety update reflect not only the addition of new cases but also follow-up obtained on previously received cases.

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Table 40 Pregnancy Outcomes

Outcome	In Period (n)	Cumulative (n)
Live infant, no apparent congenital anomaly[1]	0	1
Live infant with congenital anomaly	0	0
Elective termination, no apparent congenital anomaly[1]	0	0
Elective termination with congenital anomaly	0	0
Spontaneous abortion, no apparent congenital anomaly[1]	0	0
Spontaneous abortion with congenital anomaly	0	0
Stillbirth, no apparent congenital anomaly[1]	0	0
Stillbirth with congenital anomaly	0	0
Ectopic pregnancy	0	0
Molar pregnancy	0	0
Pregnancy ongoing, lost to follow-up or unknown	1	1
Total	**1**	**2**

1. Pregnancy outcome categories stating 'no apparent congenital anomaly' include outcomes where it is unknown whether a congenital anomaly occurred.

No new important safety information regarding use in pregnancy has been identified during the time period.

9.4.4.2. Lactation

No cases have been received during the reporting period where Infanrix hexa was given to lactating mothers.

No new important safety information regarding administration during lactation has been identified during the time period.

9.4.5. Special Patient Groups

No new important safety information related to use in children, elderly or organ impaired patients has been identified during the period.

9.4.6. Effects of long-term treatment

Not applicable to vaccines.

9.4.7. Patient/Consumer and other non-healthcare professional reports.

The events of interest described in Section 6.5 within the PSUR review period include all cases (irrespective of source, seriousness and listedness). Non-healthcare professional reports are therefore discussed in Section 6.5 as well. Separate Line Listings and Summary Tabulations are provided as appendices for consumer reports as per guideline E2C(R1).

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10. CONCLUSION

From the review of data received during the reporting period and presented in this PSUR, it has been concluded that the safety profile of Infanrix hexa is adequately reflected in the RSI.

There have been no amendments to the Reference Safety Information (RSI) in the current reporting period and no further amendments to the RSI are considered necessary at this time.

The benefit/risk profile of Infanrix hexa continues to be favourable.

The Company will continue to monitor cases of anaemia haemolytic autoimmune, thrombocytopenia, thrombocytopenic purpura, autoimmune thrombocytopenia, idiopathic thrombocytopenic purpura, haemolytic anemia, cyanosis, injection site nodule, abcess and injection site abscess, Kawasaki's disease, important neurological events (including encephalitis and encephalopathy), Henoch-Schonlein purpura, petechiae, purpura, haematochezia, allergic reactions (including anaphylactic and anaphylactoid reactions), cases of lack of effectiveness as well as fatal cases.

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APPENDIX 1 : Marketing Authorisation Status

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Country	*	Tradename	Approval	Launch	Removal from Market	Launch comment
Albania	pc	INFANRIX HEXA	25-Mar-09			Planned to be launched
Argentina	c	INFANRIX HEXA	15-May-01			Launch could be assumed as having happened not less than 3 months after approval.
Aruba		INFANRIX HEXA	20-Feb-02			Not applicable
Australia	c	INFANRIX HEXA	26-Nov-01			Launch could be assumed as having happened not less than 3 months after approval.
Austria	c	INFANRIX HEXA	23-Oct-00	22/06/2006		Launched
Azerbaijan	c	INFANRIX HEXA	01-Dec-08			Launch could be assumed as having happened not less than 3 months after approval.
Bahrain	c	INFANRIX HEXA	01-Aug-05			Launch could be assumed as having happened not less than 3 months after approval.
Bangladesh	c	INFANRIX HEXA	09-Sep-08			Launch could be assumed as having happened not less than 3 months after approval.
Belgium	c	INFANRIX HEXA	23-Oct-00	11/10/2006		Launched
Bosnia		INFANRIX HEXA	09-Mar-11			Not applicable
Brazil	c	INFANRIX HEXA	02-Apr-01			Launch could be assumed as having happened not less than 3 months after approval.
Bulgaria		INFANRIX HEXA	23-Oct-00			Not applicable
Canada	c	INFANRIX HEXA	28-May-04	04/12/2008		Launched
Chile	c	INFANRIX HEXA	26-Mar-02			Launch could be assumed as having happened not less than 3 months after approval.
Colombia	c	INFANRIX HEXA	23-Feb-00			Launch could be assumed as having happened not less than 3 months after approval.
Costa Rica	c	INFANRIX HEXA	02-Oct-01			Launch could be assumed as having happened not less than 3 months after approval.
Croatia	c	INFANRIX HEXA	18-Nov-04			Launch could be assumed as having happened not less than 3 months after approval.
Curacao		INFANRIX HEXA	28-Sep-01			Not applicable
Cyprus	c	INFANRIX HEXA	23-Oct-00	31/10/2003		Launched
Czech Republic	c	INFANRIX HEXA	23-Oct-00	01/08/2006		Launched
Denmark		INFANRIX HEXA	23-Oct-00			Not applicable
Dominican Republic	c	INFANRIX HEXA	22-Oct-01			Launch could be assumed as having happened not less than 3 months after approval.
Ecuador	c	INFANRIX HEXA	07-Feb-03			Launch could be assumed as having happened not less than 3 months after approval.
El Salvador	c	INFANRIX HEXA	11-Feb-03			Launch could be assumed as having happened not less than 3 months after approval.
Estonia	c	INFANRIX HEXA	23-Oct-00	01/03/2004		Launched
Finland		INFANRIX HEXA	23-Oct-00			Not applicable
France	c	INFANRIX HEXA	23-Oct-00	16/08/2006		Launched
Georgia	c	INFANRIX HEXA	04-Mar-09			Launch could be assumed as having happened not less than 3 months after approval.
Germany	c	INFANRIX HEXA	23-Oct-00	21/10/2000		Launched
Greece	c	INFANRIX HEXA	23-Oct-00	01/09/2003		Launched
Guatemala	c	INFANRIX HEXA	09-Apr-02			Launch could be assumed as having happened not less than 3 months after approval.
Guyana		INFANRIX HEXA	11-May-10			Not applicable

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Haiti	c	INFANRIX HEXA	25-Jun-08			Launch could be assumed as having happened not less than 3 months after approval.
Honduras	c	INFANRIX HEXA	06-Jun-02			Launch could be assumed as having happened not less than 3 months after approval.
Hong Kong	c	INFANRIX HEXA	26-Nov-01			Launch could be assumed as having happened not less than 3 months after approval.
Hungary		INFANRIX HEXA	23-Oct-00			Not applicable
Iceland		INFANRIX HEXA	23-Oct-00			Not applicable
Ireland	c	INFANRIX HEXA	23-Oct-00			Launch could be assumed as having happened not less than 3 months after approval.
Israel		INFANRIX HEXA	01-Aug-05			Not applicable
Italy	c	INFANRIX HEXA	23-Oct-00	21/02/2001		Launched
Ivory Coast		INFANRIX HEXA	14-Jun-02			Not applicable
Jamaica	c	INFANRIX HEXA	19-Jul-01			Launch could be assumed as having happened not less than 3 months after approval.
Jordan	c	INFANRIX HEXA	30-Mar-05			Launch could be assumed as having happened not less than 3 months after approval.
Kazakhstan	c	INFANRIX HEXA	16-Jan-09			Launch could be assumed as having happened not less than 3 months after approval.
Kenya	c	INFANRIX HEXA	06-Dec-01			Launch could be assumed as having happened not less than 3 months after approval.
Latvia	pc	INFANRIX HEXA	23-Oct-00			Planned to be launched
Lebanon	c	INFANRIX HEXA	25-Mar-09			Launch could be assumed as having happened not less than 3 months after approval.
Lithuania		INFANRIX HEXA	23-Oct-00	30/03/2005	01/01/2007	Not applicable
Luxembourg		INFANRIX HEXA	23-Oct-00			Not applicable
Macedonia		INFANRIX HEXA	26-Apr-10			Not applicable
Madagascar	c	INFANRIX HEXA	11-Feb-08	01/03/2008		Launched
Malaysia	c	INFANRIX HEXA	06-Jan-06			Launch could be assumed as having happened not less than 3 months after approval.
Malta	c	INFANRIX HEXA	23-Oct-00	01/11/2001		Launched
Mauritius	c	INFANRIX HEXA	22-May-06			Launch could be assumed as having happened not less than 3 months after approval.
Mexico	c	INFANRIX HEXA	15-Dec-00			Launch could be assumed as having happened not less than 3 months after approval.
Moldova	c	INFANRIX HEXA	12-May-03			Launch could be assumed as having happened not less than 3 months after approval.
Morocco	c	INFANRIX HEXA	06-Oct-03			Launch could be assumed as having happened not less than 3 months after approval.
Myanmar	c	INFANRIX HEXA	26-May-10	07/09/2011		Launched
Namibia	c	INFANRIX HEXA	07-Apr-06			Launch could be assumed as having happened not less than 3 months after approval.
Netherlands	c	INFANRIX HEXA	23-Oct-00	30/01/2005		Launched
New Zealand	c	INFANRIX HEXA	24-Apr-01			Launch could be assumed as having happened not less than 3 months after approval.
Nicaragua	c	INFANRIX HEXA	02-Apr-02			Launch could be assumed as having happened not less than 3 months after approval.
Norway		INFANRIX HEXA	13-Aug-01			Not applicable
Pakistan	c	INFANRIX HEXA	22-Nov-02			Launch could be assumed as having happened not less than 3 months after approval.
Panama	c	INFANRIX HEXA	22-Apr-02			Launch could be assumed as having happened not less than 3 months after approval.
Peru	c	INFANRIX HEXA	06-May-03			Launch could be assumed as having happened not less than 3 months after approval.
Philippines	c	INFANRIX HEXA	03-Oct-02			Launch could be assumed as having happened not less than 3 months after approval.
Poland	c	INFANRIX HEXA	23-Oct-00	06/02/2004		Launched

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Portugal		INFANRIX HEXA	23-Oct-00			Not applicable
Qatar	pc	INFANRIX HEXA	07-Oct-10			Planned to be launched
Romania	c	INFANRIX HEXA	23-Oct-00	31/01/2007		Launched
Saudi Arabia	c	INFANRIX HEXA	03-Oct-05			Launch could be assumed as having happened not less than 3 months after approval.
Serbia	pc	INFANRIX HEXA®	20-Mar-09			Planned to be launched
Singapore	c	INFANRIX HEXA	07-May-03			Launch could be assumed as having happened not less than 3 months after approval.
Slovakia	c	INFANRIX HEXA	23-Oct-00	01/01/2008		Launched
Slovenia		INFANRIX HEXA	23-Oct-00			Not applicable
South Africa	c	INFANRIX HEXA	07-Apr-06			Launch could be assumed as having happened not less than 3 months after approval.
Spain	c	INFANRIX HEXA	23-Oct-00	01/06/2001		Launched
Sri Lanka	c	INFANRIX HEXA	04-Jul-05			Launch could be assumed as having happened not less than 3 months after approval.
Sweden	c	INFANRIX HEXA	23-Oct-00	01/12/2001		Launched
Switzerland	c	INFANRIX HEXA	02-Oct-00			Launch could be assumed as having happened not less than 3 months after approval.
Syria		INFANRIX HEXA	26-Nov-06			Not applicable
Taiwan	c	INFANRIX HEXA	14-Oct-04			Launch could be assumed as having happened not less than 3 months after approval.
Thailand	c	INFANRIX HEXA	13-Sep-02	10/01/2003		Launched
Trinidad and Tobago	c	INFANRIX HEXA	24-Sep-01			Launch could be assumed as having happened not less than 3 months after approval.
Tunisia		INFANRIX HEXA	20-Aug-05			Not applicable
UK		INFANRIX HEXA	23-Oct-00			Not applicable
Ukraine	c	INFANRIX HEXA	12-Nov-02			Launch could be assumed as having happened not less than 3 months after approval.
United Arab Emirates	c	INFANRIX HEXA	18-Sep-06			Launch could be assumed as having happened not less than 3 months after approval.
Venezuela	c	INFANRIX HEXA	11-Jul-02			Launch could be assumed as having happened not less than 3 months after approval.
Vietnam	c	INFANRIX HEXA	19-Sep-05			Launch could be assumed as having happened not less than 3 months after approval.
Yemen		INFANRIX HEXA	11-Aug-08			Not applicable

*c, commercialized; pc, planned commercialized; empty, not commercialized and not planned

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APPENDIX 2 : Global Data Sheet version 010 - 21 Oct 2010

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Active Name: Combined diphtheria, tetanus, pertussis (acellular), hepatitis B, poliomyelitis (inactivated) and *Haemophilus influenzae* type b vaccine
Version Number: 010
Version Date: 21 Oct 2010

GLOBAL DATASHEET

Combined diphtheria, tetanus, pertussis (acellular), hepatitis B, poliomyelitis (inactivated) and *Haemophilus influenzae* type b vaccine

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Active Name: Combined diphtheria, tetanus, pertussis (acellular), hepatitis B, poliomyelitis (inactivated) and *Haemophilus influenzae* type b vaccine
Version Number: 010
Version Date: 21 Oct 2010

GLOBAL PRESCRIBER INFORMATION

TITLE

Combined diphtheria-tetanus-acellular pertussis, hepatitis B, enhanced inactivated polio vaccine and *Haemophilus influenzae* type b vaccine.

SCOPE

Trade Name(s)

Infanrix hexa

Formulation and Strength

Powder and suspension for suspension for injection.

1 dose (0.5 ml) contains:

Diphtheria toxoid[1]	not less than 30 International units
Tetanus toxoid[1]	not less than 40 International units
Bordetella pertussis antigens	
Pertussis toxoid[1]	25 micrograms
Filamentous Haemagglutinin[1]	25 micrograms
Pertactin[1]	8 micrograms
Hepatitis B surface antigen[2,3]	10 micrograms
Poliovirus (inactivated)	
type 1 (Mahoney strain)[4]	40 D-antigen unit
type 2 (MEF-1 strain)[4]	8 D-antigen unit
type 3 (Saukett strain)[4]	32 D-antigen unit
Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate)[3]	10 micrograms
conjugated to tetanus toxoid as carrier protein	20 - 40 micrograms

[1]adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$) 0.5 milligrams Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisiae*) by recombinant DNA technology
[3]adsorbed on aluminium phosphate ($AlPO_4$) 0.32 milligrams Al^{3+}
[4]propagated in VERO cells

The DTPa-HBV-IPV component is presented as a turbid white suspension. Upon storage, a white deposit and clear supernatant can be observed.

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The Hib component is presented as a white powder.

Excipients

It is mandatory for country product information to include both the complete list of excipients for all locally marketed presentations, and any locally imposed excipient warning statements.

Lactose

Sodium chloride (NaCl)

Medium 199 (as stabilizer including amino acids, mineral salts and vitamins)

Water for injections

Residues

Potassium chloride

Disodium phosphate

Monopotassium phosphate

Polysorbate 20 and 80

Glycine

Formaldehyde

Neomycin sulphate

Polymyxin B sulphate

CLINICAL INFORMATION

Indications

Infanrix hexa is indicated for primary and booster vaccination of infants against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and *Haemophilus influenza* type b.

Dosage and Administration

Posology

- **Primary vaccination**

The primary vaccination schedule consists of three doses of 0.5 ml (e.g. 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months) or two doses (e.g. 3, 5 months). There should be an interval

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of at least 1 month between doses. The Expanded Program on Immunisation schedule (at 6, 10, 14 weeks of age) may only be used if a dose of hepatitis B vaccine has been given at birth.

Locally established immunoprophylactic measures against hepatitis B should be maintained. Where a dose of hepatitis B vaccine is given at birth, Infanrix hexa can be used as a replacement for supplementary doses of hepatitis B vaccine from the age of 6 weeks. If a second dose of hepatitis B vaccine is required before this age, monovalent hepatitis B vaccine should be used.

- **Booster vaccination**

After a vaccination with 2 doses (e.g. 3, 5 months) of Infanrix hexa a booster dose must be given at least 6 months after the last priming dose, preferably between 11 and 13 months of age.

After vaccination with 3 doses (e.g. 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months) of Infanrix hexa a booster dose may be given at least 6 months after the last priming dose and preferably before 18 months of age.

Booster doses should be given in accordance with the official recommendations.

Infanrix hexa can be considered for the booster if the composition is in accordance with the official recommendations.

Other combinations of antigens have been studied in clinical trials following primary vaccination with Infanrix hexa and may be used for a booster dose: diphtheria, tetanus, acellular pertussis (DTPa), diphtheria, tetanus, acellular pertussis, *Haemophilus influenzae* type b (DTPa+Hib), diphtheria, tetanus, acellular pertussis, inactivated poliomyelitis, *Haemophilus influenzae* type b (DTPa-IPV+Hib) and diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliomyelitis, *Haemophilus influenzae* type b (DTPa-HBV-IPV+Hib).

Method of administration

Infanrix hexa is for deep intramuscular injection.

Contraindications

Hypersensitivity to the active substances or to any of the excipients or residues (see *Formulation and Strength*, *Excipients* and *Residues*).

Hypersensitivity after previous administration of diphtheria, tetanus, pertussis, hepatitis B, polio or Hib vaccines.

Infanrix hexa is contraindicated if the child has experienced an encephalopathy of unknown aetiology, occurring within 7 days following previous vaccination with

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pertussis containing vaccine. In these circumstances pertussis vaccination should be discontinued and the vaccination course should be continued with diphtheria-tetanus, hepatitis B, inactivated polio and Hib vaccines.

Warnings and Precautions

As with other vaccines, administration of Infanrix hexa should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor infection is not a contra-indication.

Vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable events) and a clinical examination.

If any of the following events are known to have occurred in temporal relation to receipt of pertussis-containing vaccine, the decision to give further doses of pertussis-containing vaccines should be carefully considered:

- Temperature of ≥ 40.0°C within 48 hours, not due to another identifiable cause.
- Collapse or shock-like state (hypotonic-hyporesponsiveness episode) within 48 hours of vaccination.
- Persistent, inconsolable crying lasting ≥ 3 hours, occurring within 48 hours of vaccination.
- Convulsions with or without fever, occurring within 3 days of vaccination.

There may be circumstances, such as a high incidence of pertussis, when the potential benefits outweigh possible risks.

In children with progressive neurological disorders, including infantile spasms, uncontrolled epilepsy or progressive encephalopathy, it is better to defer pertussis (Pa or Pw) immunization until the condition is corrected or stable. However, the decision to give pertussis vaccine must be made on an individual basis after careful consideration of the risks and benefits.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

Infanrix hexa should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects.

Infanrix hexa should under no circumstances be administered intravascularly or intradermally.

Infanrix hexa contains traces of neomycin and polymyxin. The vaccine should be used with caution in patients with known hypersensitivity to one of these antibiotics.

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Infanrix hexa will not prevent disease caused by pathogens other than *Corynebacterium diphtheriae*, *Clostridium tetani*, *Bordetella pertussis*, hepatitis B virus, poliovirus or *Haemophilus influenzae* type b. However, it can be expected that hepatitis D will be prevented by immunisation as hepatitis D (caused by the delta agent) does not occur in the absence of hepatitis B infection.

A protective immune response may not be elicited in all vaccinees (see *Pharmacodynamic Effects*).

A history of febrile convulsions, a family history of convulsions or Sudden Infant Death Syndrome (SIDS) do not constitute contraindications for the use of Infanrix hexa. Vaccinees with a history of febrile convulsions should be closely followed up as such adverse events may occur within 2 to 3 days post vaccination.

Human Immunodeficiency Virus (HIV) infection is not considered as a contra-indication. The expected immunological response may not be obtained after vaccination of immunosuppressed patients.

Since the Hib capsular polysaccharide antigen is excreted in the urine a positive urine test can be observed within 1-2 weeks following vaccination. Other tests should be performed in order to confirm Hib infection during this period.

Limited data in 169 premature infants indicate that Infanrix hexa can be given to premature children. However, a lower immune response may be observed and the level of clinical protection remains unknown.

The potential risk of apnoea and the need for respiratory monitoring for 48-72h should be considered when administering the primary immunization series to very premature infants (born ≤ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.

Interactions

There are insufficient data with regard to the efficacy and safety of simultaneous administration of Infanrix hexa and Measles-Mumps-Rubella vaccine to allow any recommendation to be made.

Data on concomitant administration of Infanrix hexa with Prevenar (pneumococcal saccharide conjugated vaccine, adsorbed) have shown no clinically relevant interference in the antibody response to each of the individual antigens when given as a 3 dose primary vaccination.

However, high incidence of fever (> 39.5°C) was reported in infants receiving Infanrix hexa and Prevenar compared to infants receiving the hexavalent vaccine alone.

Antipyretic treatment should be initiated according to local treatment guidelines.

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As with other vaccines, it may be expected that in patients receiving immunosuppressive therapy, an adequate response may not be achieved.

Pregnancy and Lactation

Pregnancy

As Infanrix hexa is not intended for use in adults, information on the safety of the vaccine when used during pregnancy is not available.

Lactation

As Infanrix hexa is not intended for use in adults, information on the safety of the vaccine when used during lactation is not available.

Ability to perform tasks that require judgement, motor or cognitive skills

Not relevant.

Adverse Reactions

Clinical Trial Data

The safety profile presented below is based on data from more than 16,000 subjects.

As has been observed for DTPa and DTPa-containing combinations, an increase in local reactogenicity and fever was reported after booster vaccination with Infanrix hexa with respect to the primary course.

Adverse reactions reported are listed according to the following frequency:

Very common: ≥ 1/10
Common: ≥ 1/100 to < 1/10
Uncommon: ≥ 1/1000 to < 1/100
Rare: ≥ 1/10000 to < 1/1000
Very rare: < 1/10000

Infections and infestations

Uncommon: upper respiratory tract infection

Metabolism and nutrition disorders

Very common: appetite lost

Psychiatric disorders

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Very common: irritability, crying abnormal, restlessness
Common: nervousness

Nervous system disorders

Uncommon: somnolence
Very rare: convulsions (with or without fever)

Respiratory, thoracic and mediastinal disorders

Uncommon: cough*
Rare: bronchitis

Gastrointestinal disorders

Common: vomiting, diarrhoea

Skin and subcutaneous tissue disorders

Common: pruritus*
Rare: rash
Very rare: dermatitis, urticaria*

General disorders and administration site conditions

Very common: pain, redness, local swelling at the injection site (≤ 50 mm), fever ≥ 38°C, fatigue
Common: local swelling at the injection site (> 50 mm)**, fever >39.5°C, injection site reactions, including induration
Uncommon: diffuse swelling of the injected limb, sometimes involving the adjacent joint**

Post Marketing Data

Blood and lymphatic system disorders

Lymphadenopathy, thrombocytopenia

Immune system disorders

Allergic reactions (including anaphylactic and anaphylactoid reactions)

Nervous system disorders

Collapse or shock-like state (hypotonic-hyporesponsiveness episode)

Respiratory, thoracic and mediastinal disorders

Apnoea* *[see Warnings and Precautions for apnoea in very premature infants (≤ 28 weeks of gestation)]*

Skin and subcutaneous tissue disorders

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Angioneurotic oedema*

General disorders and administration site conditions

Extensive swelling reactions, swelling of the entire injected limb**, vesicles at the injection site

* observed with other GSK DTPa-containing vaccines

** Children primed with acellular pertussis vaccines are more likely to experience swelling reactions after booster administration in comparison with children primed with whole cell vaccines. These reactions resolve over an average of 4 days.

Experience with hepatitis B vaccine:

Meningitis, mimicking serum sickness, paralysis, encephalitis, encephalopathy, neuropathy, neuritis, hypotension, vasculitis, lichen planus, erythema multiforme, arthritis, muscular weakness have been reported during post-marketing surveillance following GlaxoSmithKline Biologicals' hepatitis B vaccine in infants < 2 years old. The causal relationship to the vaccine has not been established.

Overdosage

Insufficient data are available.

Clinical Pharmacology

Pharmacodynamics

ATC Code

Pharmaco-therapeutic group: Bacterial and viral vaccines combined, ATC code J07CA09

Pharmacodynamic Effects

Result obtained in the clinical studies for each of the components are summarised in the tables below:

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Active Name: Combined diphtheria, tetanus, pertussis (acellular), hepatitis B, poliomyelitis (inactivated) and *Haemophilus influenzae* type b vaccine
Version Number: 010
Version Date: 21 Oct 2010

Percentage of subjects with antibody titres ≥ assay cut-off one month after primary vaccination with Infanrix hexa

Antibody (cut-off)	**Two doses**	**Three doses**			
	3-5 months N= 530 (4 studies)	**2-3-4 months N= 196 (2 studies)**	**2-4-6 months N= 1693 (6 studies)**	**3-4-5 months N= 1055 (6 studies)**	**6-10-14 weeks N= 265 (1 study)**
	%	**%**	**%**	**%**	**%**
Anti-diphtheria (0.1 IU/ml) †	98.0	100.0	99.8	99.7	99.2
Anti-tetanus (0.1 IU/ml) †	100.0	100.0	100.0	100.0	99.6
Anti-PT (5 EL.U/ml)	99.5	100.0	100.0	99.8	99.6
Anti-FHA (5 EL.U/ml)	99.7	100.0	100.0	100.0	100.0
Anti-PRN (5 EL.U/ml)	99.0	100.0	100.0	99.7	98.9
Anti-HBs (10 mIU/ml) †	96.8	99.5	98.9	98.0	98.5*
Anti-Polio type 1 (1/8 dilution) †	99.4	100.0	99.9	99.7	99.6
Anti-Polio type 2 (1/8 dilution) †	96.3	97.8	99.3	98.9	95.7
Anti-Polio type 3 (1/8 dilution) †	98.8	100.0	99.7	99.7	99.6
Anti-PRP (0.15 μg/ml) †	91.7	96.4	96.6	96.8	97.4

N=number of subjects
* in a subgroup of infants not administered hepatitis B vaccine at birth, 77.7% of subjects had anti-HBs titres ≥ 10 mIU/ml
† cut-off accepted as indicative of protection

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Active Name: Combined diphtheria, tetanus, pertussis (acellular), hepatitis B, poliomyelitis (inactivated) and *Haemophilus influenzae* type b vaccine
Version Number: 010
Version Date: 21 Oct 2010

Percentage of subjects with antibody titres ≥ assay cut-off one month after booster vaccination with Infanrix hexa

Antibody (cut-off)	**Booster vaccination at 11 months of age following a 3-5 month primary course N=532 (3 studies)**	**Booster vaccination during the second year of life following a three dose primary course N= 2009 (12 studies)**
	%	**%**
Anti-diphtheria (0.1 IU/ml) †	100.0	99.9
Anti-tetanus (0.1 IU/ml) †	100.0	99.9
Anti-PT (5 EL.U/ml)	100.0	99.9
Anti-FHA (5 EL.U/ml)	100.0	99.9
Anti-PRN (5 EL.U/ml)	99.2	99.5
Anti-HBs (10 mIU/ml) †	98.9	98.4
Anti-Polio type 1 (1/8 dilution) †	99.8	99.9
Anti-Polio type 2 (1/8 dilution) †	99.4	99.9
Anti-Polio type 3 (1/8 dilution) †	99.2	99.9
Anti-PRP (0.15 μg/ml) †	99.6	99.7

N= Number of subjects
† cut-off accepted as indicative of protection

As the immune response to pertussis antigens following Infanrix hexa administration is equivalent to that of Infanrix, the protective efficacy of the two vaccines is expected to be equivalent.

The protective efficacy of the pertussis component of Infanrix against WHO-defined typical pertussis (≥ 21 days of paroxysmal cough) was demonstrated in:

- a prospective blinded household contact study performed in Germany (3, 4, 5 months schedule). Based on data collected from secondary contacts in households where there was an index case with typical pertussis, the protective efficacy of the vaccine was 88.7%.

- a NIH sponsored efficacy study performed in Italy (2, 4, 6 months schedule). The vaccine efficacy was found to be 84%. In a follow-up of the same cohort, the efficacy

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was confirmed up to 60 months after completion of primary vaccination without administration of a booster dose of pertussis.

Results of long term follow-up in Sweden demonstrate that acellular pertussis vaccines are highly efficacious in infants when administered according to the 3 and 5 months primary vaccination schedule, with a booster dose administered at approximately 12 months. However, data indicate that protection against pertussis may be waning at 7-8 years of age. This suggests that a second booster dose of pertussis vaccine is warranted in children aged 5-7 years who have previously been vaccinated following this schedule.

Protective immunity against hepatitis B has been shown to persist for at least 3.5 years in more than 90% of children administered four doses of Infanrix hexa. Antibody levels were not different from what was observed in a parallel cohort administered monovalent hepatitis B vaccine.

The effectiveness of the Hib component of Infanrix hexa was investigated via an extensive post-marketing surveillance study conducted in Germany. Over a seven year follow-up period, the effectiveness of the Hib components of two hexavalent vaccines, of which one was Infanrix hexa, was 89.6% for a full primary series and 100% for a full primary series plus booster dose (irrespective of the Hib vaccine used for priming).

Pharmacokinetics

Evaluation of pharmacokinetic properties is not required for vaccines.

Clinical Studies

See *Pharmacodynamic Effects*.

NON-CLINICAL INFORMATION

Preclinical data reveal no special hazard for humans based on conventional studies of safety, specific toxicity, repeated dose toxicity and compatibility of ingredients.

PHARMACEUTICAL INFORMATION

Shelf-Life

The expiry date of the vaccine is indicated on the label and packaging. The expiry date refers to the last day of the month mentioned.

The shelf-life is 3 years.

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Storage

Infanrix hexa should be stored at +2°C to +8°C. Protect from light.

During transport, recommended conditions of storage must be respected.

The DTPa-HBV-IPV suspension and the reconstituted vaccine must not be frozen. Discard if it has been frozen.

Nature and Contents of Container

The DTPa-HBV-IPV component is presented in a pre-filled syringe or vial.

The Hib component is presented as a white pellet in a glass vial.

The vials and pre-filled syringes are made of neutral glass type I, which conforms to European Pharmacopoeia Requirements.

Vial and pre-filled syringe presentations (with or without needles) are available in packs of 1, 10, 20 and 50.
Vial and vial presentation is available in pack sizes of 1 and 50.

Incompatibilities

Infanrix hexa should not be mixed with other vaccines in the same syringe.

Use and Handling

1. Wording for vial and pre-filled syringe presentation

The DTPa-HBV-IPV suspension should be well shaken in order to obtain a homogeneous turbid white suspension. The DTPa-HBV-IPV suspension and the Hib powder should be inspected visually for any foreign particulate matter and/or variation of physical aspect. In the event of either being observed, discard the vaccine.

Infanrix hexa must be reconstituted by adding the entire content of the pre-filled syringe to the vial containing the Hib powder.

It is good clinical practice to only inject a vaccine when it has reached room temperature. In addition, a vial at room temperature ensures sufficient elasticity of the rubber closure to minimise any coring of rubber particles. To achieve this, the vial should be kept at room temperature (25 ± 3 °C) for at least five minutes before connecting the pre-filled syringe and reconstituting the vaccine.

The reconstituted vaccine presents as a slightly more cloudy suspension than the liquid component alone. This is normal and does not impair the performance of the vaccine. In the event of other variation being observed, discard the vaccine.

After reconstitution, the vaccine should be injected immediately. However the vaccine may be kept for up to 8 hours at room temperature (21°C).

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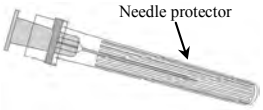
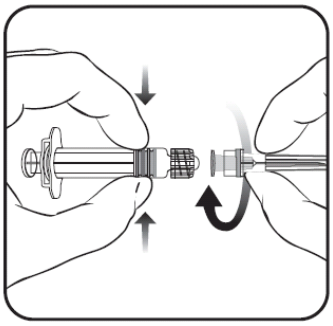
Withdraw the entire contents of the vial.

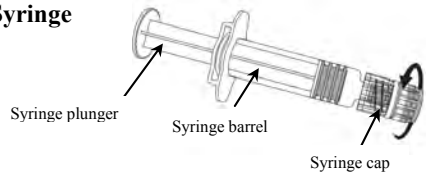
- ***Specific instructions for the pre-filled syringe with a luer lock adaptor (PRTC)***

Needle





Syringe



1. Holding the syringe **barrel** in one hand (avoid holding the syringe plunger), unscrew the syringe cap by twisting it anticlockwise.
2. To attach the needle to the syringe, twist the needle clockwise into the syringe until you feel it lock (see picture).
3. Remove the needle protector, which on occasion can be a little stiff.
4. Administer the vaccine.

2. Wording for vial and vial presentation

Upon storage, a white deposit and clear supernatant may be observed in the vial containing the DTPa-HBV-IPV suspension. This does not constitute a sign of deterioration.

Infanrix hexa must be reconstituted by adding the entire content of the vial containing the DTPa-HBV-IPV suspension to the vial containing the Hib powder. To do so, draw up the suspension with a syringe and add the suspension to the powder. The mixture should be well shaken until the powder is completely dissolved in the suspension.

The reconstituted vaccine presents as a slightly more cloudy suspension than the liquid component alone. This is normal and does not impair the performance of the vaccine.

The reconstituted vaccine should be inspected visually for any foreign particulate matter and/or abnormal physical appearance. In the event of either being observed, discard the vaccine.

A new needle should be used to administer the vaccine.

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After reconstitution, the vaccine should be used immediately.

Withdraw the entire contents of the vial.

Any unused product or waste material should be disposed of in accordance with local requirements.

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APPENDIX 3A : All serious spontaneous cases (excluding consumer reports), all serious attributable clinical trial cases and all non-serious unlisted cases (excluding consumer and regulatory reports)

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Appendix 3A: Individual Case Histories Received in Time Period of PSUR for:

Infanrix hexa

Case No.	Country	Report Source	Age/Sex	Form'n or Route	TDD	Treatment Dates†	Event Onset	TTO / TTOSLD	Events	Outcome	Comments
Blood and lymphatic system disorders											
#B0740907A	France	PH,MD,RA	4 Months/M	INJ	U	10Aug2011-10Aug2011	11Aug2011	U/1 Days	Agranulocytosis, Pyrexia, Rash	R	
#D0072751A	Germany	MD	7 Months/M	INJ	.5ML	05Jul2011-05Jul2011	02Aug2011	U/28 Days	Anaemia haemolytic autoimmune*, Autoantibody positive	N	
#B0696866A	Poland	MD,RA	1 Months/U	INJ	U	20Dec2010-20Dec2010	23Dec2010	U/3 Days	Anaemia, Hypotonic-hypore sponsive episode, Apathy, Thirst decreased, Respiratory tract infection, Somnolence	R	

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#D0070397A	Germany	MD,RP	3 Months/M	INJ	.5ML	08Feb2011-08Feb2011	09Feb2011	U/1 Days	Haemorrhagic diathesis*, Ecchymosis, Petechiae, Upper respiratory tract infection	R
#B0737478A	Poland	MD,RA	4 Months/M	INJ	U	18Feb2011-18Feb2011	18Feb2011	U/8 Hours	Haemorrhagic diathesis, Petechiae, Pyrexia	R
#B0686840A	Czech Republic	MD,RA	5 Months/M	INJ	U	07May2009-07May2009	07May2009	U/3 Hours	Idiopathic thrombocytopenic purpura, Febrile convulsion, Clonic convulsion, Tremor, Dyskinesia, Petechiae, Platelet count decreased, Pyrexia	R
#B0705987A	Ireland	PH	8 Months/M	INJ	U	01Dec2009-01Dec2009	01Jan2010	U/1 Months	Idiopathic thrombocytopenic purpura, Haemorrhage, Platelet count decreased, Petechiae, Fall, Increased tendency to bruise, Upper respiratory tract infection	U

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#D0071950A	Germany	MD	12 Months/M	INJ	.5ML	30Jun2011-30Jun2011	02Jul2011	U/2 Days	Idiopathic thrombocytopenic purpura*, Mouth haemorrhage*, Mouth haemorrhage*, Haematoma*	N
#B0740099A	Netherlands	MD,RA	4 Months/F	INJ	U	06Apr2009-06Apr2009	06Apr2009	U/Hours	Idiopathic thrombocytopenic purpura, Petechiae, Diarrhoea, Inflammation, Pyrexia	R
#B0684234A	Italy	MD,RA	10 Months/M	INJ	U	07Apr2010-07Apr2010	17Apr2010	U/10 Days	Idiopathic thrombocytopenic purpura, Thrombocytopenia, Rhinitis, Petechiae, Petechiae, Pyrexia	U
#B0715203A	Italy	MD,RA	5 Months/F	INJ	U	14Apr2009-14Apr2009	17Apr2009	U/3 Days	Leukocytosis, Inflammatory marker increased, Hyperaemia, Rhinitis, Injection site reaction, Nuchal rigidity, Irritability, Pyrexia, Crying	U
B0686750A	Poland	MD,RA	19 Months/U	INJ	U	25Aug2010-25Aug2010	27Aug2010	U/2 Days	Lymphadenopathy, Injection site oedema, Injection site erythema, Lymphadenopathy	U

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#B0691905A	Poland	RA	17 Months/U	INJ	U	02Dec2010-02Dec2010	03Dec2010	U/Hours	Lymphadenopathy, Oedema, Erythema, Lymph node palpable, Pyrexia, Restlessness, Insomnia	U
#B0695084A	France	RA	2 Years/F	INJ	U	14Sep2010-14Sep2010	14Sep2010	U/0 Days	Thrombocytopenia, Anaemia, Haematoma, Pyrexia, Gingival bleeding, Fall, Epistaxis, Blood lactate dehydrogenase increased, Incorrect route of drug administration	R
#B0699373A	Sweden	HP,RA	12 Months/F	INJ	U	08Nov2010-08Nov2010	16Nov2010	U/8 Days	Thrombocytopenia, Contusion	R
#D0071125A	Germany	HP,RA	3 Months/F	INJ	U	16Mar2011-16Mar2011	28Mar2011	U/12 Days	Thrombocytopenia, Gastroenteritis rotavirus, Leukopenia, Petechiae, Haematoma, Ureteric stenosis, Pyelocaliectasis	U

#D0072425A	Germany	MD	24 Months/M	INJ	.5ML	04Aug2011-04Aug2011	11Aug2011	U/7 Days	Thrombocytopenia*, Petechiae*, Haematoma*	R	
#B0694143A	Italy	MD,RA	2 Months/F	INJ	U	04Feb2010-04Feb2010	05Feb2010	U/1 Days	Thrombocytopenia, Petechiae, Pyrexia	R	
#B0695999A	Taiwan, ROC	LI	3 Months/U	INJ	U	10Dec2007-10Dec2007	15Dec2007	U/5 Days	Thrombocytopenic purpura*	R	Thrombocytopenic Purpura Following Vaccination in Early Childhood: Experience of a Medical Centre in the Past 2 Decades. J Clin Med Assoc. Dec2010; Vol 73: n°12
#B0693944A	Czech Republic	MD,RA	4 Months/M	INJ	U	10Dec2010-10Dec2010	11Dec2010	U/1 Days	Thrombocytopenic purpura, Petechiae, Haematoma	R	
#B0693767A	France	RA	6 Months/F	INJ	U	21Sep2010-21Sep2010	09Oct2010	U/18 Days	Thrombocytopenic purpura, Petechiae, Haematoma, Epistaxis, Splenomegaly, Thrombocytopenia, Gingival bleeding	I	

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#B0724575A	France	RA	19 Months/M	INJ	U	26Apr2011-26Apr2011	01Jan2011	U/20 Days	Thrombocytopenic purpura, Thrombocytopenia, Petechiae, Injection site haematoma	U
Cardiac disorders										
#B0716780A	Italy	MD,RA	5 Months/F	INJ, INJ	U, .5ML	10Feb2011-10Feb2011, 14Apr2011-14Apr2011		U/63 Days, U/0 Days	Cardiac arrest, Multi-organ failure, Pneumonia aspiration, Cerebral ischaemia, Sudden infant death syndrome, Unresponsive to stimuli, Peripheral coldness, Staring, Musculoskeletal stiffness, Pyrexia, Pyrexia, Somnolence	F
#D0070772A	Germany	RA	3 Months/M	INJ	U	01Mar2011-01Mar2011	13Mar2011	U/12 Days	Cardiogenic shock, Cardiac failure, Congestive cardiomyopathy, Atrial tachycardia, Supraventricular tachycardia, Acidosis, Pyrexia, Gastrointestinal pain, Hypokalaemia, Fluid intake reduced,	R

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									Hypertension, H1N1 influenza, Cholecystitis, Psychotic disorder, Crying		
#B0711289A	South Africa	HP,MD	6 Weeks/U	INJ	U	20Mar2011-20Mar2011, 21Apr2011-21Apr2011	20Mar2011	U/0 Years, U/U	Cardiopulmonary failure, Pyrexia, Bradycardia, Pyrexia	U	Possible HHE in an infant born prematurely
#B0693461A	Austria	MD,RA	3 Months/M	INJ	U	01Jan2010-01Jan2010	14Dec2010	U/Unknown	Cardiovascular disorder*	R	
#D0071453A	Germany	MD,RA	6 Months/M	INJ	U	12May2011-12May2011	12May2011	U/0 Days	Cardiovascular disorder, Apathy, Hyperpyrexia, Respiratory tract infection, Chills, Cyanosis, Pallor, Hypoventilation	R	
#D0072089A	Germany	MD,RA	11 Weeks/M	INJ	U	23May2011-23May2011	01May2011	U/7 Hours	Cardiovascular disorder, Crying, Hypotonia, Dyskinesia, Pallor	R	

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#B0694497A	Netherlands	HP,RA	8 Weeks/F	INJ	U	05Jan2011-05Jan2011	05Jan2011	U/0 Days	Cyanosis, Acidosis, Apnoea, Inflammation, Oxygen saturation decreased, Bradycardia, Injection site pain, Injection site swelling, Injection site erythema, Bacterial infection	R
#B0713567A	Poland	MD,RA	2 Months/M	INJ	U	15Mar2011-15Mar2011	15Mar2011	U/Minutes	Cyanosis, Apnoea, Hypotonic-hypore sponsive episode	R
#B0712985A	Netherlands	MD,RA	1 Months/M	INJ	.5ML	21Dec2010-21Dec2010	21Dec2010	U/4 Hours	Cyanosis, Cyanosis, Hypotonic-hypore sponsive episode, Dyspnoea, Foaming at mouth	U
#B0743683A	Netherlands	HP,MD,RA	3 Months/M	INJ, INJ	U, .5ML	07Jul2011-07Jul2011, 1 Days		U/Hours, U/Hours	Cyanosis, Cyanosis, Skin discolouration, Erythema, Gastrointestinal disorder, Injection site inflammation, Pyrexia, Erythema, Skin discolouration	R

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#B0719722A	Italy	MD,RA	11 Months/F	INJ	U	11May2011-11May2011	11May2011	U/0 Days	Cyanosis, Dyspnoea, Hypertonia	I
#B0752371A	Italy	MD,RA	2 Months/M	INJ	U	01Jun2011-01Jun2011	01Jun2011	U/0 Days	Cyanosis, Escherichia infection, Oxygen saturation decreased, C-reactive protein increased, Weight decreased, Decreased appetite, Hypotonic-hypore sponsive episode, Somnolence	R
#B0728501A	Thailand	HP	5 Months/F	INJ	U	23Jun2011-23Jun2011	23Jun2011	U/2 Hours	Cyanosis, Fatigue, Cold sweat, Pyrexia, Irritability	R
#B0683004A	Italy	RA	4 Months/M	INJ	U	28Jan2009-28Jan2009	28Jan2009	U/0 Days	Cyanosis, Hypotonia, Pallor	R
#B0741415A	Poland	MD,RA	5 Months/U	INJ	U	01Aug2011-01Aug2011	01Aug2011	U/0 Days	Cyanosis, Hypotonic-hypore sponsive episode, Crying	R

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#B0681642A	Switzerland	MD,RA	4 Months/F	INJ	U	13Sep2010-13Sep2010	13Sep2010	U/6 Hours	Cyanosis, Hypotonic-hypore sponsive episode, Pallor, Vomiting, Pyrexia	R
#B0744335A	Italy	MD,RA	2 Months/F	INJ	.5ML	09Aug2011-09Aug2011	09Aug2011	U/0 Days	Cyanosis, Injection site urticaria, Crying, Irritability	R
#B0715332A	Italy	RA	15 Months/F	INJ	U	04Apr2011-04Apr2011	04Apr2011	U/0 Days	Cyanosis, Loss of consciousness, Apnoea, Hypotonia, Crying	R
#B0726312A	Italy	RA	10 Months/F	INJ	U	26May2011-26May2011	26May2011	U/0 Days	Cyanosis, Loss of consciousness, Hypotonia	R
#B0690279A	Italy	MD,RA	3 Months/M	INJ	U	20May2010-20May2010	20May2010	U/0 Days	Cyanosis, Oculogyric crisis, Myoclonus, Pyrexia	R
#B0711564A	Italy	RA	2 Months/F	INJ	U	29Mar2011-29Mar2011	29Mar2011	U/0 Days	Cyanosis, Pallor, Hypotonia	R

#B0712499A	Italy	MD,RA	5 Months/M	INJ	U	04Apr2011-04Apr2011	04Apr2011	U/0 Days	Cyanosis, Pallor, Hypotonic-hypore sponsive episode, Crying	R
#B0730016A	Italy	RA	19 Months/M	INJ	U	18May2011-18May2011	19May2011	U/1 Days	Cyanosis, Pyrexia	R
#D0072994A	Germany	MD,RA	12 Weeks/M	INJ	U	19Apr2011-19Apr2011	19Apr2011	U/5 Hours	Cyanosis, Rash macular, Crying, Pain	R
D0071925A	Germany	CO,MD	11 Weeks/F	INJ	U	28Jun2011-28Jun2011	28Jun2011	U/Immediate	Cyanosis, Rash macular, Screaming	R
#D0071602A	Germany	P	3 Months/M	INJ	.5ML	21Jan2011-21Jan2011	22Jan2011	U/12 Hours	Cyanosis, Screaming, Flushing, Cyanosis*, Crying*	R
#B0729115A	Italy	MD,RA	6 Months/M	INJ	U	20Jul2010-20Jul2010	20Jul2010	U/Hours	Cyanosis, Unresponsive to stimuli, Dyspnoea, Glossoptosis, Staring	R

Congenital, familial and genetic disorders										
#D0071554A	Germany	MD,RA	8 Months/F	INJ	U	1 Days	01Jul2010	U/Unknown	Talipes, Posture abnormal, Decubitus ulcer, Developmental delay, Balance disorder	I
Ear and labyrinth disorders										
#D0070187A	Germany	RA	25 Months/M	INJ, INJ, INJ, INJ	.5ML, .5ML, .5ML, .5ML	18Jun2010-18Jun2010, 18Mar2009-18Mar2009, 02Apr2009-02Apr2009, 05May2009-05May2009	21Jan2011	U/7 Months, U/22 Months, U/22 Months, U/21 Months	Tympanic membrane perforation*, Haemophilus infection*, Vaccination failure*	N
#D0070501A	Germany	RA	21 Months/F	INJ, INJ, INJ, INJ	U, U, U, U	01Sep2009-01Sep2009, 10Nov2010-10Nov2010, 06Oct2009-06Oct2009, 12Nov2009-12Nov2009	17Feb2011	U/18 Months, U/16 Months, U/15 Months, U/99 Days	Tympanic membrane perforation, Vaccination failure	R
Eye disorders										
#B0696210A	Italy	MD,RA	11 Months/M	INJ	U	19Jan2011-19Jan2011	19Jan2011	U/0 Days	Eyelid oedema, Localised oedema, Urticaria, Urticaria	R
#B0722407A	Netherlands	MD,RA	2 Months/M	INJ	U	03Feb2011-03Feb2011	03Feb2011	U/14 Hours	Gaze palsy, Hypertonia, Pyrexia, Dyskinesia, Somnolence, Feeling hot	R

#B0683261A	Italy	MD,RA	3 Months/F	INJ	U	21Sep2010-21Sep2010	01Oct2010	U/10 Days	Gaze palsy, Hypotonia	R
#B0681967A	Spain	MD,RA	2 Months/F	INJ	U	27Sep2010-27Sep2010	27Sep2010	U/2 Hours	Gaze palsy, Hypotonia, Pallor	R
#B0700213A	Italy	RA	5 Months/M	INJ	U	19Jan2011-19Jan2011	22Jan2011	U/3 Days	Oculogyric crisis	U
D0069798A	Germany	MD	2 Months/M	INJ	U	25Oct2010-25Oct2010	27Oct2010	U/2 Days	Pupils unequal	N
Gastrointestinal disorders										
D0070465A	Germany	MD,RA	3 Months/M	INJ	U	05Jan2011-05Jan2011	05Jan2011	U/0 Days	Abdominal distension, Pyrexia, Hypotonia, Pallor, Restlessness, Vomiting	R

B0736768A	Poland	MD	2 Months/F	INJ	U	14Jun2011-14Jun2011	14Jun2011	U/0 Days	Abdominal pain, Anxiety, Crying	R
B0681732A	South Africa	HP	8 Weeks/U	INJ	U	20Oct2010-20Oct2010	20Oct2010	U/0 Days	Abdominal pain, Irritability, Pyrexia	W
B0743702A	Netherlands	MD,RA	2 Months/M	INJ	U	15Jul2011-15Jul2011	15Jul2011	U/Hours	Abnormal faeces	R
#B0701523A	Italy	RA	5 Months/M	INJ	U	10Jan2011-10Jan2011	10Jan2011	U/0 Days	Colitis, Pyrexia	I
#B0747304A	Poland	MD,RA	4 Months/U	INJ	U	12Aug2011-12Aug2011	14Aug2011	U/2 Days	Diarrhoea haemorrhagic, Pyrexia, Crying, Restlessness, Abnormal behaviour	R
#B0754698A	Poland	MD,RA	2 Months/U	INJ	U	18Aug2011-18Aug2011	19Aug2011	U/1 Days	Diarrhoea haemorrhagic, Pyrexia, Vomiting, Faeces discoloured, Dermatitis diaper,	U

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									Erythema, Dyspepsia	
#B0747625A	France	MD,RP	2 Months/F	INJ	U	23Aug2011-23Aug2011	23Aug2011	U/Same day	Diarrhoea, Vomiting, Gastroenteritis	R
#B0694325A	Spain	P	3 Months/M	INJ	U	18Nov2010-18Nov2010	20Nov2010	U/2 Days	Gastrooesophageal reflux disease*, Bronchial hyperreactivity*	R
#B0714317A	Czech Republic	MD	2 Months/F	INJ	U	23Mar2011-23Mar2011	30Mar2011	U/7 Days	Haematochezia, Gastrointestinal inflammation, Restlessness, Flatulence, Frequent bowel movements	I
#D0073097A	Germany	MD,RA	13 Weeks/M	INJ	.5ML	29Sep2011-29Sep2011	01Oct2011	U/2 Days	Haematochezia*, Gastrointestinal pain*	R

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#B0754377A	South Africa	HP	4 Months/F	INJ	U	29Sep2011-29Sep2011	04Oct2011	U/5 Days	Intussusception, Diarrhoea, Haematochezia	U
D0072360A	Germany	MD,RP	3 Years/F	INJ	U	21Jun2011-21Jun2011	21Jun2011	U/0 Days	Lip swelling, Dyspnoea	R
#B0749250A	France	RA	2 Months/M	INJ	U	20Mar2011-20Mar2011	21Mar2011	U/0 Days	Rectal haemorrhage	R
#B0747231A	Poland	MD,RA	1 Months/U	INJ	U	10Aug2011-10Aug2011	10Aug2011	U/0 Days	Vomiting, Pyrexia, Diarrhoea, Rash macular, Rash generalised	R
D0071405A	Germany	MD	3 Months/F	INJ	U	16May2011-16May2011	16May2011	U/0 Days	Vomiting, Underdose	R

General disorders and administration site conditions

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#D0071850A	Germany	MD,RP	8 Years/F	INJ	U	1 Days		U/Unknown	Abscess sterile	U
#D0071850B	Germany	MD,RP	8 Years/F	INJ	U	1 Days		U/Unknown	Abscess sterile	U
#D0072409A	Germany	MD,RP	7 Months/M	INJ, INJ	.5ML, .5ML	29Oct2010-29Oct2010, 1 Days	31Oct2010	U/2 Days, U/Unknown	Abscess sterile, Foreign body reaction, Allergy to metals, Lymphadenopathy, Local swelling, Induration, Local swelling, Induration	R
#D0068815B	Germany	MD,RA	19 Months/M	INJ	U	23Feb2010-23Feb2010, 11Jan2010-11Jan2010, 1 Days	01Jan2010	U/0 Years, U/Unknown, U/U	Abscess sterile*, Injection site swelling*, Injection site induration*, Scar*, Abscess drainage, Purulence, Cyst	N
#D0070025A	Germany	MD,RP	6 Years/M	INJ	U	07Oct2010-07Oct2010	10Dec2010	U/64 Days	Abscess sterile, Neoplasm skin, Induration, Injection site swelling, Injection site discolouration, Granuloma skin,	U

									Scar, Surgery, Vaccination complication	
D0069774A	Germany	MD,RP	U/U	INJ	U	1 Days		U/Unknown	Adverse event	U
#B0726474A	Italy	MD	U/F	INJ	U	1 Days		U/Unknown	Condition aggravated	U
#B0727175A	France	RA	18 Months/F	INJ	U	26Oct2010-26Oct2010	27Oct2010	U/1 Days	Death	F
#D0071496A	Germany	HP,RA	3 Months/F	INJ	U	16May2011-16May2011	17May2011	U/1 Days	Death	F
#D0072663A	Germany	RA	9 Weeks/M	INJ	.5ML	05Sep2011-05Sep2011	07Sep2011	U/2 Days	Death*	F

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#D0070336A	Germany	HP,RA	4 Months/M	INJ	U	01Jul2009-01Jul2009	15Jul2009	U/14 Days	Developmental delay, Hypotonia, Nystagmus, Speech disorder, Transaminases increased, Hypoaesthesia, Dizziness, Visual acuity reduced	N
#D0070043A	Germany	MD,RA	3 Months/M	INJ	U	12Jan2010-12Jan2010, 12Feb2010-12Feb2010, 12Mar2010-12Mar2010	01Jan2010	U/10 Days, U/U, U/U	Developmental delay*, Movement disorder*, Stereotypy*, Motor dysfunction*, Hypotonia*, Muscle twitching*, Areflexia*, Reflex test normal*, Ill-defined disorder*, Pyrexia*, Hypersensitivity*, Lip swelling*, Rash*, Cytomegalovirus test positive*, Iodine deficiency*, Hydrocele*, Convulsion*, Hypothyroidism*	N

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D0069358C	Germany	HP,RA	2 Months/M	INJ	U	13Nov2009-13Nov2009	13Nov2009	U/0 Days	Developmental delay, Psychomotor hyperactivity, Sleep disorder, Hyperhidrosis, Restlessness, Ill-defined disorder	U	
#D0069358A	Germany	HP,RA	7 Months/M	INJ	U	12Apr2010-12Apr2010	12Apr2010	U/1 Hours	Developmental delay, Weight gain poor, Psychomotor hyperactivity, Hyperhidrosis, Tremor, Injection site erythema, Injection site swelling, Sleep disorder	N	
B0703201A	Switzerland	LI	20 Months/M	INJ	U	1 Days		U/24 Hours	Extensive swelling of vaccinated limb, Injection site erythema, Injection site reaction, Injection site warmth, Pyrexia	R	B.M. Huber MD : Extensive limb swelling after vaccination : 1 case. The journal of Pediatrics 2011 Feb. http://www.jpeds.com/
B0741001A	France	MD	16 Months/U	INJ	U	01Aug2011-01Aug2011	01Aug2011	U/1 Days	Extensive swelling of vaccinated limb, Injection site erythema, Injection site warmth, Injection site induration	U	

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B0702525A	France	PH	16 Months/M	INJ	U	23Feb2011-23Feb2011	24Feb2011	U/1 Days	Extensive swelling of vaccinated limb, Injection site erythema, Injection site warmth, Injection site induration, Injection site infection, Ill-defined disorder	N
#B0703591A	France	PH	20 Months/M	INJ	U	1 Days, 1 Days, 1 Days	25Feb2011	U/See text, U/U, U/U	Extensive swelling of vaccinated limb, Injection site erythema, Injection site warmth, Injection site oedema, Pyrexia, Wrong drug administered	R
B0685430A	France	MD	18 Months/U	INJ	U	16Nov2010-16Nov2010	01Nov2010	U/0 Weeks	Extensive swelling of vaccinated limb, Injection site erythema, Injection site warmth, Injection site vesicles	N
B0705104A	France	MD	22 Months/M	INJ	U	01Mar2011-01Mar2011	01Mar2011	U/24 Hours	Extensive swelling of vaccinated limb, Injection site induration, Product quality issue	N

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B0705108A	France	MD	22 Months/M	INJ	U	01Mar2011-01Mar2011	01Mar2011	U/24 Hours	Extensive swelling of vaccinated limb, Injection site induration, Product quality issue	N
B0681184A	France	MD	18 Months/M	INJ	U	25Aug2010-25Aug2010	26Aug2010	U/1 Days	Extensive swelling of vaccinated limb, Injection site inflammation	R
#B0750035A	Poland	MD,RA	17 Months/U	INJ	U	17Aug2011-17Aug2011	18Aug2011	U/1 Days	Extensive swelling of vaccinated limb, Injection site swelling, Injection site erythema, Injection site pain	R
B0713123A	France	CO,MD	17 Months/M	INJ	U	12Apr2011-12Apr2011	13Apr2011	U/0 Days	Extensive swelling of vaccinated limb, Injection site warmth, Injection site erythema, Injection site pruritus	I
B0711364A	France	MD	2 Years/F	INJ	U	04Apr2011-04Apr2011	06Apr2011	U/2 Days	Extensive swelling of vaccinated limb, Injection site warmth, Injection site inflammation, Injection site erythema, Incorrect route of	I

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									drug administration	
B0685437A	France	MD	18 Months/M	INJ	U	17Nov2010-17Nov2010	17Nov2010	U/0 Hours	Extensive swelling of vaccinated limb, Injection site warmth, Injection site pain, Pyrexia, Injection site oedema, Skin discolouration	R
#B0751956A	Czech Republic	MD,RA	3 Months/F	INJ	U	23Aug2011-23Aug2011		U/0 Months	Fatigue, Hypotonia, Hypersomnia	U
B0709060A	Netherlands	HP,RA	10 Months/F	INJ	U	20Aug2010-20Aug2010		U/Unknown	Fibrosis, Inflammation, Pyrexia	R
#B0692411A	Italy	RA	12 Months/M	INJ	U	21Oct2010-21Oct2010	28Oct2010	U/7 Days	Gait disturbance*	R

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B0733393A	Viet Nam	MD	3 Years/F	INJ	U	04Jul2011-04Jul2011	04Jul2011	U/0 Days	Gait disturbance, Injection site swelling, Pyrexia	N
D0071920A	Germany	MD	Infant/U	INJ	U	1 Days		U/Unknown	Granuloma	U
#D0072470A	Germany	RA	20 Months/M	INJ	.5ML	22Jul2011-22Jul2011, 20May2010-20May2010	22Jul2011	U/0 Days, U/U	Hyperpyrexia*	R
#B0742490A	Greece	MD,RP	2 Months/F	INJ	U	01Feb2010-01Feb2010	01Feb2010	U/Hours	Hyperpyrexia, Rash morbilliform	R
B0742514A	Greece	MD,RP	2 Months/F	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/Hours	Hyperpyrexia, Rash morbilliform	R
B0742521A	Greece	MD,RP	2 Months/F	INJ	U	08Aug2011-08Aug2011	08Aug2011	U/Hours	Hyperpyrexia, Rash morbilliform	R

B0707224A	Argentina	MD	4 Months/F	INJ	U	01Feb2011-01Feb2011	01Feb2011	U/1 Days	Hypothermia	R
B0735139A	Netherlands	MD,RA	4 Months/F	INJ, INJ, INJ	U, U, .5ML	U, 13May2011-13May2011, U	13May2011	U/Unknown, U/Unknown, U/4 Hours	Ill-defined disorder, Eating disorder, Gastrointestinal disorder, Pyrexia, Vomiting, Pyrexia, Diarrhoea, Vomiting	R
#B0715306A	Romania	MD,RP	6 Months/M	INJ	U	14Apr2011-14Apr2011	15Apr2011	U/1 Days	Ill-defined disorder, Inflammation, Agitation, Pyrexia	R
B0705049A	Colombia	HP,MD	4 Months/M	INJ, INJ	U, U	03Mar2011-03Mar2011, 03Jan2011-03Jan2011, 17May2011-17May2011	03Mar2011	U/0 Days, U/0 Days, U/U	Ill-defined disorder, Pyrexia, Pyrexia, Irritability	U
B0756832A	Netherlands	HP,RA	2 Months/M	INJ	.5ML	07Jul2011-07Jul2011	07Jul2011	U/13 Hours	Ill-defined disorder, Pyrexia, Respiration abnormal, Hypotonic-hypore sponsive episode	R

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B0718374A	Belgium	MD	15 Months/M	INJ	U	19Apr2011-19Apr2011		U/See text	Incorrect product storage	X
B0718379A	Belgium	MD	15 Months/M	INJ	U	19Apr2011-19Apr2011		U/See text	Incorrect product storage	X
B0718380A	Belgium	MD	15 Months/F	INJ	U	19Apr2011-19Apr2011		U/See text	Incorrect product storage	X
B0681225A	France	PH	3 Months/M	INJ	U	01Sep2010-01Sep2010	01Sep2010	U/See text	Incorrect product storage	X
B0681900A	France	MD	19 Months/F	INJ	U	18Oct2010-18Oct2010	18Oct2010	U/See text	Incorrect product storage	X
B0683002A	France	MD	Infant/U	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/See text	Incorrect product storage	X

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B0683003A	France	MD	Infant/U	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/See text	Incorrect product storage	X
B0685438A	France	MD	2 Months/U	INJ	U	01Oct2010-01Oct2010	01Oct2010	U/See text	Incorrect product storage	X
B0685922A	France	PH	Infant/U	INJ	U	01Nov2010-01Nov2010	01Nov2010	U/See text	Incorrect product storage	X
B0686441A	France	PH	2 Months/F	INJ	U	24Nov2010-24Nov2010	24Nov2010	U/See text	Incorrect product storage	X
B0688412A	France	MD	U/U	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/See text	Incorrect product storage	X
B0688724A	France	MD	3 Months/M	INJ	U	01Oct2010-01Oct2010	01Oct2010	U/See text	Incorrect product storage	X

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B0689227A	France	PH	1 Years/U	INJ	U	08Dec2010-08Dec2010	08Dec2010	U/See text	Incorrect product storage	X
B0689746A	France	HP,PH	2 Months/M	INJ	U	14Dec2010-14Dec2010	14Dec2010	U/See text	Incorrect product storage	X
B0691868A	France	PH	2 Months/U	INJ	U	01Dec2010-01Dec2010	01Dec2010	U/See text	Incorrect product storage	X
B0692725A	France	MD	4 Months/M	INJ	U	19Oct2010-19Oct2010	19Oct2010	U/See text	Incorrect product storage	X
B0692728A	France	MD	6 Months/M	INJ	U	18Oct2010-18Oct2010	18Oct2010	U/See text	Incorrect product storage	X
B0692729A	France	MD	9 Months/M	INJ	U	19Oct2010-19Oct2010	19Oct2010	U/See text	Incorrect product storage	X

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B0692906A	France	MD,RP	2 Months/F	INJ	U	1 Days		U/See text	Incorrect product storage	X
B0693355A	France	MD	Neonate/U	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/See text	Incorrect product storage	X
B0694120A	France	PH	3 Months/M	INJ	U	17Jan2011-17Jan2011	17Jan2011	U/See text	Incorrect product storage	X
B0695156A	France	PH	2 Months/U	INJ	U	1 Days		U/See text	Incorrect product storage	X
B0700350A	France	CO,PH	2 Months/F	INJ	U	16Feb2011-16Feb2011	01Feb2011	U/See text	Incorrect product storage	X
B0701361A	France	PH	2 Months/F	INJ	U	17Feb2011-17Feb2011	17Feb2011	U/See text	Incorrect product storage	X

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B0705083A	France	MD	Infant/U	INJ	U	1 Days		U/See text	Incorrect product storage	X
B0707186A	France	PH	2 Months/F	INJ	U	18Mar2011-18Mar2011	18Mar2011	U/See text	Incorrect product storage	X
B0712971A	France	PH	2 Months/M	INJ	U	01Apr2011-01Apr2011	01Apr2011	U/See text	Incorrect product storage	X
B0724552A	France	MD	2 Months/U	INJ	U	26May2011-26May2011	26May2011	U/See text	Incorrect product storage	X
B0725917A	France	PH	6 Months/F	INJ	U	01Jun2011-01Jun2011	01Jun2011	U/See text	Incorrect product storage	X
B0729492A	France	PH	2 Months/F	INJ	U	01Jun2011-01Jun2011	01Jun2011	U/See text	Incorrect product storage	X

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B0729515A	France	PH	2 Months/U	INJ	U	01Jun2011-01Jun2011	01Jun2011	U/See text	Incorrect product storage	X
B0731763A	France	PH	U/U	U	U	1 Days		U/See text	Incorrect product storage	X
B0737084A	France	MD	2 Months/F	INJ	U	03Aug2011-03Aug2011	03Aug2011	U/See text	Incorrect product storage	X
B0746698A	France	MD	U/U	INJ	U	1 Days		U/See text	Incorrect product storage	X
B0750069A	France	PH	U/U	INJ	U	U	09Sep2011	U/See text	Incorrect product storage	X
B0756736A	France	PH	3 Months/U	INJ	U	19Oct2011-19Oct2011	19Oct2011	U/See text	Incorrect product storage	X

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B0684837A	France	PH,MD	2 Months/M	INJ	U	15Nov2010-15Nov2010	15Nov2010	U/See text	Incorrect product storage*	X
B0683276A	France	MD,RP	2 Months/M	INJ	U	26Oct2010-26Oct2010	26Oct2010	U/See text	Incorrect product storage, Drug administered to patient of inappropriate age	X
B0711998A	Ethiopia	MD	5 Weeks/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/See text	Incorrect product storage, Drug administration error	X
#B0702823A	Spain	HP,RA	2 Months/M	INJ	U	18Feb2011-18Feb2011	18Feb2011	U/Immediate	Induration, Erythema	R
D0069932A	Germany	MD,RA	4 Months/M	INJ	U	03Jan2011-03Jan2011	03Jan2011	U/0 Days	Induration*, Erythema*, Oedema peripheral*	U
B0719482A	Netherlands	HP,RA	1 Years/F	INJ	U	29Jul2010-29Jul2010		U/Unknown	Inflammation	U

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#B0683274A	Italy	MD	4 Months/F	INJ	U	25Oct2010-25Oct2010	28Oct2010	U/3 Days	Inflammation, Inflammatory marker increased, Pyrexia	R
B0698816A	Netherlands	HP,RA	11 Months/M	INJ	U	28Jul2010-28Jul2010	01Jul2010	U/Hours	Inflammation, Pyrexia, Otitis media, Skin discolouration	R
B0698798A	Netherlands	HP,RA	4 Months/F	INJ	U	07Dec2009-07Dec2009	17Dec2009	U/10 Days	Inflammation, Skin ulcer, Injection site discolouration, Injection site pruritus	N
#D0072316A	Germany	RA	9 Months/F	INJ, INJ	.5ML, U	30May2011-30May2011, 07Apr2011-07Apr2011	01Apr2011	U/0 Years, U/0 Months	Injection site abscess sterile*, Injection site nodule*, Injection site erythema*, Injection site swelling*, Injection site nodule	R
B0718962A	France	MD	2 Months/M	INJ	U	1 Days		U/Unknown	Injection site cyst, Injection site pruritus	U

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D0072257A	Germany	MD,RA	4 Months/F	INJ	U	25Mar2011-25Mar2011	01Apr2011	U/4 Weeks	Injection site discolouration	N
D0072258A	Germany	MD,RA	3 Months/M	INJ	U	28Mar2011-28Mar2011	01Apr2011	U/4 Weeks	Injection site discolouration	N
D0071052A	Germany	MD,RP	2 Months/M	INJ, INJ, INJ	U, U, U	17Dec2010-17Dec2010, 07Feb2011-07Feb2011, 08Mar2011-08Mar2011		U/Unknown, U/Unknown, U/Unknown	Injection site discolouration*, Injection site discolouration*, Injection site discolouration*, Product quality issue*	N
D0071085A	Germany	CO,MD,RA, RP	3 Months/M	INJ, INJ	U, U	14Mar2011-14Mar2011, 01Apr2011-01Apr2011	01Jan2011	U/0 Months, U/0 Months	Injection site discolouration*, Injection site discolouration*, Product quality issue*	U
D0071231A	Germany	MD,RA	3 Months/F	INJ, INJ	U, U	24Jan2011-24Jan2011, 04Mar2011-04Mar2011	01Jan2011	U/0 Years, U/0 Years	Injection site discolouration*, Injection site discolouration*, Product quality issue*	N

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B0743118A	Netherlands	MD,RA	2 Months/M	INJ	.5ML	16Aug2011-16Aug2011	16Aug2011	U/Seconds	Injection site discolouration, Injection site erythema, Malaise, Pyrexia	R
D0069323A	Germany	MD	9 Months/M	INJ	U	20Sep2010-20Sep2010		U/0 Days	Injection site discolouration*, Injection site induration*, Injection site erythema*	I
D0071009A	Germany	MD,RA,RP	4 Months/M	INJ	U	17Mar2011-17Mar2011	01Jan2011	U/0 Months	Injection site discolouration*, Product quality issue*	N
D0071086A	Germany	MD,RA,RP	4 Months/F	INJ	U	11Mar2011-11Mar2011	01Jan2011	U/0 Years	Injection site discolouration*, Product quality issue*	N
D0071128A	Germany	MD,RA	4 Months/M	INJ	U	17Mar2011-17Mar2011	01Apr2011	U/4 Weeks	Injection site discolouration*, Product quality issue*	N
D0071129A	Germany	MD,RA	4 Months/F	INJ	U	22Mar2011-22Mar2011	01Apr2011	U/4 Weeks	Injection site discolouration*, Product quality issue*	N

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D0071218A	Germany	MD,RA	4 Months/M	INJ	U	02Mar2011-02Mar2011	01Apr2011	U/4 Weeks	Injection site discolouration*, Product quality issue*	N
D0071219A	Germany	MD,RA	4 Months/F	INJ	U	02Mar2011-02Mar2011	01Apr2011	U/4 Weeks	Injection site discolouration*, Product quality issue*	N
B0710275A	France	MD	3 Months/F	INJ	U	1 Days		U/Unknown	Injection site erythema, Generalised erythema, Hypersensitivity	R
B0747469A	France	MD	2 Months/F	INJ	U	14Sep2011-14Sep2011	14Sep2011	U/Same day	Injection site erythema, Incorrect product storage, Incorrect route of drug administration	U
B0695756A	France	MD	34 Months/U	INJ	U	21Jan2011-21Jan2011	22Jan2011	U/1 Days	Injection site erythema, Injection site induration, Injection site swelling, Lymphadenopathy	N

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#B0716747A	Poland	MD,RA	1 Months/U	INJ	U	08Feb2011-08Feb2011	08Feb2011	U/0 Days	Injection site erythema, Injection site oedema, Crying, Pyrexia	R
B0725393A	France	MD	2 Months/F	INJ	U	01May2011-01May2011	01May2011	U/0 Days	Injection site erythema, Injection site pain, Injection site oedema, Injection site warmth	R
B0702448A	France	MD	17 Months/M	INJ	U	23Feb2011-23Feb2011	24Feb2011	U/1 Days	Injection site erythema, Injection site reaction, Injection site warmth, Injection site pain, Injection site swelling, Injection site induration, Injection site pruritus	R
D0069984A	Germany	MD	6 Months/M	INJ	U	10Jan2011-10Jan2011	10Jan2011	U/0 Days	Injection site erythema*, Injection site swelling*, Abscess*	R
D0071543A	Germany	MD	4 Years/F	INJ	U	14Apr2011-14Apr2011	14Apr2011	U/0 Days	Injection site erythema, Injection site swelling, Incorrect route of drug administration, Off label use	R

B0701152A	South Africa	HP	14 Weeks/F	INJ	U	15Feb2011-15Feb2011	01Feb2011	U/Days	Injection site erythema, Injection site swelling, Injection site induration	U
B0701172A	South Africa	HP	18 Months/F	INJ	U	16Feb2011-16Feb2011	17Feb2011	U/1 Days	Injection site erythema, Injection site swelling, Injection site induration	U
B0701171A	South Africa	HP	18 Months/F	INJ	U	16Feb2011-16Feb2011	17Feb2011	U/1 Days	Injection site erythema, Injection site swelling, Injection site induration, Injection site vesicles	U
D0070379A	Germany	MD	24 Months/M	INJ	U	14Feb2011-14Feb2011	16Feb2011	U/2 Days	Injection site erythema, Injection site swelling, Injection site nodule, Pyrexia	N
D0070791A	Germany	MD	12 Months/F	INJ	U	22Mar2011-U	22Mar2011	U/During	Injection site erythema, Injection site swelling, Wrong technique in drug usage process	R

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B0736298A	South Africa	HP	19 Months/M	INJ	U	27Jul2011-27Jul2011	29Jul2011	U/2 Days	Injection site erythema, Injection site warmth	N
D0070442A	Germany	MD,RG,RA	22 Months/F	INJ	.5ML	18Feb2011-18Feb2011	19Feb2011	U/1 Days	Injection site erythema*, Injection site warmth*	U
B0710891A	France	MD	2 Years/M	INJ	U	29Mar2011-29Mar2011	29Mar2011	U/3 Hours	Injection site erythema, Injection site warmth, Injection site induration, Pyrexia, Inflammation	U
B0720201A	France	CO,MD	16 Months/M	INJ	U	04May2011-04May2011	01May2011	U/0 Weeks	Injection site erythema, Injection site warmth, Injection site swelling, Injection site haematoma, Injection site vesicles	I
D0070872A	Germany	HP,RA	16 Months/F	INJ	U	09Dec2010-09Dec2010	01Jan2011	U/0 Months	Injection site extravasation, Injection site scar	N

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B0750616A	France	MD	1 Years/M	INJ	U	15Oct2010-15Oct2010	22Oct2010	U/7 Days	Injection site haematoma, Injection site pruritus, Injection site dermatitis, Injection site induration	N
#B0717663A	South Africa	HP	3 Months/M	INJ	.5ML	26Apr2011-26Apr2011	26Apr2011	U/0 Days	Injection site haemorrhage, Injection site rash, Injection site swelling, Injection site erythema, Irritability, Crying	U
B0709384A	Belgium	MD,RP	Infant/U	INJ	U	1 Days		U/Unknown	Injection site induration	R
B0718963A	France	MD	3 Months/F	INJ	U	1 Days		U/Unknown	Injection site induration	U
B0718964A	France	MD	Infant/M	INJ	U	1 Days		U/Unknown	Injection site induration	U

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D0071088A	Germany	MD,RP	5 Months/F	INJ	U	04Mar2011-04Mar2011	01Mar2011	U/0 Weeks	Injection site induration	N
D0071420A	Germany	MD,RP	U/U	INJ	U	1 Days		U/Unknown	Injection site induration	U
#B0729084A	France	RA	2 Years/F	INJ	U	12Apr2011-12Apr2011	12Apr2011	U/Same day	Injection site induration, Disability, Oedema, Extensive swelling of vaccinated limb	I
B0719704A	France	MD	20 Months/F	INJ	U	11May2011-11May2011	12May2011	U/1 Days	Injection site induration, Injection site erythema, Injection site pruritus	N
#B0727606A	Poland	MD,RA	18 Months/U	INJ	U	20May2011-20May2011	21May2011	U/1 Days	Injection site induration, Injection site erythema, Pyrexia	R

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B0727001A	France	MD	18 Months/F	INJ	U	01Jun2011-01Jun2011	01Jun2011	U/0 Months	Injection site induration, Injection site inflammation, Injection site warmth, Injection site pain, Product quality issue	U
B0727004A	France	MD	2 Years/F	INJ	U	01Jun2011-01Jun2011	01Jun2011	U/0 Months	Injection site induration, Injection site inflammation, Injection site warmth, Injection site pain, Product quality issue	U
B0750870A	France	PH	Infant/F	INJ	U	09Sep2011-09Sep2011	01Jan2010	U/0 Months	Injection site induration, Injection site swelling, Injection site warmth, Injection site erythema, Rash	I
B0753352A	France	PH	17 Months/F	INJ	U	15Sep2011-15Sep2011	15Sep2011	U/0 Days	Injection site induration, Injection site warmth, Injection site erythema, Injection site pain, Injection site oedema	I
#B0738500A	France	RA	4 Months/U	INJ, INJ	U, U	01Aug2011-01Aug2011, 01Aug2011-01Aug2011	01Aug2011	U/See text, U/See text	Injection site induration, Pyrexia, Wrong technique in drug usage process, Overdose	U

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B0683368A	Netherlands	HP,RA	12 Months/M	INJ	U	08Apr2010-08Apr2010	08Apr2010	U/0 Days	Injection site inflammation	R
B0736271A	Netherlands	MD,RA	3 Months/F	INJ	.5ML	11Jul2011-11Jul2011	13Jul2011	U/0 Days	Injection site inflammation, Extensive swelling of vaccinated limb, Injection site erythema, Injection site warmth, Injection site discolouration	N
B0735199A	Netherlands	HP,RA	3 Months/F	INJ	U	10Mar2010-10Mar2010		U/3 Days	Injection site inflammation, Injection site discolouration	N
B0726647A	Poland	MD,RA	16 Months/U	INJ	U	16Apr2011-16Apr2011	27Apr2011	U/11 Days	Injection site inflammation, Injection site erythema, Injection site oedema	R
B0755890A	Netherlands	MD,RA	12 Months/F	INJ	U	19Jan2010-19Jan2010	19Jan2010	U/0 Days	Injection site inflammation, Injection site pain, Fibrosis, Injection site haematoma, Injection site swelling, Injection site haemorrhage, Dermatitis	U

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#B0757275A	France	RA	21 Months/M	INJ	U	24Aug2011-24Aug2011		U/0 Days	Injection site inflammation, Injection site rash, Injection site warmth, Injection site induration, Injection site pain, Injection site erythema, Eczema, Impetigo	I
B0681516A	France	MD	2 Months/U	INJ	U	01Sep2010-01Sep2010	01Sep2010	U/0 Days	Injection site inflammation*, Injection site warmth*, Injection site erythema*, Injection site pain*, Pyrexia*	R
B0707830A	Netherlands	HP,RA	2 Months/M	INJ	.5ML	01Dec2010-01Dec2010	01Dec2010	U/Hours	Injection site inflammation, Pyrexia	R
B0727488A	Netherlands	MD,RA	3 Months/F	INJ	U	12Oct2010-12Oct2010	12Oct2010	U/2 Hours	Injection site inflammation, Pyrexia, Crying, Injection site pain	R
B0733456A	Netherlands	HP,RA	2 Months/F	INJ	U	04Oct2010-04Oct2010	04Oct2010	U/3 Minutes	Injection site inflammation, Pyrexia, Crying, Injection site pain, Crying	R

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B0737614A	Netherlands	HP,RA	11 Months/M	INJ	U	12Nov2010-12Nov2010	13Nov2010	U/1 Days	Injection site inflammation, Pyrexia, Crying, Injection site pain, Fibrosis, Malaise, Nasopharyngitis	R
B0751103A	Netherlands	HP,RA	4 Months/F	INJ	U	15Oct2010-15Oct2010	15Oct2010	U/0 Days	Injection site inflammation, Pyrexia, Crying, Injection site pain, Listless, Malaise	R
B0756895A	Netherlands	HP,RA	2 Months/F	INJ	U	09Nov2010-09Nov2010	09Nov2010	U/2 Hours	Injection site inflammation, Pyrexia, Crying, Injection site pain, Skin discolouration, Respiration abnormal, Hypotonia, Malaise	U
B0731185A	Netherlands	HP,RA	12 Months/M	INJ	U	31May2011-31May2011	31May2011	U/0 Days	Injection site inflammation, Rash generalised, Pyrexia	I
B0697403A	France	HP	2 Months/M	INJ	U	19Jan2011-19Jan2011	19Jan2011	U/0 Days	Injection site nodule	N

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B0691683A	France	MD	Infant/F	INJ, INJ	U, U	01Sep2009-01Sep2009, 01Sep2010-01Sep2010	01Jan2009	U/Unknown, U/Unknown	Injection site nodule, Injection site discolouration	N
B0684107A	France	MD,RP	Infant/F	INJ	U	1 Days		U/Unknown	Injection site nodule, Injection site pruritus	N
B0709808A	France	MD	2 Years/F	INJ	U	01Jun2010-01Jun2010	01Jan2010	U/3 Weeks	Injection site nodule, Injection site pruritus	U
B0716281A	France	MD,RP	3 Years/M	INJ	U	1 Days		U/Unknown	Injection site nodule, Injection site pruritus	N
#B0746455A	France	RA	5 Months/M	INJ, INJ	U, U	13Nov2010-13Nov2010, 14Jan2011-14Jan2011	01Jan2011	U/2 Months, U/0 Months	Injection site nodule, Injection site pruritus	N
B0741005A	France	MD	Infant/F	INJ	U	01Sep2010-01Sep2010	01Sep2010	U/0 Months	Injection site nodule, Injection site pruritus, Hypertrichosis	N

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#B0683007A	France	HP,MD	5 Months/F	INJ	U	01Feb2009-01Feb2009, 01May2009-01May2009, 01Mar2009-01Mar2009	01May2009	U/0 Months, U/U, U/U	Injection site nodule, Injection site pruritus, Hypertrichosis, Injection site discolouration, Injection site nodule, Injection site inflammation, Papule, Wrong drug administered	N
D0070912A	Germany	HP,RA	6 Months/M	INJ, INJ	U, U	26Jan2011-26Jan2011, 22Dec2010-22Dec2010	01Dec2010	U/0 Months, U/0 Weeks	Injection site nodule, Scar, Injection site nodule, Scar	N
B0708070A	France	MD	18 Months/F	INJ	U	10Mar2011-10Mar2011	10Mar2011	U/Same day	Injection site oedema, Injection site nodule, Injection site induration	N
B0756102A	Ecuador	MD,RP	9 Months/F	INJ	U	01Sep2011-01Sep2011, 01Jan2011-01Jan2011, 1 Days	27Sep2011	U/3 Weeks, U/0 Months, U/U	Injection site papule	N
B0708548A	Peru	MD	18 Months/M	INJ	U	18Feb2011-18Feb2011	18Feb2011	U/Hours	Injection site rash, Injection site erythema, Injection site oedema, Injection site swelling	R

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D0071230A	Germany	MD	U/U	INJ	U	27Aug2010-27Aug2010		U/0 Years	Injection site reaction	U
B0685692A	Ukraine	CO,MD	6 Months/F	INJ	U	09Nov2010-09Nov2010	09Nov2010	U/0 Days	Injection site reaction	N
D0071777A	Germany	MD	19 Months/M	INJ	.5ML	20Sep2010-20Sep2010	20Sep2010	U/Unknown	Injection site reaction*	N
B0734425A	France	MD	8 Weeks/F	INJ	U	08Jul2011-08Jul2011	08Jul2011	U/Immediate	Injection site reaction, Injection site erythema, Injection site swelling, Injection site induration, Pyrexia, Injection site oedema	R
#B0747299A	Poland	MD,RA	19 Months/U	INJ	U	16Aug2011-16Aug2011	16Aug2011	U/0 Days	Injection site reaction, Injection site extravasation, Injection site erythema, Pharyngeal erythema	R

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B0734171A	France	MD	Infant/F	INJ	U	01Nov2010-01Nov2010		U/Unknown	Injection site reaction, Injection site pruritus, Injection site nodule	N
#B0727676A	Poland	MD,RA	18 Months/U	INJ	U	21May2011-21May2011	22May2011	U/1 Days	Injection site reaction, Injection site swelling, Injection site erythema, Injection site warmth, Body temperature increased	R
B0714712A	Poland	MD,RA	6 Months/U	INJ	U	08Feb2011-08Feb2011	08Feb2011	U/0 Days	Injection site reaction, Injection site warmth, Body temperature, Injection site erythema, Injection site pain	R
#B0756170A	Poland	MD,RA	19 Months/U	INJ	U	15Sep2011-15Sep2011	15Sep2011	U/0 Days	Injection site reaction, Injection site warmth, Pyrexia, Urticaria	R
B0743179A	Netherlands	MD,RA	10 Months/M	INJ	.5ML	16Aug2011-16Aug2011	16Aug2011	U/4 Hours	Injection site reaction, Pyrexia, Crying, Rash	N

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B0740908A	Poland	MD	4 Months/M	INJ	U	21Jul2011-21Jul2011	22Jul2011	U/1 Days	Injection site reaction, Subcutaneous nodule	U
#B0743545A	France	RA	4 Months/F	INJ, INJ	U, U	09Aug2011-09Aug2011, 09Aug2011-09Aug2011	10Aug2011	U/1 Days, U/1 Days	Injection site reaction, Wrong technique in drug usage process, Medication error, Overdose, Injection site induration, Pyrexia	R
B0728595A	South Africa	HP,MD	2 Months/F	INJ	U	12Apr2011-12Apr2011	26Apr2011	U/14 Days	Injection site swelling, Injection site abscess, Discomfort	R
D0070911A	Germany	MD,RA	17 Months/M	INJ	U	01Jul2009-01Jul2009	01Jul2009	U/0 Days	Injection site swelling, Injection site erythema, Injection site warmth	U
#D0069419A	Germany	RA	2 Years/M	INJ	U	01Jan2006-01Jan2006	01Jan2006	U/Unknown	Injection site swelling*, Injection site erythema*, Injection site warmth*, Injection site pain*, Lymphadenopathy*, Injection site reaction*	N

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#D0069690A	Germany	MD,RP	18 Months/M	INJ	U	06Dec2010-06Dec2010	07Dec2010	U/1 Days	Injection site swelling, Injection site erythema, Sepsis	R
D0071985A	Germany	MD,RP	4 Months/M	INJ	U	07Jul2011-07Jul2011		U/Unknown	Injection site swelling, Injection site warmth, Injection site erythema, Injection site pain	R
D0072079A	Germany	MD,RP	30 Months/M	INJ	U	05Jul2011-05Jul2011		U/Unknown	Injection site swelling, Injection site warmth, Injection site erythema, Injection site pain	R
D0072080A	Germany	MD,RP	24 Months/M	INJ	U	04Jul2011-04Jul2011		U/Unknown	Injection site swelling, Injection site warmth, Injection site erythema, Injection site pain	R
D0072081A	Germany	MD,RP	3 Months/F	INJ	U	16Jun2011-16Jun2011		U/Unknown	Injection site swelling, Injection site warmth, Injection site erythema, Injection site pain	R
#B0741418A	Poland	MD,RA	19 Months/U	INJ	U	13Jul2011-13Jul2011	14Jul2011	U/1 Days	Injection site warmth, Injection site erythema, Injection site oedema, Extensive	R

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									swelling of vaccinated limb	
#B0709244A	Poland	MD,RA	26 Months/U	INJ	U	07Feb2011-07Feb2011	08Feb2011	U/1 Days	Injection site warmth, Injection site oedema, Injection site erythema	U
B0751948A	Poland	MD,RA	17 Months/U	SUS	U	13Jul2011-13Jul2011	14Jul2011	U/1 Days	Injection site warmth, Injection site oedema, Injection site erythema, Body temperature increased, Extensive swelling of vaccinated limb	U
#B0713570A	Poland	MD,RA	18 Months/U	INJ	U	01Mar2011-01Mar2011	02Mar2011	U/1 Days	Injection site warmth, Injection site oedema, Injection site erythema, Injection site pain, Restlessness, Body temperature increased	R
B0726162A	Poland	MD,RA	18 Months/M	INJ	U	23Mar2011-23Mar2011	24Mar2011	U/1 Days	Injection site warmth, Injection site reaction	R

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B0726175A	Poland	MD,RA	20 Months/U	INJ	U	22Mar2011-22Mar2011	22Mar2011	U/0 Days	Injection site warmth, Injection site reaction, Urticaria, Pyrexia	R
B0729606A	South Africa	HP	19 Months/M	INJ	U	08Jun2011-08Jun2011	08Jun2011	U/0 Days	Injection site warmth, Tenderness, Injection site nodule, Injection site induration, Injection site swelling, Injection site erythema, Injection site pain	I
B0729497A	France	MD	2 Months/M	INJ	U	27May2011-27May2011	29May2011	U/2 Days	Irritability, Crying, Middle insomnia	R
B0685920A	France	MD	4 Months/M	INJ, INJ	U, U	23Nov2010-23Nov2010, 23Nov2010-23Nov2010	23Nov2010	U/See text, U/See text	Irritability, Overdose, Wrong technique in drug usage process	R
#B0730845A	Italy	MD,RA	5 Months/F	INJ	U	16Jun2011-16Jun2011	16Jun2011	U/0 Days	Irritability, Pyrexia	R

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B0701338A	France	PH,MD	4 Months/M	INJ	U	21Feb2011-21Feb2011	21Feb2011	U/See text	Irritability, Sleep disorder, Pyrexia, Injection site induration, Nodule, Incorrect product storage	R
B0690212A	Netherlands	MD,RA	11 Months/F	INJ	U	12Apr2010-12Apr2010	01Apr2010	U/0 Days	Malaise, Abnormal behaviour, Pyrexia	R
B0708970A	Netherlands	HP,RA	4 Months/F	INJ	U	19Mar2009-19Mar2009	01Mar2009	U/1 Days	Malaise, Faeces discoloured, Crying, Pyrexia	U
B0732140A	Netherlands	HP,RA	4 Months/F	INJ	U	22Sep2010-22Sep2010	01Sep2010	U/3 Days	Malaise, Fatigue, Crying, Pyrexia, Diarrhoea, Nasopharyngitis, Somnolence	U
#B0689818A	France	RA	10 Weeks/F	INJ	U	23Nov2010-23Nov2010	23Nov2010	U/5 Hours	Malaise, Hypotonia	R
#B0716345A	France	RA	2 Months/F	INJ	U	22Feb2011-22Feb2011	22Feb2011	U/7 Hours	Malaise, Hypotonia, Cyanosis	R

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B0731042A	Netherlands	MD,RA	2 Months/M	INJ	U	12May2011-12May2011	12May2011	U/0 Days	Malaise, Ill-defined disorder	R
B0727512A	Netherlands	MD,RA	4 Months/F	INJ	U	18Aug2010-18Aug2010	18Aug2010	U/0 Days	Malaise, Injection site inflammation, Crying, Pyrexia, Somnolence	R
B0707085A	Netherlands	MD,RA	2 Months/M	INJ	U	03Nov2010-03Nov2010		U/Unknown	Malaise, Pallor, Insomnia, Pyrexia, Crying	R
B0711155A	Netherlands	HP,RA	5 Months/M	INJ	U	17Aug2010-17Aug2010	01Aug2010	U/4 Days	Malaise, Rash, Crying, Pyrexia	R
B0726560A	Sweden	HP,MD	3 Months/F	INJ, INJ	U, U	20Dec2010-20Dec2010, 01Oct2010-01Oct2010		U/Unknown, U/Unknown	Nodule, Injection site extravasation, Abscess, Erythema	U
B0692240A	Belgium	MD	3 Years/M	INJ, INJ	U, U	01Jan2008-01Jan2008, 1 Days		U/1 Years, U/During	No therapeutic response, Expired drug administered	U

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B0692241A	Belgium	MD	6 Years/F	INJ	U	22Jun2005-22Jun2005		U/3 Years	No therapeutic response, Expired drug administered	X
B0695165A	France	MD	2 Months/F	INJ, INJ	U, U	01Jan2010-01Jan2010, 01Jan2009-01Jan2009	01Jan2009	U/See text, U/9 Months	No therapeutic response, Incorrect dose administered	X
#B0744411A	France	PH,MD,RA	2 Months/F	INJ	U	25Aug2011-25Aug2011	25Aug2011	U/5 Days	Oedema, Diarrhoea, Vomiting, Urticaria, Transaminases increased, Drug administered to patient of inappropriate age, Papule, Crying, Pain	R
#B0700208A	France	RA	4 Months/M	INJ	U	24Sep2010-24Sep2010	25Sep2010	U/1 Days	Oedema, Extensive swelling of vaccinated limb, Skin warm, Pyrexia, Vomiting	R
D0072570A	Germany	MD,RA	30 Months/F	INJ	U	17Feb2011-17Feb2011	18Feb2011	U/1 Days	Oedema peripheral	R

#B0755892A	Czech Republic	MD,RA	3 Months/M	INJ	U	06Oct2011-06Oct2011	06Oct2011	U/10 Minutes	Oedema peripheral, Crying, Erythema, Skin discolouration	R
D0072932A	Germany	MD	2 Months/M	INJ	U	20Sep2011-20Sep2011	20Sep2011	U/2 Hours	Oedema peripheral, Erythema	R
#B0688647A	Slovakia	MD	5 Months/F	INJ	U	01Dec2010-01Dec2010	01Dec2010	U/2 Minutes	Oedema peripheral*, Erythema*	R
D0072448A	Germany	MD	2 Months/M	INJ, INJ	U, U	11Sep2009-11Sep2009, 27Oct2009-27Oct2009		U/Unknown, U/Unknown	Oedema peripheral, Erythema, Screaming	R
D0072142A	Germany	CO,MD	13 Months/F	INJ	U	20Jul2011-20Jul2011	21Jul2011	U/1 Days	Oedema peripheral, Haematoma	R
#B0691164A	Netherlands	HP,RA	7 Weeks/M	INJ	U	30Aug2010-30Aug2010	31Aug2010	U/25 Hours	Oedema peripheral*, Oedema peripheral*, Cardiac murmur*	R

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B0695380A	South Africa	HP	19 Months/M	INJ	.5ML	10Dec2010-10Dec2010	10Dec2010	U/Hours	Oedema peripheral, Oedema peripheral, Contusion, Induration, Contusion, Vomiting, Pyrexia	R
D0072585A	Germany	MD	11 Months/M	INJ	U	29Aug2011-29Aug2011	01Jan2011	U/Unknown	Oedema peripheral, Pain in extremity, Skin warm, Oedema peripheral, Pain in extremity, Skin discolouration	U
B0737868A	Netherlands	MD,RA	3 Months/F	INJ	U	14Jun2011-14Jun2011	14Jun2011	U/0 Days	Oedema peripheral, Pyrexia	U
#B0709202A	Italy	MD,RA	3 Months/M	INJ	U	06Aug2009-06Aug2009, 27May2010-27May2010	07Aug2009	U/1 Days, U/U	Oedema peripheral, Rash erythematous, Pain in extremity, Hyperaemia, Pallor, Cerumen impaction, Crying, Pyrexia	R
D0069390A	Germany	CO,MD	3 Months/M	INJ	U	28Oct2010-28Oct2010	31Oct2010	U/3 Days	Oedema peripheral, Screaming, Erythema, Haematoma, Pain	R

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#D0069502A	Germany	MD,RP	20 Months/F	INJ	.5ML	11Nov2010-11Nov2010	12Nov2010	U/1 Days	Oedema peripheral*, Sepsis*, Swelling*, Erythema*	R
B0724153A	Austria	MD	17 Months/U	INJ	U	11Apr2011-11Apr2011	12Apr2011	U/1 Days	Pain, Ill-defined disorder, Injection site swelling, Injection site erythema	U
B0724155A	Austria	MD	20 Months/U	INJ	U	14Apr2011-14Apr2011	15Apr2011	U/1 Days	Pain, Ill-defined disorder, Injection site swelling, Injection site erythema	U
B0724160A	Austria	MD	17 Months/U	INJ	U	17Apr2011-17Apr2011	18Apr2011	U/1 Days	Pain, Ill-defined disorder, Injection site swelling, Injection site erythema	U
#B0725047A	France	RA	2 Months/M	INJ	U	13May2011-13May2011	13May2011	U/Same day	Pyrexia	R
#B0738737A	Ireland	MD,RA	4 Months/M	INJ	.5ML	28Jun2011-28Jun2011	28Jun2011	U/8 Hours	Pyrexia	R

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#B0705446A	Italy	HP,RA	13 Months/M	INJ	U	25Jan2011-25Jan2011	25Jan2011	U/0 Days	Pyrexia	R
#B0692084A	Latvia	HP,RA	10 Months/F	INJ	U	02Nov2010-02Nov2010	03Nov2010	U/18 Hours	Pyrexia	R
#B0733016A	Latvia	HP,RA	4 Months/F	INJ	.5ML	02Jun2011-02Jun2011	02Jun2011	U/6 Hours	Pyrexia	R
#B0755542A	Latvia	HP,RA	19 Months/F	INJ	.5ML	09Sep2011-09Sep2011	09Sep2011	U/6 Hours	Pyrexia	R
#B0688816A	Poland	MD,RA	17 Months/U	INJ	U	17Nov2010-17Nov2010	19Nov2010	U/48 Hours	Pyrexia	R
#B0696766A	Poland	MD,RA	21 Months/U	INJ	U	05Jan2011-05Jan2011	05Jan2011	U/0 Days	Pyrexia	R

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#B0750972A	Poland	MD,RA	2 Months/U	INJ	U	04Aug2011-04Aug2011	04Aug2011	U/7 Hours	Pyrexia	R
#B0686714A	Spain	HP,RA	4 Months/F	INJ	U	16Sep2010-16Sep2010	16Sep2010	U/0 Days	Pyrexia	R
#D0072635A	Germany	RA	6 Months/M	INJ	.5ML	19May2011-19May2011	21May2011	U/2 Days	Pyrexia*	R
#B0684627A	Italy	MD,RA	5 Months/M	INJ	U	26Apr2010-26Apr2010	26Apr2010	U/0 Days	Pyrexia*	R
B0706993A	France	MD	2 Months/F	INJ	U	18Feb2011-18Feb2011	19Feb2011	U/1 Days	Pyrexia, Crying	R
#B0728225A	Namibia	HP	3 Months/F	INJ, INJ	U, U	01Jan2011-01Jan2011, 10Jun2011-10Jun2011		U/0 Days, U/Unknown	Pyrexia, Decreased appetite, Fluid intake reduced, Pyrexia, Diarrhoea	U

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#B0728546A	France	MD	2 Months/F	INJ	U	19May2011-19May2011	19May2011	U/7 Hours	Pyrexia, Decreased appetite, Somnolence, Fatigue	R
B0736206A	Netherlands	MD,RA	2 Months/M	INJ	U	12Jul2011-12Jul2011	12Jul2011	U/Hours	Pyrexia, Decreased appetite, Wrong drug administered, Overdose	U
#B0705783A	France	RA	6 Months/M	INJ, INJ	U, U	14Dec2010-14Dec2010, 14Aug2010-14Aug2010	14Aug2010	U/6 Hours, U/6 Hours	Pyrexia, Diarrhoea, Nausea, Vomiting, Inappropriate schedule of drug administration	R
D0070922A	Germany	HP	16 Months/F	INJ	U	06Apr2011-06Apr2011	06Apr2011	U/0 Days	Pyrexia, Ear infection, Bronchitis, Wrong technique in drug usage process, Incorrect route of drug administration	U
B0745305A	France	MD	3 Months/U	INJ, INJ	U, U	01Sep2010-01Sep2010, 01Aug2010-01Aug2010, 01Jul2010-01Jul2010	01Aug2010	U/Unknown, U/0 Days, U/U	Pyrexia, Erythema, Diarrhoea, Acne, Wrong drug administered	R

B0729547A	France	MD	26 Months/M	INJ	U	27Jun2011-27Jun2011	27Jun2011	U/See text	Pyrexia, Expired drug administered	R
#D0072494A	Germany	MD,RP	13 Weeks/M	INJ	.5ML	07Jul2011-07Jul2011, 09Jun2011-09Jun2011	07Jul2011	U/4 Hours, U/U	Pyrexia*, Fluid intake reduced*, Food aversion*	R
#B0704596A	Spain	P	4 Months/F	INJ	U	07Feb2011-07Feb2011	08Feb2011	U/1 Days	Pyrexia*, Gastroenteritis rotavirus*	R
B0722680A	France	MD	2 Months/F	INJ	U	25May2011-25May2011	25May2011	U/12 Hours	Pyrexia, Incorrect product storage	R
D0072069A	Germany	MD,RP	28 Months/M	INJ	U	28Jun2011-28Jun2011		U/0 Weeks	Pyrexia, Injection site erythema, Injection site swelling, Skin induration, Injection site pruritus	R

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#B0724988A	Latvia	HP,RA	2 Months/M	INJ	U	10May2011-10May2011	10May2011	U/7 Hours	Pyrexia, Injection site extravasation, Injection site erythema	R
D0070161A	Germany	MD	5 Months/F	INJ	U	24Jan2011-24Jan2011	25Jan2011	U/1 Days	Pyrexia, Injection site extravasation, Injection site erythema, Injection site swelling, Scab, Injection site haematoma	N
#B0740301A	Austria	MD,RA	1 Years/M	INJ	U	06Jul2011-06Jul2011	06Jul2011	U/10 Hours	Pyrexia, Injection site haematoma, Injection site erythema	R
B0727206A	Netherlands	MD,RA	13 Months/M	INJ	U	13Oct2010-13Oct2010	14Oct2010	U/24 Hours	Pyrexia, Injection site inflammation, Decreased appetite, Fibrosis	N
D0071584A	Germany	PH	25 Months/M	INJ, INJ	U, U	23May2011-23May2011, 01Jan2010-01Jan2010	01Jan2010	U/1 Days, U/Unknown	Pyrexia, Injection site pain, Eczema	I

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D0070985A	Germany	MD,RP	15 Months/M	INJ	U	08Apr2011-08Apr2011	09Apr2011	U/1 Days	Pyrexia, Injection site swelling, Hyperaesthesia, Flatulence, Abdominal pain, Cow's milk intolerance	N
#D0070119A	Germany	PH,MD	5 Months/M	INJ	U	21Jan2011-21Jan2011	21Jan2011	U/0 Days	Pyrexia, Injection site swelling, Pain in extremity, Screaming	U
D0070134A	Germany	PH,MD	5 Months/M	INJ	U	21Jan2011-21Jan2011	21Jan2011	U/0 Days	Pyrexia, Injection site swelling, Pain in extremity, Screaming	R
D0070136A	Germany	PH,MD	6 Months/F	INJ	U	25Jan2011-25Jan2011	25Jan2011	U/0 Days	Pyrexia, Injection site swelling, Pain in extremity, Screaming	U
D0070135A	Germany	PH	6 Months/F	INJ	U	25Jan2011-25Jan2011	25Jan2011	U/0 Days	Pyrexia, Injection site swelling, Pain in extremity, Screaming, Rash generalised	R

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B0710855A	Kenya	CO,HP	6 Weeks/U	INJ	.5ML	1 Days	U/Unknown	Pyrexia, Overdose	R
B0710871A	Kenya	CO,HP	6 Weeks/U	INJ	.5ML	1 Days	U/Unknown	Pyrexia, Overdose	R
B0710875A	Kenya	CO,HP	6 Weeks/U	INJ	.5ML	1 Days	U/Unknown	Pyrexia, Overdose	R
B0710876A	Kenya	CO,HP	6 Weeks/U	INJ	.5ML	1 Days	U/Unknown	Pyrexia, Overdose	R
B0710877A	Kenya	CO,HP	6 Weeks/U	INJ	.5ML	1 Days	U/Unknown	Pyrexia, Overdose	R
B0710878A	Kenya	CO,HP	6 Weeks/U	INJ	.5ML	1 Days	U/Unknown	Pyrexia, Overdose	R

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B0710879A	Kenya	CO,HP	6 Weeks/U	INJ	.5ML	1 Days		U/Unknown	Pyrexia, Overdose	R
B0708048A	France	MD	4 Months/M	INJ	U	23Mar2011-23Mar2011	23Mar2011	U/Same day	Pyrexia, Overdose, Wrong drug administered	R
D0070270A	Germany	MD	3 Months/F	INJ	U	10Feb2011-10Feb2011	10Feb2011	U/0 Days	Pyrexia, Restlessness, Accidental overdose	R
D0072493A	Germany	MD,RP	Child/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/0 Months	Pyrexia, Restlessness, Ill-defined disorder	U
D0072684A	Germany	MD,RP	Child/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/0 Months	Pyrexia, Restlessness, Ill-defined disorder	U
D0072685A	Germany	MD,RP	Child/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/0 Months	Pyrexia, Restlessness, Ill-defined disorder	U

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D0072686A	Germany	MD,RP	Child/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/0 Months	Pyrexia, Restlessness, Ill-defined disorder	U
D0072687A	Germany	MD,RP	Child/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/0 Months	Pyrexia, Restlessness, Ill-defined disorder	U
D0072688A	Germany	MD,RP	Child/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/0 Months	Pyrexia, Restlessness, Ill-defined disorder	U
D0072689A	Germany	MD,RP	Child/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/0 Months	Pyrexia, Restlessness, Ill-defined disorder	U
D0072690A	Germany	MD,RP	Child/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/0 Months	Pyrexia, Restlessness, Ill-defined disorder	U
D0072691A	Germany	MD,RP	Child/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/0 Months	Pyrexia, Restlessness, Ill-defined disorder	U

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D0072692A	Germany	MD,RP	Child/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/0 Months	Pyrexia, Restlessness, Ill-defined disorder	U
D0072693A	Germany	MD,RP	Child/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/0 Months	Pyrexia, Restlessness, Ill-defined disorder	U
D0072694A	Germany	MD,RP	Child/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/0 Months	Pyrexia, Restlessness, Ill-defined disorder	U
D0070466A	Germany	MD	4 Months/F	INJ	U	25Jul2007-25Jul2007	25Jul2007	U/0 Days	Pyrexia, Salmonellosis	R
#D0071783A	Germany	HP,RA	4 Months/M	INJ	U	07Jun2011-07Jun2011	07Jun2011	U/0 Days	Pyrexia, Vaccination complication	R
#B0705290A	France	OT,MD,RA	10 Months/M	INJ	U	07Mar2011-07Mar2011	07Mar2011	U/4 Hours	Sudden death, Pyrexia, Lymphadenopathy, Emphysema, Product quality issue,	F

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									Cardio-respiratory arrest, Asphyxia, Febrile convulsion	
#D0070324A	Germany	OM,MD,RP	3 Months/M	INJ	.5ML	18Jan2011-18Jan2011	23Jan2011	U/5 Days	Sudden infant death syndrome*, Death*, Vomiting*, Cardiomyopathy*	F
#B0688734A	France	RA	10 Weeks/F	INJ	U	09Nov2010-09Nov2010	10Nov2010	U/1 Days	Sudden infant death syndrome, Respiratory tract congestion, Cough, Nasal congestion	F
B0730530A	Austria	PH	U/U	INJ	U	1 Days		U/Unknown	Swelling, Erythema	U
B0686436A	France	PH	20 Months/F	INJ	U	01Nov2010-01Nov2010	01Nov2010	U/See text	Therapeutic response decreased, Incorrect product storage	X
D0070885A	Germany	MD	3 Months/F	INJ, INJ	U, U	14Feb2011-14Feb2011, 28Mar2011-28Mar2011	01Feb2011	U/2 Days, U/2 Days	Vaccination site induration, Vaccination site induration	I

Hepatobiliary disorders										
#B0736978A	Italy	RA	7 Years/F	INJ	U	14Jul2011-14Jul2011	14Jul2011	U/0 Days	Hypertransamina saemia, Vomiting	R
Immune system disorders										
#B0735456A	Italy	MD,RA	4 Months/M	INJ	U	12Jul2011-12Jul2011, 10May2011-10May2011	12Jul2011	U/0 Days, U/U	Allergy to vaccine, Urticaria, Pyrexia, Rash maculo-papular	R
#B0698663A	Italy	MD,RA	4 Months/M	INJ	U	01Feb2011-01Feb2011	01Feb2011	U/0 Days	Anaphylactic reaction, Circulatory collapse, Slow response to stimuli, Cyanosis, Hypotonia, Hypothermia, Pallor, Bradycardia, Oxygen saturation decreased, Pyrexia	R
#D0072050A	Germany	MD,RA,RP	3 Months/M	INJ	U	12Jul2011-12Jul2011	12Jul2011	U/0 Days	Anaphylactic reaction, Swelling, Erythema, Crying, Petechiae	R

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#D0071107A	Germany	MD	8 Months/M	INJ	U	10Jan2008-10Jan2008		U/Unknown	Anaphylactic shock	U
#B0741646A	Italy	MD,RA	2 Months/F	INJ	.5ML	17Aug2011-17Aug2011	17Aug2011	U/0 Days	Anaphylactic shock, Stridor, Respiratory disorder, Pulse pressure decreased, Heart rate increased, Crying	I
#B0680987A	Belgium	MD,RP	2 Months/F	INJ	U	20Oct2010-20Oct2010	20Oct2010	U/Minutes	Anaphylactic shock, Syncope, Apnoea, Bronchospasm, Blood pressure decreased, Pallor, Respiratory rate decreased, Crying, Hypoventilation	R
#D0072500A	Germany	PH,MD,RP, VR	13 Weeks/M	INJ	.5ML	24Aug2011-24Aug2011, 15Jun2011-15Jun2011	24Aug2011	U/5 Minutes, U/U	Anaphylactoid reaction*, Hypersensitivity*, Product quality issue, Urticaria*, Rash*, Apathy*, Anaphylactic reaction*, Erythema*, Petechiae*, Injection site erythema*	U

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#B0747751A	Czech Republic	MD,RA	4 Months/F	INJ	U	04Feb2010-04Feb2010	01Apr2010	U/2 Months	Hypersensitivity, Eye oedema, Rhinorrhoea, Pyrexia	U
#D0071600A	Germany	MD,RA	33 Months/M	INJ	U	17May2011-17May2011	19May2011	U/2 Days	Hypersensitivity, Injection site swelling, Injection site erythema, Injection site warmth	R
#B0743870A	France	RA	33 Months/M	INJ	U	26Aug2011-26Aug2011	26Aug2011	U/0 Days	Hypersensitivity, Pyrexia, Face oedema, Urticaria, Injection site inflammation	R
#B0683194A	Sweden	HP,RA	3 Months/M	INJ, INJ	U, .5ML	21Oct2010-21Oct2010, 01Jan2010-01Jan2010	26Aug2010	U/Unknown, U/20 Minutes	Hypersensitivity, Rash, Skin discolouration, Rash, Rash, Pyrexia	R
#D0072638A	Germany	RA	3 Months/F	INJ	.5ML	31Aug2011-31Aug2011	31Aug2011	U/0 Days	Hypersensitivity*, Swollen tongue*, Eyelid oedema*	R

Infections and infestations

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#D0070332A	Germany	RA	11 Months/M	INJ	U	06Aug2010-06Aug2010	28Sep2010	U/53 Days	Abscess	R
D0072966A	Germany	MD,RA	17 Months/M	INJ	.5ML	19Jan2011-19Jan2011	11Apr2011	U/82 Days	Abscess*	N
D0071349A	Germany	HP,RA	26 Months/F	INJ	U	15Oct2010-15Oct2010	11Apr2011	U/6 Months	Abscess, Granuloma	N
#D0072765A	Germany	RA	9 Months/F	INJ	.5ML	22Mar2011-22Mar2011, 18Jan2011-18Jan2011, 15Feb2011-15Feb2011	12Jul2011	U/3 Months, U/U, U/U	Abscess*, Haematoma*	R
D0072015A	Germany	PH,MD	4 Months/F	INJ, INJ	U, U	04May2011-04May2011, 22Jun2011-22Jun2011	04May2011	U/0 Days, U/0 Days	Abscess, Induration, Erythema, Abscess, Induration, Erythema, Product quality issue	S

#B0740389A	Italy	MD,RA	10 Months/F	INJ	U	29Jun2011-29Jun2011	30Jun2011	U/1 Days	Abscess limb, Pyrexia, Oedema peripheral, Erythema, Pain, Inflammation	I
#B0747749A	Czech Republic	MD,RA	6 Months/F	INJ	U	01Sep2010-01Sep2010, 01Aug2010-01Aug2010, 01Jul2010-01Jul2010	01Sep2010	U/0 Months, U/U, U/U	Bronchitis, Pyrexia	R
#B0713564A	Serbia	MD,RP	2 Years/M	INJ	U	08Apr2011-08Apr2011	10Apr2011	U/2 Days	Cellulitis, Erythema, Body temperature increased, Injection site swelling	N
#B0730177A	Spain	HP,RA	9 Months/F	INJ	U	22Feb2011-22Feb2011	01Mar2011	U/7 Days	Cellulitis, Streptococcal bacteraemia, Local reaction, Pyrexia	R
#B0687557A	Poland	MD,RA	11 Months/U	INJ	U	10Nov2010-10Nov2010	10Nov2010	U/0 Days	Ear infection, Injection site inflammation, Pyrexia, Vomiting	U
#B0692285A	France	RA	21 Months/F	INJ	U	08Dec2010-08Dec2010	08Dec2010	U/0 Days	Encephalitic infection, Convulsion, Dyskinesia, Fatigue, Pyrexia, Hypertonia,	U

									Depressed level of consciousness, Electroencephalogram abnormal	
#B0712285A	Austria	MD,RA	3 Years/F	INJ	U	08Mar2011-08Mar2011	09Mar2011	U/1 Days	Erysipelas, Erythema, Feeling hot, Swelling, Pyrexia	R
#B0735649A	Italy	MD,RA	5 Months/F	INJ	U	10May2011-10May2011, 08Mar2011-08Mar2011	26May2011	U/16 Days, U/U	Gastroenteritis, Convulsion, Central nervous system inflammation, Conjunctivitis, Cheilitis, Pyrexia, Rash papular, Viral rash	R
#B0714131A	Czech Republic	MD,RA	7 Months/M	INJ	U	30Nov2010-30Nov2010, 05Jan2011-05Jan2011, 01Feb2011-01Feb2011	16Feb2011	U/15 Days, U/U, U/U	Gastroenteritis rotavirus, Vaccination failure	R
#D0071047A	Germany	MD	12 Months/F	INJ	U	22Sep2010-22Sep2010	09Apr2011	U/6 Months	Gastroenteritis rotavirus, Vaccination failure, Gastroenteritis astroviral, Gastroenteritis Escherichia coli	R

#D0070948A	Germany	MD,RP	19 Months/M	INJ	U	21Jan2011-21Jan2011	01Mar2011	U/0 Years	Gastroenteritis rotavirus, Vaccination failure, Pyrexia, Vomiting, Diarrhoea, Ear infection	R
#B0684636A	Austria	MD	3 Months/M	INJ	U	18Oct2010-18Oct2010	22Oct2010	U/4 Days	Gastroenteritis rotavirus*, Vomiting, Rash, Diarrhoea, Viral rash	R
#D0069326A	Germany	MD	4 Months/M	INJ	U	1 Days		U/0 Months	Gastroenteritis staphylococcal, Diarrhoea, Vomiting, Pyrexia, Fatigue	U
#B0748231A	Czech Republic	MD,RA	4 Months/M	INJ	U	05Apr2011-05Apr2011, 28Feb2011-28Feb2011	11Apr2011	U/6 Days, U/U	Groin abscess, Abscess	N
#B0711894A	Australia	HP	28 Months/M	INJ, INJ, INJ, INJ	U, U, U, U	06Jan2009-06Jan2009, 02Mar2009-02Mar2009, 11May2009-11May2009, 10Nov2009-10Nov2009	17Mar2011	U/2 Years, U/2 Years, U/22 Months, U/16 Months	Haemophilus infection, Bacteraemia, Pharyngitis, Lethargy, Pyrexia, Dyspnoea, Vaccination failure	R

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#B0727263A	Australia	HP	10 Months/M	INJ	U	17Dec2010-17Dec2010, 17Sep2010-17Sep2010	30May2011	U/5 Months, U/U	Haemophilus infection, Irritability, Pyrexia, Abasia	R
#B0685659A	France	MD	2 Months/M	INJ	U	01Oct2010-01Oct2010	01Nov2010	U/10 Days	Herpes zoster	U
B0692979A	France	MD	18 Months/M	INJ	U	09Dec2010-09Dec2010	18Dec2010	U/9 Days	Herpes zoster	S
B0697049A	Sweden	HP,MD	3 Months/M	INJ, INJ	U, U	01Jan2010-01Jan2010, 17Jan2011-17Jan2011		U/1 Weeks, U/1 Weeks	Impetigo, Urticaria papular, Rash erythematous, Rash vesicular, Rash erythematous, Rash vesicular, Rash pruritic, Rash macular	U
B0705097A	Austria	MD	5 Years/F	INJ, INJ, INJ, INJ, INJ, INJ	U, U, U, U, U, U	01Feb2007-01Feb2007, 01May2007-01May2007, 01Jun2007-01Jun2007, 01Oct2007-01Oct2007, 01Jan2008-01Jan2008, 17Feb2011-17Feb2011	01Jan2009	U/0 Years, U/0 Years, U/0 Years, U/0 Years, U/1 Years, U/0 Months	Infection, Injection site swelling, Injection site erythema, Pyrexia, No therapeutic response	U

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B0756153A	Ecuador	MD,RP	4 Months/F	INJ	.5ML	01Jan2010-01Jan2010	U/1 Weeks	Injection site abscess	U
D0072769A	Germany	MD	4 Months/M	INJ	U	1 Days	U/2 Days	Injection site abscess	U
D0072948A	Germany	MD	4 Months/M	INJ	U	1 Days	U/2 Days	Injection site abscess	U
D0071422A	Germany	MD,RA	6 Months/F	INJ	U	28Jun2010-28Jun2010	U/3 Months	Injection site abscess, Injection site erythema, Injection site swelling, Foreign body reaction, Incision site abscess	S
D0071422B	Germany	MD,RA	14 Months/F	INJ	U	17Feb2011-17Feb2011	U/6 Weeks	Injection site abscess, Injection site inflammation, Injection site swelling, Foreign body reaction, Incision site abscess	S

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#B0718957A	France	MD	2 Months/M	INJ	U	1 Days		U/Unknown	Injection site abscess, Injection site nodule, Injection site erythema	R
#B0686567A	Czech Republic	MD,RA	9 Months/U	INJ	U	13Oct2010-13Oct2010	01Oct2010	U/16 Days	Injection site abscess, Injection site oedema, Injection site swelling	R
B0747623A	Belgium	MD,RP	6 Months/M	INJ	U	U	10Sep2011	U/Unknown	Injection site cellulitis, Extensive swelling of vaccinated limb, Injection site oedema	U
#B0696664A	France	RA	17 Months/M	INJ	U	29Dec2010-29Dec2010	30Dec2010	U/1 Days	Injection site infection, Erythema, Oedema, Feeling hot, C-reactive protein increased	R
B0683076A	Poland	MD,RA	21 Months/U	INJ	U	14Apr2010-14Apr2010	14Apr2010	U/0 Days	Injection site pustule, Body temperature increased, Injection site erythema, Injection site pain, Injection site oedema	R

D0069888A	Germany	MD	U/F	INJ	U	01Jan2005-01Jan2005	01Jan2005	U/1 Days	Labyrinthitis, Gait disturbance, Balance disorder	R
#B0741331A	South Africa	HP	16 Weeks/U	INJ	U	1 Days		U/10 Days	Meningitis	U
#B0714940A	France	RA	4 Months/F	INJ	U	26Mar2011-26Mar2011	30Mar2011	U/4 Days	Meningitis aseptic	R
#B0711853A	Australia	HP	11 Months/M	INJ, INJ, INJ	U, U, U	18May2010-18May2010, 04Aug2010-04Aug2010, 21Oct2010-21Oct2010	05Mar2011	U/10 Months, U/7 Months, U/4 Months	Meningitis haemophilus, Bacteraemia, Vaccination failure	R
#B0727262A	Australia	HP	11 Months/F	INJ, INJ, INJ	U, U, U	16Nov2010-16Nov2010, 18Jan2011-18Jan2011, 31Aug2010-31Aug2010	28May2011	U/9 Months, U/6 Months, U/4 Months	Meningitis haemophilus, Pyrexia, Headache, Lethargy, Decreased appetite, Vomiting, Vaccination failure	R

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#B0685610A	Andorra	RA,RP	10 Months/M	INJ, INJ	U, U	04Feb2010-04Feb2010, 04Jun2010-04Jun2010	17Nov2010	U/9 Months, U/5 Months	Meningitis haemophilus, Vaccination failure	R
#B0735156A	South Africa	MD	3 Years/F	INJ, INJ, INJ, INJ	U, U, U, U	12Sep2007-12Sep2007, 10Oct2007-10Oct2007, 07Nov2007-07Nov2007, 08Jan2009-08Jan2009	05Jun2011	U/4 Years, U/4 Years, U/4 Years, U/2 Years	Meningitis haemophilus, Vaccination failure	R
#D0072024A	Germany	MD,RA	3 Months/M	INJ	U	24May2011-24May2011	25May2011	U/1 Days	Meningitis pneumococcal, Gastroenteritis rotavirus, Respiratory syncytial virus infection, Pneumococcal sepsis, Pharyngitis, Somnolence, Pyrexia, Fluid intake reduced, Respiration abnormal, Crying, Diarrhoea, Cardiovascular insufficiency, Pallor, Tachypnoea, Anaemia, Thrombocytosis	U

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#D0069889A	Germany	OM,MD	4 Months/M	INJ	U	01Oct2010-01Oct2010	04Oct2010	U/3 Days	Meningitis pneumococcal, Grand mal convulsion, Epilepsy, Hydrocephalus, Subdural hygroma, Subdural empyema, Anaemia, Generalised oedema, Ileus paralytic, Conjunctivitis, Septic shock, Pneumonia primary atypical, Neurosurgery, Pyrexia, Abdominal distension, Ill-defined disorder, Restlessness, Hyperaesthesia, Oligodipsia, Eye movement disorder, Hypertonia, Tachycardia, Oxygen saturation decreased, Ascites, Respiratory arrest, Drug	N

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									ineffective, Cyanosis, Splenomegaly	
#B0700040A	Sweden	CO,HP	9 Months/F	INJ	U	20May2010-20May2010, 17Aug2010-17Aug2010	26Nov2010	U/101 Days, U/U	Meningitis, Sepsis, Shock, Pneumococcal infection, Renal impairment, Hepatic function abnormal, Pyrexia, Diarrhoea, Vomiting	F
#B0683335A	Netherlands	HP,RA	2 Months/M	INJ	U	13Sep2010-13Sep2010	13Sep2010	U/3 Minutes	Meningitis viral, Convulsion, Yellow skin, Cyanosis, Dehydration, Diarrhoea, Somnolence, Crying, Vomiting	F
B0719600A	Netherlands	HP,RA	11 Months/F	INJ	U	04Oct2010-04Oct2010	04Oct2010	U/4 Hours	Nasopharyngitis, Insomnia, Injection site haematoma, Injection site inflammation, Injection site pain, Pyrexia, Crying	R

#D0069814A	Germany	MD,RA	9 Weeks/M	INJ	.5ML	29Oct2010-29Oct2010	03Nov2010	U/5 Days	Osteomyelitis*, Bone abscess*	R
#D0070068A	Germany	RA	11 Months/M	INJ, INJ	U, U	13Dec2007-13Dec2007, 04Mar2008-04Mar2008	01Mar2008	U/2 Months, U/0 Months	Otitis media	N
#B0748257A	Czech Republic	MD,RA	4 Months/M	INJ	U	01Dec2010-01Dec2010		U/Unknown	Otitis media, Increased upper airway secretion, Snoring, Mucous membrane disorder, Lymphadenopathy	U
#D0069222A	Germany	MD	11 Months/M	INJ, INJ, INJ	U, U, U	14Jan2010-14Jan2010, 11Feb2010-11Feb2010, 26Apr2010-26Apr2010	04May2010	U/110 Days, U/82 Days, U/8 Days	Pertussis	R
D0070831A	Germany	MD	Child/U	INJ	U	1 Days		U/Unknown	Pertussis	U

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D0071749A	Germany	HP,RA	5 Months/F	INJ	U	26Apr2011-26Apr2011	27Apr2011	U/1 Days	Pertussis	R
D0072909A	Germany	PH	4 Years/U	INJ	U	U		U/U	Pertussis	U
#D0072273A	Germany	MD,RP	5 Months/M	INJ, INJ	U, U	15Jun2011-15Jun2011, 08Apr2011-08Apr2011	27Jun2011	U/80 Days, U/12 Days	Pertussis, Choking, Cyanosis, Apnoea, Bronchopneumonia, Cough, Vomiting	N
#D0069277A	Germany	MD,RP	5 Years/F	INJ, INJ, INJ, INJ	U, U, U, U	19Oct2006-19Oct2006, 03Jan2006-03Jan2006, 29Nov2005-29Nov2005, 25Oct2005-25Oct2005	01Aug2010	U/3 Years, U/4 Years, U/4 Years, U/4 Years	Pertussis*, Cough*, Cough*, Vomiting*, Rhinitis*, Decreased appetite*, Weight decreased*, Vaccination failure*	R
#D0071988A	Germany	MD,RP	2 Years/F	INJ, INJ, INJ, INJ	U, U, U, U	04Sep2009-04Sep2009, 06Oct2009-06Oct2009, 15Jul2010-15Jul2010, 07Aug2009-07Aug2009	01Jul2011	U/23 Months, U/22 Months, U/21 Months, U/12 Months	Pertussis, Cough, Vaccination failure	I

#D0072008A	Germany	MD,RP	8 Years/F	INJ, INJ, INJ, INJ	U, U, U, U	15Jan2003-15Jan2003, 25Feb2003-25Feb2003, 25Mar2003-25Mar2003, 03Nov2003-03Nov2003	05Jul2011	U/8 Years, U/8 Years, U/8 Years, U/7 Years	Pertussis, Cough, Vaccination failure	I
#D0072212A	Germany	MD,RA	6 Years/M	INJ	U	06Apr2006-06Apr2006	14Jul2011	U/5 Years	Pertussis, Cough, Vaccination failure	I
#D0072947A	Germany	HP,RA	3 Years/M	INJ, INJ, INJ, INJ	U, U, U, U	18Dec2007-18Dec2007, 30Jan2008-30Jan2008, 04Apr2008-04Apr2008, 26Nov2008-26Nov2008	01Aug2011	U/3 Years, U/3 Years, U/3 Years, U/2 Years	Pertussis, Cough, Vaccination failure	U
#D0072725A	Germany	MD	6 Months/M	INJ, INJ, INJ	U, U, U	05Apr2011-05Apr2011, 03May2011-03May2011, 31May2011-31May2011	05Jul2011	U/91 Days, U/63 Days, U/35 Days	Pertussis, Cough, Vomiting, Vaccination failure	I
#B0745561A	Switzerland	MD	9 Months/F	INJ, INJ, INJ	U, U, U	05Jan2011-05Jan2011, 08Mar2011-08Mar2011, 24May2011-24May2011	09Aug2011	U/7 Months, U/5 Months, U/77 Days	Pertussis, Cyanosis, Cough, Pyrexia, Vaccination failure	I
#D0072016A	Germany	MD	31 Months/F	INJ, INJ, INJ, INJ	U, U, U, U	30Mar2009-30Mar2009, 30Apr2009-30Apr2009, 25Jun2009-25Jun2009, 12Jan2010-12Jan2010	07Jul2011	U/2 Years, U/2 Years, U/24 Months, U/17 Months	Pertussis, Pertussis, Vomiting, Rhinitis, Vaccination failure	U

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D0072007A	Germany	MD,RP	6 Months/F	INJ, INJ, INJ	U, U, U	29Mar2011-29Mar2011, 03May2011-03May2011, 31May2011-31May2011	29Jun2011	U/92 Days, U/57 Days, U/29 Days	Pertussis, Pyrexia, Cough, Rhinitis, Lymphadenopathy	U
#B0735430A	South Africa	HP	18 Months/F	INJ	U	U		U/Unknown	Pertussis, Sneezing, Post-tussive vomiting, Rhinorrhoea, Respiratory syncytial virus infection, Pyrexia, Cough, Vaccination failure	U
#B0687509A	Austria	MD	5 Years/F	INJ	U	1 Days		U/Unknown	Pertussis, Vaccination failure	U
#D0069221A	Germany	MD	2 Years/M	INJ	U	17Dec2008-17Dec2008	06Sep2010	U/21 Months	Pertussis, Vaccination failure	R
#D0069673A	Germany	MD,RP	1 Years/M	INJ	U	01Jul2010-01Jul2010	01Jan2010	U/0 Years	Pertussis, Vaccination failure	I

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#D0069696A	Germany	MD,RP	12 Years/M	INJ	U	1 Days		U/Unknown	Pertussis, Vaccination failure	I
#D0069697A	Germany	MD,RP	7 Years/M	INJ	U	1 Days		U/Unknown	Pertussis, Vaccination failure	I
#D0069698A	Germany	MD,RP	Adult/F	INJ	U	1 Days		U/Unknown	Pertussis, Vaccination failure	I
#D0069825A	Germany	MD,RP	3 Years/F	INJ, INJ, INJ, INJ	U, U, U, U	10Dec2007-10Dec2007, 26Jan2008-26Jan2008, 25Sep2008-25Sep2008, 24Oct2007-24Oct2007	01Aug2010	U/3 Years, U/3 Years, U/2 Years, U/23 Months	Pertussis, Vaccination failure	R
#D0070091A	Germany	MD	11 Months/F	INJ, INJ, INJ	U, U, U	20May2010-20May2010, 04Mar2010-04Mar2010, 22Apr2010-22Apr2010	20Oct2010	U/8 Months, U/6 Months, U/5 Months	Pertussis, Vaccination failure	R
#D0070092A	Germany	MD	5 Years/U	INJ, INJ, INJ, INJ	U, U, U, U	25Oct2005-25Oct2005, 22Nov2005-22Nov2005, 20Dec2005-20Dec2005, 03Apr2007-03Apr2007	20Oct2010	U/5 Years, U/5 Years, U/5 Years, U/4 Years	Pertussis, Vaccination failure	R

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#D0070099A	Germany	RA	9 Years/F	INJ, INJ, INJ, INJ	U, U, U, U	29Oct2001-29Oct2001, 07Dec2001-07Dec2001, 17Jan2002-17Jan2002, 1 Days	08Nov2010	U/9 Years, U/9 Years, U/9 Years, U/Unknown	Pertussis, Vaccination failure	U
#D0070108A	Germany	HP	4 Years/M	INJ, INJ, INJ, INJ	U, U, U, U	01Sep2006-01Sep2006, 13Oct2006-13Oct2006, 09Nov2006-09Nov2006, 27Jul2007-27Jul2007	01Jan2010	U/4 Years, U/4 Years, U/4 Years, U/3 Years	Pertussis, Vaccination failure	U
#D0070132A	Germany	HP	4 Years/M	INJ, INJ, INJ, INJ	U, U, U, U	18Jul2006-18Jul2006, 16Aug2006-16Aug2006, 05Oct2006-05Oct2006, 08Jun2007-08Jun2007	01Jan2010	U/4 Years, U/4 Years, U/4 Years, U/3 Years	Pertussis, Vaccination failure	U
#D0070264A	Germany	MD,RP	Child/U	INJ	U	1 Days		U/Unknown	Pertussis, Vaccination failure	U
#D0070268A	Germany	MD,RP	Child/U	INJ	U	1 Days		U/Unknown	Pertussis, Vaccination failure	U
#D0071806A	Germany	MD,RP	8 Years/F	INJ	U	1 Days	01Jun2011	U/Unknown	Pertussis, Vaccination failure	R

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#D0072784A	Germany	MD,RP	6 Years/F	INJ	U	1 Days	17Aug2011	U/Unknown	Pertussis, Vaccination failure	U
#D0072839A	Germany	MD,RP	Child/M	INJ	U	1 Days		U/3 Years	Pertussis, Vaccination failure	U
#D0072968A	Germany	MD,RA	5 Months/M	INJ, INJ, INJ	U, U, U	15Dec2010-15Dec2010, 19Jan2011-19Jan2011, 03Feb2011-03Feb2011	01Apr2011	U/107 Days, U/72 Days, U/57 Days	Pertussis, Vaccination failure	U
#D0073001A	Germany	MD	6 Years/M	INJ, INJ, INJ, INJ	U, U, U, U	16Aug2005-16Aug2005, 20Sep2005-20Sep2005, 18Oct2005-18Oct2005, 25Jul2006-25Jul2006	21Jul2011	U/6 Years, U/5 Years, U/5 Years, U/5 Years	Pertussis, Vaccination failure	U
#D0073013A	Germany	HP,RA	5 Years/F	INJ, INJ, INJ, INJ	U, U, U, U	01Jun2006-01Jun2006, 01Sep2006-01Sep2006, 01Dec2006-01Dec2006, 01Apr2007-01Apr2007	12Sep2011	U/5 Years, U/5 Years, U/4 Years, U/4 Years	Pertussis, Vaccination failure	N
#D0073015A	Germany	HP,RA	27 Months/F	INJ	U	01Aug2009-01Aug2009	26Sep2011	U/2 Years	Pertussis, Vaccination failure	N

#B0682709A	Australia	MD,RP	9 Years/F	INJ, INJ, INJ, INJ	U, U, U, U	1 Days, 1 Days, 1 Days, 1 Days		U/Unknown, U/Unknown, U/Unknown, U/Unknown	Pertussis, Vaccination failure, Bordetella test negative	U
#D0071888A	Germany	MD,RP	4 Years/M	INJ, INJ, INJ, INJ	U, U, U, U	20Sep2007-20Sep2007, 20Nov2007-20Nov2007, 23Oct2007-23Oct2007, 30Jun2008-30Jun2008	01May2011	U/4 Years, U/4 Years, U/4 Years, U/3 Years	Pertussis, Vaccination failure, Cough, Infection	R
#D0070138A	Germany	HP	5 Years/F	INJ, INJ, INJ, INJ	U, U, U, U	31May2005-31May2005, 11Aug2005-11Aug2005, 08Sep2005-08Sep2005, 24Apr2006-24Apr2006	11Aug2005	U/5 Years, U/0 Days, U/5 Years, U/4 Years	Pertussis, Vaccination failure, Inappropriate schedule of drug administration	U
#D0071587A	Germany	MD	9 Months/F	INJ, INJ, INJ	U, U, U	18Aug2010-18Aug2010, 13Oct2010-13Oct2010, 15Sep2010-15Sep2010	21Mar2011	U/7 Months, U/6 Months, U/5 Months	Pertussis, Vaccination failure, Pertussis	N
D0071872A	Germany	MD	8 Months/F	INJ, INJ	U, U	03Mar2011-03Mar2011, 28Apr2011-28Apr2011	20Jun2011	U/3 Months, U/2 Months	Purulent discharge, Injection site erythema	I
#B0685226A	Netherlands	HP,RA	11 Months/F	INJ	U	27Jul2010-27Jul2010	28Jul2010	U/1 Days	Pyelonephritis, Urinary tract infection, Oligodipsia, Oliguria, C-reactive protein	U

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									increased, Escherichia infection, Pyrexia, Crying, Decreased appetite	
#B0712429A	Czech Republic	MD	7 Months/F	INJ	U	01Mar2011-01Mar2011, 27Jan2011-27Jan2011	01Mar2011	U/0 Days, U/U	Salmonella sepsis, Rash generalised, Pyrexia, Diarrhoea, Drug hypersensitivity, Hypersensitivity	R
#B0707174A	France	RA	21 Months/M	INJ	U	25Nov2010-25Nov2010	01Dec2010	U/0 Weeks	Staphylococcal abscess, Injection site abscess, Pyrexia, Injection site swelling, Leukocytosis, C-reactive protein increased, Injection site inflammation	R
#B0698641A	Czech Republic	MD	3 Months/M	INJ	U	03Jan2011-03Jan2011	01Jan2011	U/1 Weeks	Staphylococcal abscess, Streptococcal abscess, Injection site abscess	R
#B0698651A	Czech Republic	MD	4 Months/M	INJ	U	03Jan2011-03Jan2011, 1 Days	01Jan2011	U/2 Weeks, U/U	Staphylococcal abscess, Streptococcal abscess, Injection site abscess	R

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B0698608A	Poland	MD,RA	20 Months/M	INJ	U	14Dec2010-14Dec2010	15Dec2010	U/1 Days	Tonsillitis, Injection site extravasation, Injection site erythema, Pyrexia	U
D0069721A	Germany	MD	18 Months/F	INJ	U	06Dec2010-06Dec2010, 07Sep2010-07Sep2010	06Dec2010	U/0 Days, U/U	Tonsillitis, Pyrexia, Incorrect dose administered	U
#B0716727A	Austria	MD	Infant/M	INJ	U	19Apr2011-19Apr2011	20Apr2011	U/1 Days	Transmission of an infectious agent via a medicinal product, Pain, Ill-defined disorder, Injection site erythema, Injection site swelling, Product quality issue	U
#B0696094A	Poland	P	2 Months/M	INJ	U	02Nov2010-02Nov2010	03Nov2010	U/1 Days	Urinary tract infection*	R
#D0069935A	Germany	MD	35 Months/M	INJ	U	18Jul2009-18Jul2009	13Dec2010	U/16 Months	Varicella*, Papule*, Rash vesicular*, Scab*, Vaccination failure*	R

#B0728665A	Netherlands	HP,RA	3 Months/M	INJ	U	14Oct2010-14Oct2010	14Oct2010	U/8 Hours	Viral infection, Petechiae, Pyrexia, Vomiting	R
#D0070215A	Germany	MD,RP	8 Months/M	INJ	U	06Jan2011-06Jan2011	26Jan2011	U/20 Days	Viral rash, Rash generalised, Hepatosplenomegaly, Upper respiratory tract infection	N
Injury, poisoning and procedural complications										
B0730790A	France	MD	Adult/F	INJ	U	30Jun2011-30Jun2011	30Jun2011	U/See text	Accidental exposure	X
B0700347A	France	MD	2 Months/F	INJ	U	1 Days		U/See text	Accidental overdose	X
B0720905A	France	PH	3 Years/M	INJ	U	19May2011-19May2011	19May2011	U/See text	Accidental overdose	X

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D0070893A	Germany	MD	17 Years/F	INJ	U	05May2008-05May2008	05May2008	U/0 Days	Accidental overdose	X
B0741664A	France	MD	14 Months/F	INJ	U	20Aug2011-20Aug2011, 20Aug2011-20Aug2011	20Aug2011	U/Same day, U/Same day	Accidental overdose, Pyrexia	R
B0700269A	South Africa	HP	5 Months/F	INJ, INJ	U, U	11Feb2011-11Feb2011, 11Feb2011-11Feb2011	11Feb2011	U/See text, U/See text	Accidental overdose, Wrong technique in drug usage process	X
B0705307A	France	MD	3 Months/M	INJ	U	23Dec2010-23Dec2010	23Dec2010	U/See text	Drug administered to patient of inappropriate age	X
B0706474A	France	PH	1 Months/M	INJ	U	01Mar2011-01Mar2011	01Mar2011	U/See text	Drug administered to patient of inappropriate age	X
B0708594A	France	MD	3 Years/U	INJ, INJ	U, U	01Sep2008-01Sep2008, 01Dec2008-01Dec2008	01Sep2008	U/See text, U/See text	Drug administered to patient of inappropriate age	X

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B0743865A	France	MD	5 Weeks/M	INJ	U	30Aug2011-30Aug2011	30Aug2011	U/See text	Drug administered to patient of inappropriate age	X
B0756536A	Belgium	MD	20 Months/U	INJ	U	05Oct2011-05Oct2011, 28Aug2011-28Aug2011	05Oct2011	U/During, U/U	Drug administration error	X
B0698939A	France	MD	1 Months/U	INJ	U	01Dec2010-01Dec2010	01Dec2010	U/See text	Drug administration error	X
B0711341A	France	MD	7 Weeks/U	INJ	U	1 Days		U/See text	Drug administration error	X
B0718226A	France	MD	5 Weeks/U	INJ	U	01Apr2011-01Apr2011	01Apr2011	U/See text	Drug administration error	X
B0725884A	France	MD	6 Weeks/U	INJ	U	09Jun2011-09Jun2011	09Jun2011	U/See text	Drug administration error	X

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B0735279A	France	MD	6 Weeks/M	INJ	U	21Jun2011-21Jun2011	21Jun2011	U/See text	Drug administration error	X
B0735351A	France	MD	6 Weeks/U	INJ	U	22Jun2011-22Jun2011	22Jun2011	U/See text	Drug administration error	X
B0741923A	France	MD	5 Weeks/U	INJ	U	08Aug2011-08Aug2011	08Aug2011	U/See text	Drug administration error	X
B0742889A	France	MD	1 Months/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/See text	Drug administration error	X
B0745772A	France	MD	1 Months/U	INJ	U	01Aug2011-01Aug2011	01Aug2011	U/See text	Drug administration error	X
B0755871A	France	HP	4 Weeks/U	INJ	U	05Sep2011-05Sep2011	05Sep2011	U/See text	Drug administration error	X

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D0070350A	Germany	MD	7 Years/F	INJ	U	01Apr2009-01Apr2009	01Apr2009	U/0 Days	Drug administration error	X
D0071025A	Germany	MD	1 Months/F	INJ	U	1 Days		U/During	Drug administration error	X
D0071150A	Germany	MD,RP	1 Months/F	INJ	U	07Feb2011-07Feb2011	07Feb2011	U/0 Days	Drug administration error	X
D0071390A	Germany	MD	Neonate/M	INJ	U	10May2011-10May2011	10May2011	U/During	Drug administration error	X
D0071673A	Germany	MD	4 Weeks/F	INJ	U	24Feb2011-24Feb2011	24Feb2011	U/0 Days	Drug administration error	X
B0690209A	France	MD	8 Weeks/F	INJ, INJ	U, U	30Nov2010-30Nov2010, 20Dec2010-20Dec2010	30Nov2010	U/See text, U/See text	Drug administration error, Inappropriate schedule of drug administration	X

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B0735329A	France	MD	7 Weeks/M	INJ, INJ	U, U	13Jul2010-13Jul2010, 27Feb2010-27Feb2010, 15Jun2010-15Jun2010	27Feb2010	U/See text, U/See text, U/U	Drug administration error, Inappropriate schedule of drug administration	X
D0072087A	Germany	MD,RP	4 Months/F	INJ	U	15Jul2011-15Jul2011	15Jul2011	U/0 Days	Drug administration error, Wrong technique in drug usage process, Incorrect route of drug administration	X
B0732003A	Australia	MD	4 Months/U	INJ	U	27Jun2011-27Jun2011	03Jun2011	U/During	Expired drug administered	X
B0752903A	Australia	HP	Infant/U	INJ	U	18Sep2011-18Sep2011	18Sep2011	U/During	Expired drug administered	X
A0947255A	Canada	HP	8 Weeks/F	INJ	U	27Sep2011-27Sep2011	27Sep2011	U/See text	Expired drug administered	X

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B0733807A	France	MD	Infant/U	INJ	U	23May2011-23May2011	23May2011	U/See text	Expired drug administered	X
B0731311A	Ireland	MD	6 Months/M	INJ	U	20May2011-20May2011	20May2011	U/During	Expired drug administered	X
B0731312A	Ireland	MD	6 Months/F	INJ	U	20May2011-20May2011	20May2011	U/During	Expired drug administered	X
B0680981A	France	PH	9 Months/M	INJ	U	01Oct2010-01Oct2010	01Oct2010	U/See text	Inappropriate schedule of drug administration	X
B0683449A	France	MD	10 Months/U	INJ	U	03Jun2010-03Jun2010	03Jun2010	U/See text	Inappropriate schedule of drug administration	X
B0691618A	France	MD	12 Months/U	INJ	U	01Dec2010-01Dec2010, 01Jan2010-01Jan2010, 01Jan2010-01Jan2010	01Dec2010	U/See text, U/U, U/U	Inappropriate schedule of drug administration	X

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B0696263A	France	MD	10 Months/M	INJ	U	26Jan2011-26Jan2011, 19Jul2010-19Jul2010, 06May2010-06May2010	26Jan2011	U/See text, U/U, U/U	Inappropriate schedule of drug administration	X
B0698753A	France	MD	6 Months/M	INJ	U	15Feb2010-15Feb2010, 02Oct2009-02Oct2009, 16Dec2009-16Dec2009	15Feb2010	U/See text, U/U, U/U	Inappropriate schedule of drug administration	X
B0704539A	France	PH	2 Months/U	INJ	U	04Mar2011-04Mar2011, 18Feb2011-18Feb2011	04Mar2011	U/See text, U/U	Inappropriate schedule of drug administration	X
B0707438A	France	MD	9 Months/F	INJ	U	23Aug2010-23Aug2010	23Aug2010	U/See text	Inappropriate schedule of drug administration	X
B0713996A	France	MD	4 Months/M	INJ	U	18Apr2011-18Apr2011, 18Feb2011-18Feb2011	18Apr2011	U/See text, U/U	Inappropriate schedule of drug administration	X
B0719764A	France	MD	14 Months/F	INJ	U	16May2011-16May2011	16May2011	U/See text	Inappropriate schedule of drug administration	X

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B0727092A	France	MD	9 Months/M	INJ	U	05Nov2010-05Nov2010	05Nov2010	U/See text	Inappropriate schedule of drug administration	X
B0735327A	France	MD	Infant/U	INJ	U	30Jun2011-30Jun2011	30Jun2011	U/See text	Inappropriate schedule of drug administration	X
B0735328A	France	MD	5 Months/M	INJ	U	01Oct2010-01Oct2010	01Oct2010	U/See text	Inappropriate schedule of drug administration	X
B0748243A	France	MD	13 Months/M	INJ	U	03Aug2011-03Aug2011, 07Sep2010-07Sep2010, 10Nov2010-10Nov2010	03Aug2011	U/See text, U/U, U/U	Inappropriate schedule of drug administration	X
B0750549A	France	MD	3 Years/U	INJ	U	04Jan2011-04Jan2011	04Jan2011	U/See text	Inappropriate schedule of drug administration	X
D0069396A	Germany	MD,RP	6 Months/F	INJ	U	09Nov2010-09Nov2010, 18Oct2010-18Oct2010	09Nov2010	U/0 Days, U/U	Inappropriate schedule of drug administration	X

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D0069403A	Germany	MD	6 Months/M	INJ	U	1 Days		U/0 Days	Inappropriate schedule of drug administration	X
B0707392A	France	MD,RP	2 Months/F	INJ	U	19Mar2011-19Mar2011, 12Mar2011-12Mar2011	19Mar2011	U/See text, U/U	Inappropriate schedule of drug administration, Decreased appetite, Weight decreased	U
B0702048A	France	MD	3 Months/F	INJ	U	27Jan2011-27Jan2011, 04Jan2011-04Jan2011	27Jan2011	U/See text, U/U	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	X
B0713125A	France	MD,RP	7 Months/M	INJ	U	06Apr2011-06Apr2011	06Apr2011	U/See text	Inappropriate schedule of drug administration, Incorrect route of drug administration	X
B0703975A	France	MD	3 Months/U	INJ	U	03Aug2009-03Aug2009, 15Jul2009-15Jul2009	03Aug2009	U/See text, U/U	Inappropriate schedule of drug administration, Wrong drug administered	X
B0682314A	France	MD	Infant/U	INJ	U	1 Days		U/See text	Incorrect dose administered	X

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B0687936A	France	MD	Infant/U	INJ, INJ	U, U	28May2010-28May2010, 20Jul2010-20Jul2010, 20Oct2009-20Oct2009, 08Jan2010-08Jan2010	28May2010	U/See text, U/See text, U/U, U/U	Incorrect dose administered	X
B0698031A	France	MD	18 Months/M	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/See text	Incorrect dose administered	X
B0703977A	France	MD	6 Months/U	INJ	U	04Mar2011-04Mar2011, 07Jan2011-07Jan2011	04Mar2011	U/See text, U/U	Incorrect dose administered	X
B0705846A	France	MD,RP	5 Months/F	INJ	U	01Jan2010-01Jan2010	01Jan2011	U/See text	Incorrect dose administered	X
B0711997A	France	MD	7 Months/F	INJ	U	1 Days, 1 Days, 1 Days		U/See text, U/U, U/U	Incorrect dose administered	X
B0712293A	France	MD	1 Years/U	INJ	U	01Jan2010-01Jan2010	01Aug2009	U/See text	Incorrect dose administered	X

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B0719605A	France	CO,MD	5 Months/M	INJ	U	16May2011-16May2011	16May2011	U/See text	Incorrect dose administered	X
B0728502A	France	MD	8 Months/M	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/See text	Incorrect dose administered	X
B0729496A	France	HP	5 Months/U	INJ	U	24Jun2011-24Jun2011	24Jun2011	U/See text	Incorrect dose administered	X
B0745443A	France	MD	11 Months/F	INJ	U	03Sep2011-03Sep2011, 13May2011-13May2011, 16Feb2011-16Feb2011	03Sep2011	U/See text, U/U, U/U	Incorrect dose administered	X
B0746444A	France	MD	5 Months/U	INJ	U	25Jul2011-25Jul2011, 01Jun2011-01Jun2011	25Jul2011	U/See text, U/U	Incorrect dose administered	X
B0747140A	France	MD	7 Months/F	INJ	U	01Mar2011-01Mar2011, 01Jan2011-01Jan2011	01Mar2011	U/See text, U/U	Incorrect dose administered	X

B0748238A	France	MD	16 Months/M	INJ	U	15Sep2011-15Sep2011, 01Apr2010-01Apr2010, 10Jun2010-10Jun2010, 27May2011-27May2011	15Sep2011	U/See text, U/U, U/U, U/U	Incorrect dose administered	X
B0755884A	France	MD	8 Months/U	INJ	U	14Nov2010-14Nov2010	14Nov2010	U/See text	Incorrect dose administered	X
B0730220A	Singapore	MD,RP	7 Months/F	INJ	U	11Jun2011-11Jun2011	11Jun2011	U/During	Incorrect dose administered	X
B0691022A	Spain	HP	6 Months/F	INJ	U	1 Days, 1 Days		U/During, U/U	Incorrect dose administered	X
B0756912A	Belgium	MD	7 Months/M	INJ	U	05Jan2011-05Jan2011, 18Oct2010-18Oct2010, 20Sep2010-20Sep2010, 02Aug2010-02Aug2010	05Jan2011	U/During, U/U, U/U, U/U	Incorrect dose administered, Irritability, Vomiting	R
B0754991A	France	MD	3 Years/F	INJ	U	01Dec2008-01Dec2008, 01Nov2008-01Nov2008, 02Jan2009-02Jan2009	01Dec2008	U/See text, U/See text, U/See text	Incorrect dose administered, Wrong drug administered	X

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B0681952A	Australia	MD	6 Months/F	INJ	U	U, U		U/See text, U/U	Incorrect route of drug administration	X
B0686563A	Belgium	MD,RP	15 Months/F	INJ	U	23Nov2010-23Nov2010	23Nov2010	U/During	Incorrect route of drug administration	X
B0733788A	Sweden	HP,MD	1 Years/M	INJ	U	U		U/During	Incorrect route of drug administration, Dyskinesia, Underdose, Injection site erythema, Injection site swelling, Injection site swelling	U
B0742113A	Australia	CO,HP	6 Months/U	INJ	U	10Aug2011-10Aug2011	10Aug2011	U/During	Incorrect route of drug administration, Injection site haematoma, Injection site swelling, Injection site pain, Injection site erythema	R
D0069542A	Germany	HP	Adult/U	INJ	U	1 Days		U/0 Days	Incorrect route of drug administration, Overdose, Off label use, Wrong technique in drug	X

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									usage process	
B0731030A	France	CO,MD	2 Months/U	INJ	U	05Jul2011-05Jul2011	05Jul2011	U/See text	Incorrect route of drug administration, Wrong technique in drug usage process	X
B0688919A	Andorra	HP	2 Months/M	INJ	U	07Dec2010-07Dec2010	07Dec2010	U/See text	Incorrect storage of drug	X
B0686265A	Australia	HP	2 Months/U	INJ	U	12Oct2010-12Oct2010		U/See text	Incorrect storage of drug	X
B0686993A	Australia	HP	6 Months/U	INJ	U	12Oct2010-12Oct2010		U/See text	Incorrect storage of drug	X
B0686994A	Australia	HP	6 Months/U	INJ	U	12Oct2010-12Oct2010		U/See text	Incorrect storage of drug	X

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B0687001A	Australia	HP	2 Months/U	INJ	U	25Oct2010-25Oct2010	U/See text	Incorrect storage of drug	X
B0687004A	Australia	HP	6 Months/U	INJ	U	27Oct2010-27Oct2010	U/See text	Incorrect storage of drug	X
B0687005A	Australia	HP	4 Months/U	INJ	U	27Oct2010-27Oct2010	U/See text	Incorrect storage of drug	X
B0687006A	Australia	HP	7 Months/U	INJ	U	27Oct2010-27Oct2010	U/See text	Incorrect storage of drug	X
B0687007A	Australia	HP	2 Months/U	INJ	U	28Oct2010-28Oct2010	U/See text	Incorrect storage of drug	X
B0687009A	Australia	HP	2 Months/U	INJ	U	04Nov2010-04Nov2010	U/See text	Incorrect storage of drug	X

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B0687011A	Australia	HP	2 Months/U	INJ	U	05Nov2010-05Nov2010	U/See text	Incorrect storage of drug	X
B0687018A	Australia	HP	2 Months/U	INJ	U	08Nov2010-08Nov2010	U/See text	Incorrect storage of drug	X
B0687024A	Australia	HP	4 Years/U	INJ	U	09Nov2010-09Nov2010	U/See text	Incorrect storage of drug	X
B0730020A	Australia	PH	U/U	INJ	U	1 Days	U/See text	Incorrect storage of drug	X
B0731392A	Spain	HP	6 Months/M	INJ	U	01Jun2011-01Jun2011	U/See text	Incorrect storage of drug	X
B0731394A	Spain	HP	2 Months/M	INJ	U	01Jun2011-01Jun2011	U/See text	Incorrect storage of drug	X

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B0731396A	Spain	HP	4 Months/M	INJ	U	01Jun2011-01Jun2011		U/See text	Incorrect storage of drug	X
B0747719A	Belgium	HP	5 Months/M	INJ	U	29Jun2011-29Jun2011, 27Jul2011-27Jul2011, 14Sep2011-14Sep2011	14Sep2011	U/See text, U/U, U/U	Incorrect storage of drug, Pyrexia, Irritability, Diarrhoea, Abdominal pain	R
B0681410A	France	MD	20-29 Years/F	INJ	U	01Oct2010-01Oct2010		U/See text	Maternal exposure during pregnancy, Off label use	X
B0726436A	France	MD	4 Months/M	INJ	U	15Jun2011-15Jun2011	15Jun2011	U/See text	Overdose	X
D0069306A	Germany	MD	Adult/U	INJ	U	1 Days		U/0 Days	Overdose	X
D0072554A	Germany	MD	8 Years/M	INJ	U	01Jan2006-01Jan2006, 05Aug2011-05Aug2011	05Aug2011	U/0 Days, U/U	Overdose	X

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B0692789A	Italy	MD,RP	5 Months/F	INJ	U	1 Days		U/During	Overdose	X
B0749458A	New Zealand	PH	6 Weeks/F	INJ	U	20Sep2011-20Sep2011	20Sep2011	U/During	Overdose	X
D0072383A	Germany	MD	4 Months/F	INJ	U	12Aug2011-12Aug2011	12Aug2011	U/0 Days	Overdose, Wrong drug administered	X
D0072476A	Germany	MD	23 Years/M	INJ	U	20Aug2011-20Aug2011	20Aug2011	U/0 Days	Overdose, Wrong technique in drug usage process	X
B0707441A	France	MD	20 Months/F	INJ	U	18Mar2011-18Mar2011	18Mar2011	U/See text	Underdose	X
B0713124A	France	MD	3 Months/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/See text	Underdose	X

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B0715660A	France	MD	20 Months/U	INJ	U	22Apr2011-22Apr2011	22Apr2011	U/See text	Underdose	X
B0730789A	France	MD	Infant/U	INJ	U	30Jun2011-30Jun2011	30Jun2011	U/See text	Underdose	X
B0733973A	France	MD	Infant/F	INJ	U	14May2011-14May2011	14May2011	U/See text	Underdose	X
B0746437A	France	MD	18 Months/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/See text	Underdose	X
B0748270A	France	PH	16 Months/M	INJ	U	15Sep2011-15Sep2011	15Sep2011	U/See text	Underdose	X
B0750072A	France	MD,RP	1 Years/U	INJ	U	01Sep2011-01Sep2011	01Sep2011	U/See text	Underdose	X

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B0751895A	France	MD	Infant/M	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/See text	Underdose	X
D0071408A	Germany	MD	6 Months/F	INJ	U	1 Days		U/During	Underdose	X
D0071608A	Germany	MD	15 Months/M	INJ	U	13May2011-13May2011	13May2011	U/During	Underdose	X
B0741475A	Hong Kong	MD,RP	6 Months/M	INJ	U	U		U/During	Underdose	X
B0703093A	France	MD	1 Years/U	INJ	U	01Feb2011-01Feb2011	01Feb2011	U/See text	Underdose, Wrong technique in drug usage process	X
#B0686701A	Poland	MD,RA	3 Months/U	INJ, INJ, INJ	U, U, U	01Jan2009-01Jan2009, 01Jan2009-01Jan2009, 08Jul2009-08Jul2009	01Jan2009	U/Unknown, U/Unknown, U/4 Hours	Vaccination complication*, Hypotonic-hypore sponsive episode*, Pallor*, Pyrexia*,	R

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									Immobile*, Pallor*, Hypotonia*, Pyrexia*	
#B0743708A	Switzerland	MD,RA	2 Years/M	INJ	.5ML	01Jul2011-01Jul2011	02Jul2011	U/20 Hours	Vaccination complication, Injection site swelling, Injection site pruritus, Injection site warmth, Injection site erythema, Injection site pain	R
B0737216A	Australia	CO,HP	4 Weeks/U	INJ	U	U		U/During	Wrong drug administered	X
B0683434A	France	MD	4 Years/M	INJ	U	04Nov2010-04Nov2010, 15May2007-15May2007, 01Feb2008-01Feb2008	04Nov2010	U/See text, U/U, U/U	Wrong drug administered	X
B0683447A	France	MD	7 Years/F	INJ	U	19May2010-19May2010	19May2010	U/See text	Wrong drug administered	X

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B0693149A	France	PH	9 Years/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/See text	Wrong drug administered	X
B0742693A	France	MD	4 Years/F	INJ, INJ	U, U	01Apr2008-01Apr2009, 01Sep2009-01Sep2009	01Apr2008	U/See text, U/See text	Wrong drug administered	X
B0742696A	France	MD	5 Years/M	INJ	U	01May2010-01May2010	01May2010	U/See text	Wrong drug administered	X
D0069467A	Germany	MD	7 Years/F	INJ	U	17Nov2010-17Nov2010	17Nov2010	U/0 Days	Wrong drug administered	X
D0069776A	Germany	PH	19 Years/F	INJ	U	01Jul2010-01Jul2010	01Jul2010	U/During	Wrong drug administered	X
D0070452A	Germany	MD,RP	U/U	INJ	U	1 Days		U/During	Wrong drug administered	X

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D0070458A	Germany	MD	9 Years/M	INJ	U	1 Days		U/0 Days	Wrong drug administered	X
D0070469A	Germany	MD,RP	10 Years/F	INJ	U	28Feb2011-28Feb2011	28Feb2011	U/During	Wrong drug administered	X
D0070961A	Germany	PH	Adult/U	INJ	U	1 Days		U/0 Days	Wrong drug administered	X
D0071742A	Germany	PH	Adult/U	INJ	U	1 Days		U/During	Wrong drug administered	X
D0072391A	Germany	MD	7 Years/M	INJ	U	05Aug2011-05Aug2011, 01Jan2006-01Jan2006	05Aug2011	U/0 Days, U/U	Wrong drug administered	X
B0695871A	Italy	MD	3 Months/M	INJ	U	1 Days		U/During	Wrong drug administered	X

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B0726160A	Spain	HP	6 Years/M	INJ	U	18May2011-18May2011	18May2011	U/During	Wrong drug administered	X	
B0703605A	France	MD	3 Months/F	INJ	U	25Feb2011-25Feb2011	31Jan2011	U/See text	Wrong drug administered, Drug prescribing error, Inappropriate schedule of drug administration	X	
B0685825A	France	MD	6 Months/U	INJ	U	26Apr2010-26Apr2010	26Apr2010	U/See text	Wrong drug administered, Incorrect dose administered	X	
B0683553A	Australia	HP	U/U	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/During	Wrong technique in drug usage process	X	Several subjects are concerned by this case.
B0705458A	Australia	HP	2 Months/U	INJ	U	08Mar2011-08Mar2011	08Mar2011	U/During	Wrong technique in drug usage process	X	

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B0729237A	Australia	MD	U/M	INJ	U	1 Days	U/During	Wrong technique in drug usage process	X	
B0732276A	Australia	HP	Infant/U	INJ	U	1 Days	U/See text	Wrong technique in drug usage process	X	
B0734749A	Austria	MD	U/U	INJ	U	1 Days	U/During	Wrong technique in drug usage process	X	
B0756904A	Belgium	PH	Child/U	INJ	U	U	U/During	Wrong technique in drug usage process	X	
A0901113A	Canada	HP	Infant/U	INJ	U	U	U/See text	Wrong technique in drug usage process	X	3 subjects were vaccinated with infanrix hexa without hib.
A0901399A	Canada	PH	Infant/U	INJ	U	01Dec2010-01Dec2010	U/See text	Wrong technique in drug usage process	X	One subject was 67 day old male, MW. The second subject was a 77 day old female, JK.

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A0912540A	Canada	MD	21 Months/U	INJ	U	U, U, U		U/See text, U/U, U/U	Wrong technique in drug usage process	X
A0936897A	Canada	MD	Infant/U	INJ	U	1 Days		U/See text	Wrong technique in drug usage process	X
A0942606A	Canada	HP	8 Months/F	INJ	U	25Aug2011-25Aug2011, 17Mar2011-17Mar2011, 12Apr2011-12Apr2011	25Aug2011	U/See text, U/U, U/U	Wrong technique in drug usage process	X
B0686842A	France	MD,RP	2 Months/M	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/See text	Wrong technique in drug usage process	X
B0689063A	France	MD	4 Months/M	INJ	U	11Dec2010-11Dec2010	11Dec2010	U/See text	Wrong technique in drug usage process	X
B0689740A	France	MD	3 Months/F	INJ	U	16Dec2010-16Dec2010	16Dec2010	U/See text	Wrong technique in drug usage process	X

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B0693142A	France	MD	4 Months/F	INJ	U	10Jan2011-10Jan2011	10Jan2011	U/See text	Wrong technique in drug usage process	X
B0693632A	France	PH	Infant/M	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/See text	Wrong technique in drug usage process	X
B0693832A	France	MD	Neonate/F	INJ	U	14Jan2011-14Jan2011	14Jan2011	U/See text	Wrong technique in drug usage process	X
B0694085A	France	MD	12 Weeks/F	INJ	U	06Jan2011-06Jan2011	06Jan2011	U/See text	Wrong technique in drug usage process	X
B0695154A	France	MD	Infant/U	INJ	U	20Jan2011-20Jan2011	20Jan2011	U/See text	Wrong technique in drug usage process	X
B0695607A	France	PH	4 Months/F	INJ	U	21Jan2011-21Jan2011	21Jan2011	U/See text	Wrong technique in drug usage process	X

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B0697401A	France	MD	18 Months/F	INJ	U	19Jul2010-19Jul2010	01Jul2010	U/See text	Wrong technique in drug usage process	X
B0705091A	France	MD	4 Months/U	INJ	U	09Mar2011-09Mar2011	09Mar2011	U/See text	Wrong technique in drug usage process	X
B0711335A	France	MD	Infant/U	INJ	U	01Apr2011-01Apr2011	01Apr2011	U/See text	Wrong technique in drug usage process	X
B0716261A	France	PH,MD	3 Months/F	INJ	U	01Apr2011-01Apr2011	01Apr2011	U/See text	Wrong technique in drug usage process	X
B0716546A	France	MD	15 Months/F	INJ	U	27Apr2011-27Apr2011	27Apr2011	U/See text	Wrong technique in drug usage process	X
B0724340A	France	MD	3 Months/F	INJ	U	01May2011-01May2011	01May2011	U/See text	Wrong technique in drug usage process	X

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B0724548A	France	MD	Infant/U	INJ	U	03Jun2011-03Jun2011	03Jun2011	U/See text	Wrong technique in drug usage process	X
B0725882A	France	MD	20 Months/U	INJ	U	10Jun2011-10Jun2011	10Jun2011	U/See text	Wrong technique in drug usage process	X
B0731268A	France	MD	2 Months/U	INJ	U	05Jul2011-05Jul2011	05Jul2011	U/See text	Wrong technique in drug usage process	X
B0733974A	France	PH,MD	4 Months/M	INJ	U	18Jul2011-18Jul2011	18Jul2011	U/See text	Wrong technique in drug usage process	X
B0734159A	France	MD	20 Months/U	INJ	U	20Jul2011-20Jul2011	20Jul2011	U/See text	Wrong technique in drug usage process	X
B0739075A	France	PH	Infant/F	INJ	U	01Jul2011-01Jul2011	01Jul2011	U/See text	Wrong technique in drug usage process	X

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B0741941A	France	MD	2 Months/F	INJ	U	18Aug2011-18Aug2011	01Aug2011	U/See text	Wrong technique in drug usage process	X
B0743864A	France	MD	Infant/U	INJ	U	31Aug2011-31Aug2011	31Aug2011	U/See text	Wrong technique in drug usage process	X
B0745767A	France	MD	2 Months/F	INJ	U	06Sep2011-06Sep2011	06Sep2011	U/See text	Wrong technique in drug usage process	X
B0746700A	France	MD	2 Months/M	INJ, INJ	U, U	12Nov2009-12Nov2009, 11Jan2010-11Jan2010	12Nov2009	U/See text, U/See text	Wrong technique in drug usage process	X
B0747182A	France	MD	2 Months/M	INJ	U	13Sep2011-13Sep2011	13Sep2011	U/See text	Wrong technique in drug usage process	X
B0748276A	France	PH	18 Months/F	INJ	U	22Aug2011-22Aug2011	22Aug2011	U/See text	Wrong technique in drug usage process	X

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B0752261A	France	MD	4 Months/U	INJ	U	28Sep2011-28Sep2011	28Sep2011	U/See text	Wrong technique in drug usage process	X
B0755901A	France	MD	Infant/U	INJ	U	12Oct2011-12Oct2011	12Oct2011	U/See text	Wrong technique in drug usage process	X
B0756751A	France	MD	Infant/F	INJ	U	1 Days		U/See text	Wrong technique in drug usage process	X
D0069906A	Germany	MD	58 Days/M	INJ	U	10Jan2011-10Jan2011	10Jan2011	U/0 Days	Wrong technique in drug usage process	X
D0069929A	Germany	MD	4 Months/M	INJ	U	10Jan2011-10Jan2011	10Jan2011	U/0 Days	Wrong technique in drug usage process	X
D0070289A	Germany	PH	U/U	INJ	U	1 Days		U/0 Days	Wrong technique in drug usage process	X

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D0070361A	Germany	MD	6 Months/F	INJ	U	18Feb2011-18Feb2011		U/0 Days	Wrong technique in drug usage process	X
D0070400A	Germany	PH,MD,RP	4 Months/F	INJ	U	1 Days		U/During	Wrong technique in drug usage process	X
D0070741A	Germany	MD	U/U	INJ	U	1 Days		U/0 Days	Wrong technique in drug usage process	X
D0071160A	Germany	MD	13 Months/F	INJ	U	10Feb2011-10Feb2011	01Feb2011	U/During	Wrong technique in drug usage process	X
D0071690A	Germany	MD	4 Months/M	INJ	U	09Jun2011-09Jun2011	09Jun2011	U/0 Days	Wrong technique in drug usage process	X
D0072181A	Germany	MD	7 Months/U	INJ	U	1 Days		U/0 Days	Wrong technique in drug usage process	X

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D0072443A	Germany	MD	3 Months/M	INJ	U	18Aug2011-18Aug2011	18Aug2011	U/0 Days	Wrong technique in drug usage process	X
D0072513A	Germany	PH	15 Months/M	INJ	U	25Aug2011-25Aug2011	25Aug2011	U/0 Days	Wrong technique in drug usage process	X
B0719869A	Greece	MD	4 Months/M	INJ	U	08May2011-08May2011	08May2011	U/During	Wrong technique in drug usage process	X
B0735350A	Ireland	HP	4 Months/U	INJ	U	U		U/During	Wrong technique in drug usage process	X
B0740627A	Ireland	PH	4 Months/F	INJ	U	10Aug2011-10Aug2011	10Aug2011	U/During	Wrong technique in drug usage process	X
#B0755514A	Ireland	MD,RA	4 Months/M	INJ	U	22Sep2011-22Sep2011	22Sep2011	U/During	Wrong technique in drug usage process	X

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#B0682380A	New Zealand	PH	47 Days/F	INJ	.5ML	23Oct2010-23Oct2010	23Oct2010	U/During	Wrong technique in drug usage process	X
B0693373A	Spain	PH	4 Months/U	INJ	U	10Jan2011-10Jan2011	10Jan2011	U/During	Wrong technique in drug usage process	X
B0719758A	Spain	HP,RP	3 Months/F	INJ	U	26Apr2011-26Apr2011	26Apr2011	U/During	Wrong technique in drug usage process	X
B0722815A	Spain	HP,MD	4 Months/M	INJ	U	02May2011-02May2011	02May2011	U/During	Wrong technique in drug usage process	X
B0722819A	Spain	HP,MD	2 Months/M	INJ	U	02May2011-02May2011	02May2011	U/During	Wrong technique in drug usage process	X
B0722820A	Spain	HP,MD	2 Months/F	INJ	U	02May2011-02May2011	02May2011	U/During	Wrong technique in drug usage process	X

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B0703738A	Sweden	HP	U/U	INJ	U	1 Days		U/During	Wrong technique in drug usage process	X
B0703874A	Sweden	HP	3 Months/F	INJ	U	1 Days		U/During	Wrong technique in drug usage process	X
B0719890A	Sweden	HP	5 Months/F	INJ	U	10May2011-10May2011		U/During	Wrong technique in drug usage process	X
B0740544A	France	MD	12 Weeks/M	INJ, INJ	U, U	11Aug2011-11Aug2011, 17Aug2011-17Aug2011	11Aug2011	U/See text, U/See text	Wrong technique in drug usage process, Inappropriate schedule of drug administration	X
B0697148A	France	HP	18 Months/M	INJ	U	31Jan2011-31Jan2011	31Jan2011	U/See text	Wrong technique in drug usage process, Incorrect route of drug administration	X
B0749413A	France	MD	21 Months/F	INJ, INJ	U, U	14Sep2011-14Sep2011, 14Sep2011-14Sep2011	14Sep2011	U/See text, U/See text	Wrong technique in drug usage process, Overdose	X

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B0753350A	France	MD	4 Months/F	INJ, INJ	U, U	04Oct2011-04Oct2011, 04Oct2011-04Oct2011, 01Aug2011-01Aug2011	04Oct2011	U/See text, U/See text, U/U	Wrong technique in drug usage process, Overdose, Inappropriate schedule of drug administration	X
D0069699A	Germany	MD	16 Months/M	INJ	U	10Dec2010-10Dec2010, 1 Days	10Dec2010	U/During, U/U	Wrong technique in drug usage process, Underdose	X
Investigations										
#D0070846A	Germany	MD,RP	10 Months/M	INJ, INJ, INJ	U, U, U	25Jan2011-25Jan2011, 27Oct2010-27Oct2010, 22Feb2011-22Feb2011		U/5 Months, U/55 Days, U/27 Days	Aspartate aminotransferase increased, Alanine aminotransferase increased, Injection site nodule, Injection site induration, Injection site erythema, Febrile convulsion, Soft tissue infection, Abscess sterile, Respiratory tract infection	N
#D0071115A	Germany	MD	4 Years/F	INJ, INJ, INJ, INJ	U, U, U, U	11Jun2007-11Jun2007, 15Jul2007-15Jul2007, 09Oct2007-09Oct2007, 15Oct2008-15Oct2008	01Apr2011	U/4 Years, U/4 Years, U/4 Years, U/2 Years	Aspartate aminotransferase increased, No therapeutic response, Infection	U

#B0756166A	Poland	MD,RA	1 Months/M	INJ	U	27Jul2011-27Jul2011	28Jul2011	U/1 Days	Body temperature increased, Hypotonic-hypore sponsive episode, Somnolence	R
#D0070133A	Germany	HP	4 Years/F	INJ, INJ, INJ, INJ	U, U, U, U	03Apr2006-03Apr2006, 08May2006-08May2006, 12Jun2006-12Jun2006, 11May2007-11May2007	01Jan2010	U/4 Years, U/4 Years, U/4 Years, U/3 Years	Bordetella test positive, Vaccination failure	U
#D0070137A	Germany	HP	5 Years/F	INJ, INJ, INJ, INJ	U, U, U, U	28Oct2005-28Oct2005, 25Nov2005-25Nov2005, 22Aug2006-22Aug2006, 14Dec2006-14Dec2006	01Jan2010	U/5 Years, U/5 Years, U/4 Years, U/4 Years	Bordetella test positive, Vaccination failure	U
B0681488A	Belgium	MD,RP	30 Months/F	INJ	U	1 Days	01Jan2010	U/See text	Clostridium test	X
D0072013A	Germany	MD	4 Years/M	INJ	U	1 Days		U/Unknown	Clostridium test negative	X
B0718002A	France	MD	4 Months/U	INJ	U	01Oct2010-01Oct2010	01Oct2010	U/See text	Clostridium test negative, Underdose	X

B0699787A	France	PH	2 Years/U	INJ, INJ, INJ	U, U, U	01Feb2009-01Feb2009, 01Apr2009-01Apr2009, 01May2010-01May2010	01Jan2011	U/2 Years, U/2 Years, U/1 Years	Corynebacterium test negative	X
B0717163A	France	MD	18 Months/F	INJ, INJ	U, U	01Jan2010-01Jan2010, 01Jan2010-01Jan2010	01Apr2011	U/1 Years, U/1 Years	Corynebacterium test negative	X
B0731677A	Austria	MD	4 Years/M	INJ, INJ, INJ, INJ	U, U, U, U	19Mar2007-19Mar2007, 12May2007-12May2007, 31Mar2008-31Mar2008, 28Dec2006-28Dec2006		U/See text, U/See text, U/See text, U/See text	Corynebacterium test negative, Clostridium test negative, Hepatitis B antibody negative	X
B0686689A	Poland	MD,RA	5 Months/U	INJ	U	21Jul2010-21Jul2010	21Jul2010	U/0 Days	C-reactive protein increased, Restlessness, Decreased appetite, Pyrexia	R
B0728114A	France	MD	Child/F	INJ, INJ, INJ	U, U, U	1 Days, 1 Days, 1 Days		U/Unknown, U/Unknown, U/Unknown	Hepatitis B antibody negative	X
D0072530A	Germany	MD	U/U	INJ	U	1 Days		U/1 Years	Hepatitis B antibody negative	X

B0682838A	Australia	MD,RP	6 Years/M	INJ	U	U		U/During	Immunology test abnormal	X
#B0736764A	Viet Nam	HP,RP	4 Months/M	INJ	U	02Aug2011-02Aug2011, 19May2011-19May2011, 28Jun2011-28Jun2011	02Aug2011	U/Hours, U/U, U/U	Pulse absent, Dyspnoea, Injection site erythema, Injection site swelling, Crying	U
#B0720306A	Spain	MD,RP	21 Months/F	INJ	U	21Feb2010-21Feb2010, 21Dec2009-21Dec2009, 21Oct2009-21Oct2009		U/14 Months, U/U, U/U	Transaminases increased, Hepatitis B antibody positive, Jaundice, Hepatomegaly, Diarrhoea, Pyrexia	N
#B0721308A	Italy	MD,RA	11 Months/F	INJ	U	19Apr2010-19Apr2010	19Apr2010	U/0 Days	Transaminases increased, Pyrexia	R
Metabolism and nutrition disorders										
#B0752539A	Italy	MD,RA	7 Months/F	INJ	U	14Sep2011-14Sep2011	14Sep2011	U/0 Days	Decreased appetite, Pyrexia, Weight decreased, Hyperaemia, Tympanic membrane disorder, Rhinitis, Rash pustular,	U

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									Upper respiratory tract inflammation	
B0727603A	Netherlands	MD,RA	3 Months/M	INJ	U	13Sep2010-13Sep2010	14Sep2010	U/Hours	Oligodipsia, Injected limb mobility decreased, Injection site inflammation, Insomnia, Injection site pain, Crying, Pyrexia	R
B0733486A	Netherlands	HP,RA	2 Months/F	INJ	U	09Nov2010-09Nov2010	09Nov2010	U/5 Hours	Oligodipsia, Insomnia, Malaise, Nasopharyngitis, Vomiting, Crying, Pyrexia, Erythema	R
#B0714244A	Netherlands	HP,RA	5 Months/M	INJ, INJ	.5ML, U	25Feb2011-25Feb2011, 1 Days		U/6 Hours, U/1 Days	Oligodipsia, Oligodipsia, Dehydration, Pyrexia, Diarrhoea, Diarrhoea, Crying	R
#B0752361A	Italy	MD,RA	17 Months/F	INJ	U	23Jul2010-23Jul2010	01Aug2010	U/9 Days	Type 1 diabetes mellitus, Diabetic ketoacidosis, Polydipsia, Polyuria, Somnolence, Tachypnoea, Increased appetite,	S

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									Vomiting, Dermal cyst, Ketosis, Lip dry, Dehydration, Lymphadenopathy	
D0069358B	Germany	HP,RA	4 Months/M	INJ	U	07Jan2010-07Jan2010	07Jan2010	U/1 Hours	Weight gain poor, Psychomotor hyperactivity, Pyrexia, Hyperhidrosis, Tremor, Injection site erythema, Injection site swelling, Sleep disorder	N
Musculoskeletal and connective tissue disorders										
#B0705706A	France	RA	18 Months/F	INJ	U	03Nov2010-03Nov2010	03Nov2010	U/Same day	Arthralgia, Injection site oedema, Pain, Injected limb mobility decreased, Incorrect route of drug administration	R
#B0754191A	Poland	MD,RA	26 Months/U	INJ	U	04Jul2011-04Jul2011	06Jul2011	U/2 Days	Joint swelling, Gait disturbance, Body temperature increased, Arthritis	U

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#B0720309A	Belgium	RA	2 Months/F	INJ	U	22Apr2011-22Apr2011	22Apr2011	U/0 Days	Muscle contracture, Muscle spasms, Erythema, Staring, Heart rate increased	U
#B0702855A	Greece	MD,RA	5 Months/F	INJ	U	03Nov2010-03Nov2010	03Nov2010	U/0 Days	Muscle spasms, Pyrexia, Escherichia urinary tract infection	U
D0070972A	Germany	MD	2 Months/F	INJ, INJ	U, U	02Mar2011-02Mar2011, 08Apr2011-08Apr2011	02Mar2011	U/0 Days, U/0 Days	Muscle spasms, Underdose, Muscle spasms, Underdose	U
B0756767A	Netherlands	HP,RA	2 Months/M	INJ	U	09Dec2010-09Dec2010	01Dec2010	U/4 Hours	Muscle twitching, Pyrexia, Malaise	R
B0755146A	South Africa	HP	18 Months/U	INJ	U	21Sep2011-21Sep2011	22Sep2011	U/1 Days	Musculoskeletal stiffness, Injection site erythema, Injection site swelling	N
#D0069239A	Germany	MD,RA	1 Years/M	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/During	Soft tissue necrosis, Debridement, Incorrect route of drug administration	R

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Nervous system disorders

#D0070015A	Germany	RA	16 Months/M	INJ	.5ML	09Dec2010-09Dec2010, 28Sep2009-28Sep2009, 04Jan2010-04Jan2010, 20Apr2010-20Apr2010	09Dec2010	U/0 Days, U/U, U/U, U/U	Ataxia*, Balance disorder*, Balance disorder*, Encephalitis*, Encephalitis*, Gait disturbance*, Gait disturbance*, Pyrexia*, Upper respiratory tract infection*, Otitis media acute*, Cerebellar ataxia*	R
#B0705768A	Italy	MD,RA	1 Years/M	INJ	U	27Jan2011-27Jan2011	02Feb2011	U/6 Days	Balance disorder, Irritability, Upper respiratory tract infection	U
#B0682833A	France	RA	17 Months/M	INJ	U	06Jul2010-06Jul2010	13Jul2010	U/7 Days	Balance disorder, Lymphadenopathy, Fall, Otitis media, Pharyngeal erythema	R
D0069517A	Germany	HP,RA	13 Months/F	INJ	U	06Aug2010-06Aug2010	08Aug2010	U/2 Days	Balance disorder, Vestibular neuronitis, Gait disturbance, Fall	R

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#B0686955A	Austria	RA	1 Years/M	INJ	U	23Sep2010-23Sep2010	01Sep2010	U/Days	Balance disorder*, Vomiting*, Body temperature increased*	R
#B0717146A	Belgium	RA	4 Months/F	INJ	U	01Mar2011-01Mar2011	17Mar2011	U/12 Hours	Clonic convulsion	R
#B0708930A	Italy	MD,RA	3 Months/F	INJ	U	11Nov2010-11Nov2010	12Nov2010	U/1 Days	Clonic convulsion	U
#B0720877A	Australia	HP	7 Months/M	INJ	U	18May2011-18May2011	19May2011	U/1 Days	Convulsion	U
#D0072923A	Germany	MD	U/U	INJ	U	1 Days		U/Unknown	Convulsion	U
#B0699990A	Italy	RA	4 Months/M	INJ	U	08Feb2011-08Feb2011	08Feb2011	U/3 Hours	Convulsion	R

#B0746101A	Italy	RA	10 Months/F	INJ	U	22Mar2011-22Mar2011	22Mar2011	U/0 Days	Convulsion	R
#B0727831A	Spain	MD,RA	6 Months/M	INJ	U	04May2010-04May2010	04May2010	U/0 Days	Convulsion	R
#B0733815A	Spain	PH,MD,RA	4 Months/F	INJ	U	05Jul2011-05Jul2011	05Jul2011	U/0 Days	Convulsion	R
#B0696081A	Chile	MD,RP	4 Months/M	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/3 Hours	Convulsion*	R
#D0070030A	Germany	HP,RA	3 Months/M	INJ	U	19Nov2010-19Nov2010	19Nov2010	U/0 Days	Convulsion, Acute respiratory failure	U
#B0735347A	Poland	MD,RA	7 Weeks/U	INJ	U	07Jun2011-07Jun2011	08Jun2011	U/1 Days	Convulsion, Apnoea, Hypotonic-hypore sponsive episode, Pallor, Dyspnoea, Musculoskeletal	R

									stiffness	
#B0734875A	Italy	MD,RA	12 Months/F	INJ	U	07Jun2011-07Jun2011	07Jun2011	U/0 Days	Convulsion, Clonus	R
#D0071407A	Germany	MD	4 Years/U	INJ, INJ	U, U	1 Days, 1 Days		U/Unknown, U/Unknown	Convulsion, Convulsion	U
#B0686062A	Poland	MD,RA	1 Months/U	INJ	U	09Sep2010-09Sep2010	09Sep2010	U/0 Days	Convulsion, Crying	R
#B0750925A	Singapore	MD	4 Months/F	INJ	U	24Aug2011-24Aug2011	01Aug2011	U/0 Days	Convulsion, Crying, Somnolence, Staring, Abnormal behaviour, Dyskinesia	R
#D0071366A	Germany	HP,RA	12 Months/F	INJ	U	06May2011-06May2011	07May2011	U/1 Days	Convulsion, Depressed level of consciousness, Gaze palsy, Hypochromic anaemia, Pyrexia,	U

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									Injection site erythema, Musculoskeletal stiffness, Iron deficiency	
#D0071441A	Germany	MD,RA	15 Months/M	INJ	U	28Apr2011-28Apr2011	28Apr2011	U/0 Days	Convulsion, Depressed level of consciousness, Staring, Pyrexia, Asthenia, Upper respiratory tract infection, Vaccination complication	I
#D0070499A	Germany	RA	18 Months/M	INJ	.5ML	15Feb2011-15Feb2011, 26Oct2009-26Oct2009, 01Dec2009-01Dec2009, 25Jan2010-25Jan2010	16Feb2011	U/1 Days, U/U, U/U, U/U	Convulsion*, Endotracheal intubation*, Status epilepticus*, Pyrexia*, Febrile convulsion*	R
#D0070292A	Germany	RA	3 Months/F	INJ	U	22Oct2010-22Oct2010	25Oct2010	U/3 Days	Convulsion, Eye movement disorder, Dyskinesia, Pallor, Somnolence	R
#D0070470A	Germany	MD,RA	2 Months/F	INJ	U	21Feb2011-21Feb2011	01Jan2011	U/0 Years	Convulsion, Flushing, Autonomic nervous system imbalance	U

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#B0739945A	Italy	RA	5 Months/M	INJ	.5MG	21Jul2011-21Jul2011	22Jul2011	U/1 Days	Convulsion, Gaze palsy, Clonus, Pyrexia	U
#D0071548A	Germany	MD,RA	8 Months/F	INJ	U	10May2011-10May2011	11May2011	U/1 Days	Convulsion*, Gaze palsy*, Cyanosis*, Vaccination complication*, Restlessness*, Feeling hot*, Staring*, Muscle twitching*, Dyspnoea*, Hypotonia*, Somnolence*, General physical health deterioration*, Body temperature increased*	U
#B0697392A	Italy	MD,RA	16 Months/M	INJ	U	17Aug2010-17Aug2010	17Aug2010	U/0 Days	Convulsion, Grand mal convulsion, Hypotonia	R
#B0719212A	Australia	HP,MD,RA	3 Years/F	INJ	U	09May2011-09May2011	10May2011	U/16 Hours	Convulsion, Hepatotoxicity, Macrocephaly, Renal impairment, Irritability, Restlessness	N

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#B0682745A	Netherlands	HP,RA	6 Months/M	INJ	U	23Aug2010-23Aug2010	23Aug2010	U/Hours	Convulsion, Loss of consciousness, Gaze palsy, Pallor, Pyrexia, Crying	N
#B0713916A	Sweden	HP,RA	1 Years/F	INJ	U	30Aug2010-30Aug2010	30Aug2010	U/0 Days	Convulsion, Muscle twitching, Hypotonia, Staring, Body temperature increased	R
#B0704556A	Italy	RA	12 Months/M	INJ	U	09Aug2010-09Aug2010	09Aug2010	U/0 Days	Convulsion, Muscular weakness, Pyrexia	R
#D0071067A	Germany	MD,RA	6 Months/F	INJ, INJ	U, U	31Mar2011-31Mar2011, 03Mar2011-03Mar2011	01Apr2011	U/0 Months, U/0 Days	Convulsion, Myoclonus	U
#D0072213A	Germany	HP,RA	11 Weeks/F	INJ	U	05Jul2011-05Jul2011	06Jul2011	U/1 Days	Convulsion, Myoclonus, Crying, Muscle twitching	R
#D0073004A	Germany	MD,RA	16 Months/F	INJ	.5ML	03May2011-03May2011	05May2011	U/48 Hours	Convulsion*, Pallor*, Gaze palsy*, Depressed level of consciousness*,	U

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									Joint hyperextension*	
#B0681626A	Italy	MD,RA	13 Months/M	INJ	U	05Feb2010-05Feb2010	07Feb2010	U/2 Days	Convulsion, Pyrexia	R
#D0072126A	Germany	RA	3 Months/M	INJ, INJ	.5ML, .5ML	25Jun2010-25Jun2010, 19May2010-19May2010	19May2010	U/Unknown, U/0 Days	Convulsion*, Pyrexia*, Dyskinesia*, Convulsion*, Crying*, Pyrexia*	I
#D0070473A	Germany	HP,RA	4 Months/F	INJ	U	10Feb2011-10Feb2011	10Feb2011	U/0 Days	Convulsion, Pyrexia, Eye movement disorder, Muscle twitching	R
#D0071376A	Germany	OM,MD,RA	3 Months/F	INJ	.5ML	10May2011-10May2011	10May2011	U/0 Days	Convulsion, Pyrexia, Myoclonus, Salivary hypersecretion	R
#D0069319A	Germany	RA	6 Months/M	INJ, INJ, INJ, INJ	U, U, U, U	25Oct2010-25Oct2010, 03Aug2009-03Aug2009, 09Sep2009-09Sep2009, 13Oct2009-13Oct2009	01Jan2009	U/0 Days, U/0 Years, U/0 Years, U/0 Years	Convulsion, Pyrexia, Pyrexia	R

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#D0071014A	Germany	MD,RA	6 Months/M	INJ, INJ	U, U	04Apr2011-04Apr2011, 17Jan2011-17Jan2011	01Mar2011	U/0 Days, U/0 Years	Convulsion, Pyrexia, Vomiting, Febrile convulsion, Partial seizures, Partial seizures	R
#B0716693A	Italy	RA	5 Months/M	INJ	U	31Mar2011-31Mar2011	31Mar2011	U/0 Days	Convulsion, Slow response to stimuli, Cyanosis, Grand mal convulsion, Hypotonia, Pallor, Tremor, Staring, Salivary hypersecretion, Hypertonia, Tachycardia, Oxygen saturation decreased	U
#D0070906A	Germany	MD,RA	2 Months/F	INJ	U	31Mar2011-31Mar2011	01Apr2011	U/1 Days	Convulsion, Staring, Pharyngeal erythema, Seborrhoeic dermatitis	U
#B0689913A	Italy	MD,RA	12 Months/M	INJ	U	13Sep2010-13Sep2010	13Sep2010	U/0 Days	Convulsion, Stupor, Vomiting	R

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#B0685462A	France	RA	2 Months/F	INJ	U	21Oct2010-21Oct2010	21Oct2010	U/5 Hours	Convulsion, Tonic clonic movements, Tremor, Eye disorder, Pyrexia	R
#B0731868A	Italy	MD,RA	8 Months/F	INJ	U	27Jun2011-27Jun2011	02Jul2011	U/5 Days	Convulsion, Viral infection, Pyrexia, Rash maculo-papular	R
B0701150A	France	MD	3 Months/U	INJ	U	01May2010-01May2010	01May2010	U/Same day	Crying	R
B0708609A	France	MD	10 Weeks/M	INJ	U	05Jan2011-05Jan2011	05Jan2011	U/Same day	Crying	R
B0718228A	France	MD	4 Months/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/24 Hours	Crying	R
#B0730602A	Italy	MD,RA	3 Months/M	INJ	U	01Jun2011-01Jun2011	01Jun2011	U/0 Days	Crying	R

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#B0692151A	Latvia	HP,RA	2 Months/F	INJ	U	10Nov2010-10Nov2010	10Nov2010	U/Immediate	Crying	R
#B0730049A	France	RA	2 Months/M	INJ	U	26May2011-26May2011	28May2011	U/48 Hours	Crying, Decreased appetite	I
B0721457A	France	MD	2 Months/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/10 Hours	Crying, Diarrhoea	R
B0753926A	France	MD,RP	3 Months/M	INJ	U	24Aug2011-24Aug2011, 08Aug2011-08Aug2011	24Aug2011	U/See text, U/U	Crying, Inappropriate schedule of drug administration	R
B0695532A	Viet Nam	MD	2 Months/M	INJ	U	12Jan2011-12Jan2011	12Jan2011	U/10 Minutes	Crying, Injection site erythema, Erythema	R
B0727510A	Netherlands	HP,RA	4 Months/F	INJ	U	11Oct2010-11Oct2010	11Oct2010	U/0 Days	Crying, Injection site pain, Rash, Insomnia, Pruritus	R

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B0745247A	Czech Republic	MD	20 Months/M	INJ	U	02Sep2011-02Sep2011	02Sep2011	U/2 Days	Crying, Muscle spasms, Injection site erythema	R
#B0725460A	Italy	MD,RA	3 Months/M	INJ	.5ML	01Jun2011-01Jun2011	01Jun2011	U/0 Days	Crying, Oedema peripheral, Erythema	R
B0702044A	Austria	MD	5 Months/M	INJ	U	1 Days		U/2 Hours	Crying, Peripheral coldness, Chills, Tremor, Pyrexia, Agitation	R
B0719498A	Netherlands	HP,RA	10 Months/F	INJ	U	28Sep2010-28Sep2010	28Sep2010	U/Hours	Crying, Pyrexia, Malaise	U
#B0736219A	France	RA	2 Months/M	INJ	U	05May2011-05May2011	05May2011	U/6 Hours	Crying, Pyrexia, Pain in extremity	R
B0707083A	Netherlands	MD,RA	5 Months/F	INJ	U	11Nov2010-11Nov2010	11Nov2010	U/6 Hours	Crying, Pyrexia, Pain, Nasopharyngitis, Eczema, Rash, Rash, Rash	R

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#B0754599A	Czech Republic	RA	4 Months/F	INJ	U	23Sep2011-23Sep2011, 23Aug2011-23Aug2011	23Sep2011	U/0 Days, U/U	Crying*, Pyrexia*, Restlessness*, Tachycardia*	U
#B0741601A	Italy	MD,RA	5 Months/F	INJ	U	27Jul2011-27Jul2011	27Jul2011	U/0 Days	Crying, Respiratory tract inflammation	R
#B0681485A	Poland	MD,RA	3 Months/M	INJ	U	05Jul2010-05Jul2010	06Jul2010	U/1 Days	Crying, Restlessness	R
#B0689246A	Saudia Arabia	MD,RP	4 Months/M	INJ	U	01Nov2010-01Nov2010	01Nov2010	U/0 Days	Demyelination, Extrapyramidal disorder, Neurological symptom, Irritability, Crying, Pyrexia, Strabismus	I
#B0746088A	Netherlands	HP,RA	2 Months/M	INJ	U	12Oct2010-12Oct2010	12Oct2010	U/3 Seconds	Depressed level of consciousness, Crying, Injection site inflammation, Pallor, Hypotonia, Oligodipsia, Somnolence, Respiratory disorder	I

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#B0707035A	Netherlands	HP,MD,RA	3 Months/F	INJ	U	10Sep2010-10Sep2010		U/Unknown	Depressed level of consciousness, Crying, Pyrexia, Injection site inflammation, Injection site pain, Insomnia, Nasopharyngitis	R
D0069325A	Germany	OM,MD	3 Months/M	INJ	U	04Oct2010-04Oct2010	04Oct2010	U/8 Hours	Depressed level of consciousness, Hypotonic-hypore sponsive episode, Pallor, Fatigue, Eye movement disorder	R
#B0727317A	Netherlands	MD,RA	2 Months/M	INJ	U	29Apr2011-29Apr2011	01May2011	U/2 Days	Depressed level of consciousness, Hypotonic-hypore sponsive episode, Pallor, Ill-defined disorder, Feeling abnormal, Pyrexia	U
#B0719423A	Netherlands	HP,RA	9 Months/M	INJ	U	17Sep2010-17Sep2010	17Sep2010	U/0 Days	Depressed level of consciousness, Inflammation, Pain, Injected limb mobility decreased, Pyrexia, Crying	R
#B0712989A	Netherlands	HP,RA	3 Months/M	INJ, INJ, INJ	U, U, U	16Mar2011-16Mar2011, 01Apr2011-01Apr2011, 11May2011-11May2011	16Mar2011	U/2 Minutes, U/0 Months, U/0 Days	Depressed level of consciousness, Pallor, Crying, Somnolence, Malaise, Malaise	R

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#B0755401A	Netherlands	HP,RA	2 Months/M	INJ	U	08Apr2010-08Apr2010	09Apr2010	U/1 Days	Depressed level of consciousness, Pyrexia, Inflammation, Pain, Vomiting, Somnolence, Diarrhoea, Staring	R
#B0732346A	Netherlands	HP,RA	2 Months/F	INJ	U	10May2011-10May2011	10May2011	U/4 Hours	Depressed level of consciousness, Pyrexia, Somnolence	U
#B0712012A	Netherlands	HP,RA	2 Months/F	INJ	U	22Jul2010-22Jul2010	22Jul2010	U/Hours	Depressed level of consciousness, Skin warm, Staring, Hypotonia, Respiration abnormal, Crying, Pyrexia, Injection site pain	R
#B0756437A	Netherlands	HP,RA	2 Months/M	INJ	.5ML	11Oct2011-11Oct2011	11Oct2011	U/5 Minutes	Depressed level of consciousness, Staring, Pallor	R
#D0071549A	Germany	MD,RA	4 Months/M	INJ	U	07Apr2011-07Apr2011	07Apr2011	U/0 Days	Encephalitis, Bronchitis, Lactic acidosis, Hyperglycaemia, Convulsion, Injection site induration, Pyrexia,	N

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										Somnolence, Hypotonia, Depressed level of consciousness, Respiration abnormal, Cough, Pallor, Lip haematoma, General physical health deterioration, Moaning, Respiratory tract infection, Restlessness, Rhinitis, Body temperature fluctuation	
406	#B0686208A	Italy	MD,RP	3 Months/U	INJ	U	08Nov2010-08Nov2010		U/0 Months	Encephalitis, Epilepsy	U
	#D0071841A	Germany	MD,RA,RP	4 Months/F	INJ	U	09Feb2011-U	10Feb2011	U/0 Days	Encephalopathy, Infantile spasms, Lennox-Gastaut syndrome, Dyskinesia, Developmental delay, Eye movement disorder, Motor dysfunction, Posture abnormal, Fatigue,	N

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#R0014765A	Spain	C	4 Months/M	INJ	U	22Nov2010-22Nov2010	29Nov2010	U/7 Days	Hyperhidrosis, Crying, Pallor, Diarrhoea, Musculoskeletal stiffness, Depressed level of consciousness, Headache, Hypotonia, Myoclonus, Constipation, Infantile spasms, Abdominal pain Epilepsy*	I
#B0686639A	Italy	MD,RA	3 Months/F	INJ	U	08Nov2010-08Nov2010	18Nov2010	U/10 Days	Epilepsy, Cerebral ischaemia, Partial seizures	U
#B0737600A	Latvia	HP,RA	3 Months/M	INJ	.5ML	14Dec2010-14Dec2010	26Dec2010	U/12 Days	Epilepsy, Convulsion	U
#B0720048A	Czech Republic	MD,RA	6 Months/F	INJ	U	29Mar2011-29Mar2011	30Mar2011	U/1 Days	Epilepsy, Infantile spasms, Tearfulness, Dyskinesia	N

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#B0700168A	Italy	MD,RA	5 Months/M	INJ	U	04Nov2010-04Nov2010	04Nov2010	U/0 Days	Epilepsy, Petit mal epilepsy, Staring, Clonus, Clonus, Dyskinesia, Pyrexia	U
#D0070004A	Germany	RA	4 Months/M	INJ	.5ML	28Jun2010-28Jun2010	01Jan2010	U/0 Years	Facial paresis*	R
#D0070963A	Germany	MD,RP	22 Months/M	INJ	U	06Apr2011-06Apr2011	01Apr2011	U/0 Weeks	Febrile convulsion	R
#D0072063A	Germany	MD,RP	15 Months/F	INJ	U	12Jul2011-12Jul2011	01Jul2011	U/8 Hours	Febrile convulsion	R
#B0683431A	Italy	MD,RA	2 Months/F	INJ	U	21Oct2010-21Oct2010	22Oct2010	U/1 Days	Febrile convulsion	R
#B0690567A	Italy	MD,RA	14 Months/M	INJ	U	06Dec2010-06Dec2010	06Dec2010	U/0 Days	Febrile convulsion	R

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#B0710862A	Italy	RA	2 Months/F	INJ	U	13Sep2010-13Sep2010	13Sep2010	U/0 Days	Febrile convulsion	R
#B0722025A	Italy	RA	8 Months/M	INJ	U	21Sep2010-21Sep2010	22Sep2010	U/1 Days	Febrile convulsion	R
#B0735096A	Italy	MD,RA	10 Months/M	INJ	U	19Jul2011-19Jul2011	19Jul2011	U/0 Days	Febrile convulsion	R
#B0751261A	Italy	MD,RA	16 Months/M	INJ	U	19Sep2011-19Sep2011	20Sep2011	U/1 Days	Febrile convulsion	R
#B0709252A	Netherlands	HP,RA	12 Months/F	INJ	U	20Jan2011-20Jan2011	20Jan2011	U/Hours	Febrile convulsion	R
#B0744547A	Philippines	MD	0-9 Years/U	INJ	U	01Jan2011-01Jan2011		U/1 Days	Febrile convulsion	R

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#D0072283A	Germany	RA	20 Months/M	INJ	.5ML	08Jun2011-08Jun2011	01Jan2011	U/0 Years	Febrile convulsion*	R
#B0747746A	Poland	MD,RA	4 Months/F	INJ	U	11Aug2011-11Aug2011	11Aug2011	U/5 Hours	Febrile convulsion, Cyanosis, Lividity, Pyrexia	R
#B0716294A	Italy	MD,RA	13 Months/M	INJ	U	16Feb2011-16Feb2011	16Feb2011	U/0 Days	Febrile convulsion, Cyanosis, Loss of consciousness, Clonus, Salivary hypersecretion, Hypertonia	R
#D0070029A	Germany	RA	14 Months/M	INJ	.5ML	06Oct2010-06Oct2010	06Oct2010	U/0 Days	Febrile convulsion, Dyskinesia	R
#B0693711A	Italy	MD,RA	12 Months/F	INJ	U	02Feb2010-02Feb2010	03Feb2010	U/1 Days	Febrile convulsion*, Febrile convulsion*	

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#D0072871A	Germany	MD,RA	4 Months/M	INJ	U	21Sep2011-21Sep2011	21Sep2011	U/7 Hours	Febrile convulsion, Hypotonia, Pallor, Staring, Muscle twitching	R
#B0741648A	Italy	MD,RA	5 Months/F	INJ	.5ML	12Aug2011-12Aug2011	12Aug2011	U/0 Days	Febrile convulsion, Irritability	I
#B0692681A	Netherlands	HP,RA	18 Months/M	INJ	U	11Nov2010-11Nov2010	11Nov2010	U/4 Hours	Febrile convulsion, Loss of consciousness, Pallor, Tremor, Hypotonia, Peripheral coldness, Respiratory disorder, Cyanosis, Chills, Postictal state, Pyrexia	R
#B0728516A	Italy	MD,RA	12 Months/M	INJ	U	26May2011-26May2011	27May2011	U/1 Days	Febrile convulsion, Loss of consciousness, Tremor, Complex partial seizures, Grand mal convulsion, Pyrexia	R

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#B0740272A	France	PH	17 Months/M	INJ	U	17Jun2011-17Jun2011	28Jun2011	U/11 Days	Febrile convulsion, Lung infection, Hypertonia, Clonic convulsion, Pharyngeal erythema, Otitis media, Lymphadenopathy, Lung disorder, Pyrexia	R
#D0072315A	Germany	RA	4 Months/F	INJ	.5ML	24May2011-24May2011	25May2011	U/1 Days	Febrile convulsion*, Muscle rigidity*, Opisthotonus*, Gaze palsy*, Pyrexia*	R
#B0696414A	France	MD	16 Months/U	INJ	U	26Jan2011-26Jan2011	26Jan2011	U/Same day	Febrile convulsion, Pyrexia	R
#D0070007A	Germany	RA	8 Months/F	INJ	U	04Nov2010-04Nov2010	04Nov2010	U/0 Days	Febrile convulsion, Pyrexia	R
#B0692011A	Italy	MD,RA	1 Years/F	INJ	U	07Jan2010-07Jan2010	07Jan2010	U/0 Days	Febrile convulsion, Pyrexia	R

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#B0741635A	Italy	RA	11 Months/F	INJ	U	25Jul2011-25Jul2011	25Jul2011	U/0 Days	Febrile convulsion, Pyrexia	R
#B0743123A	Italy	RA	11 Months/F	INJ	U	22Jul2011-22Jul2011	22Jul2011	U/0 Days	Febrile convulsion, Pyrexia	R
#D0072318A	Germany	RA	15 Months/F	INJ	.5ML	26Jul2011-26Jul2011, 24Jun2010-24Jun2010, 23Jul2010-23Jul2010, 20Aug2010-20Aug2010	26Jul2011	U/0 Days, U/U, U/U, U/U	Febrile convulsion*, Pyrexia*, Chills*, Gaze palsy*, Eye movement disorder*, Cyanosis*, Unresponsive to stimuli*, Tremor*, Grand mal convulsion*, Upper respiratory tract infection*	R
#B0730181A	France	RA	2 Months/M	INJ	U	15Mar2011-15Mar2011	15Mar2011	U/8 Hours	Febrile convulsion, Pyrexia, Eye disorder, Hypertonia	R
#D0069309A	Germany	MD,RA	4 Months/M	INJ	U	22Sep2010-22Sep2010	22Sep2010	U/0 Days	Febrile convulsion, Pyrexia, Musculoskeletal stiffness, Gaze palsy,	U

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									Somnolence, Transaminases increased, Pharyngeal erythema, Tympanic membrane hyperaemia	
#B0733980A	Italy	PH,RA	27 Months/M	INJ	U	30Jun2011-30Jun2011	30Jun2011	U/0 Days	Febrile convulsion, Pyrexia, Tonsillar hypertrophy, Hyperaemia	R
#D0072920A	Germany	HP,RA	15 Months/M	INJ, INJ, INJ, INJ	U, U, U, U	20Sep2011-20Sep2011, 30Jul2010-30Jul2010, 30Aug2010-30Aug2010, 30Sep2010-30Sep2010	01Jan2010	U/6 Hours, U/Unknown, U/Unknown, U/Unknown	Febrile convulsion, Rash, Pyrexia, Pyrexia	N
#D0071016A	Germany	OM,MD	22 Months/M	INJ	U	06Apr2011-06Apr2011	06Apr2011	U/1 Hours	Febrile convulsion, Vomiting, Unresponsive to stimuli, Staring, Muscle twitching	R
#B0683700A	Italy	MD,RA	5 Months/M	INJ	U	04Oct2010-04Oct2010	04Oct2010	U/0 Days	Fontanelle bulging, Pyrexia, Hyperaemia	R

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#B0691640A	Spain	RA	6 Years/F	INJ	U	18Aug2010-18Aug2010	18Aug2010	U/0 Days	Grand mal convulsion*	R
#B0733550A	Austria	MD,RA	4 Months/F	INJ	.5ML	20Jun2011-20Jun2011	20Jun2011	U/0 Days	Grand mal convulsion, Agitation, Crying, Decreased appetite	R
#B0689285A	Slovakia	MD,RA	3 Months/M	INJ	U	09Nov2010-09Nov2010	09Nov2010	U/Minutes	Grand mal convulsion, Altered state of consciousness, Apnoea	R
#D0070812A	Germany	MD,RA	12 Months/F	INJ	U	14Mar2011-14Mar2011	11Feb2011	U/2 Days	Grand mal convulsion, Convulsion, Hypersensitivity, Rash macular, Crying, Eye movement disorder, Dyskinesia, Salivary hypersecretion	R
#B0706275A	Italy	MD,RA	4 Months/M	INJ	U	24Feb2011-24Feb2011	24Feb2011	U/0 Days	Grand mal convulsion, Loss of consciousness, Staring, Hypertonia, Erythema, Gastrooesophageal reflux disease,	R

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									Regurgitation	
#D0071096A	Germany	HP,OM	5 Months/M	INJ	U	02Dec2008-02Dec2008	02Dec2008	U/0 Days	Grand mal convulsion, Muscle twitching, Somnolence, Pyrexia, Somnolence	R
#B0711246A	Italy	MD,RP	2 Months/F	INJ	U	10Mar2011-10Mar2011	10Mar2011	U/0 Days	Grand mal convulsion, Myoclonus, Staring, Pyrexia	N
#B0733530A	Italy	MD,RA	5 Months/F	INJ	U	06Jul2011-06Jul2011	06Jul2011	U/0 Days	Grand mal convulsion, Pyrexia	I
#B0749797A	Italy	MD,RA	5 Months/M	INJ	U	30Aug2011-30Aug2011	30Aug2011	U/0 Days	Grand mal convulsion, Pyrexia	R
#B0702457A	Italy	MD,RA	12 Months/M	INJ	U	01Feb2011-01Feb2011	01Feb2011	U/0 Days	Grand mal convulsion, Respiratory tract infection	R

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#D0069554A	Germany	MD,RA	2 Months/F	INJ, INJ, INJ	U, U, U	22Aug2006-U, 26Sep2006-U, 24Oct2006-U	01Jan2006	U/Unknown, U/Unknown, U/Unknown	Guillain-Barre syndrome, Congenital neuropathy, Demyelinating polyneuropathy, Hip deformity, Foot deformity, Motor developmental delay	U
#B0691863A	Italy	RA	15 Months/M	INJ	U	08Sep2010-08Sep2010	10Sep2010	U/2 Days	Guillain-Barre syndrome*, Neuropathy peripheral*, Pyrexia*, General physical health deterioration*, Restlessness*, Asthma*, Decreased appetite*, Gait disturbance*, Dysstasia*, Nuchal rigidity*, General physical health deterioration*, Hyperaemia*, Dysphonia*, Hyporeflexia*, Hypotonia*, Asthenia*	R

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#B0749283A	Italy	MD,RA	7 Months/M	INJ	U	25Jan2011-25Jan2011	25Jan2011	U/0 Days	Hypertonia, Eye disorder, Pyrexia	R
#B0715581A	France	RA	2 Months/F	INJ	U	30Nov2010-30Nov2010	30Nov2010	U/Hours	Hypertonia, Loss of consciousness, Cyanosis, Clonus, Eye disorder, Apathy, Convulsion	R
B0706811A	Colombia	MD	Child/F	INJ, INJ	U, U	1 Days, 1 Days		U/Unknown, U/Unknown	Hypotonia	I
B0744733A	Netherlands	MD,RA	2 Months/F	INJ	U	22Jul2011-22Jul2011	22Jul2011	U/9 Hours	Hypotonia	R
#B0686828A	France	RA	17 Months/M	INJ	U	29Oct2010-29Oct2010	29Oct2010	U/Immediate	Hypotonia, Cerebellar ataxia, Gait disturbance, Pain, Hyperthermia, C-reactive protein increased	R

#B0712016A	Italy	MD,RA	11 Months/M	INJ	U	25Mar2011-25Mar2011	26Mar2011	U/1 Days	Hypotonia, Hyperhidrosis, Pyrexia	F
#B0747819A	France	RA	7 Weeks/F	INJ	U	23May2011-23May2011	24May2011	U/0 Days	Hypotonia, Hypersomnia, Feeding disorder neonatal, Drug administration error	R
#B0705448A	Italy	MD,RA	5 Months/F	INJ	U	25Jan2010-25Jan2010, 05Nov2010-05Nov2010	26Jan2010	U/1 Days, U/U	Hypotonia, Hypokinesia, Musculoskeletal stiffness	R
B0693444A	Netherlands	HP,RA	3 Months/F	INJ	U	28Jun2010-28Jun2010	28Jun2010	U/1 Hours	Hypotonia, Inflammation, Pyrexia, Crying	R
#B0703590A	Italy	MD,RA,RP	3 Months/M	INJ	U	08Feb2011-08Feb2011	08Feb2011	U/0 Days	Hypotonia, Pyrexia	R
#B0716297A	France	RA	2 Months/M	INJ	U	1 Days		U/1 Days	Hypotonia, Slow response to stimuli, Pallor, Incorrect route of drug administration	R

#D0071308A	Germany	MD	5 Months/M	INJ	U	05May2011-05May2011	05May2011	U/0 Days	Hypotonic-hypore sponsive episode	R
#D0071532A	Germany	RA	4 Months/F	INJ	U	1 Days	09Nov2010	U/U	Hypotonic-hypore sponsive episode	R
B0707733A	Netherlands	MD,RA	2 Months/M	INJ	U	25Jan2011-25Jan2011	25Jan2011	U/10 Hours	Hypotonic-hypore sponsive episode	R
#B0685055A	Poland	MD,RA	4 Months/U	INJ	U	29Oct2010-29Oct2010	29Oct2010	U/0 Days	Hypotonic-hypore sponsive episode	R
#B0687935A	Poland	P	2 Months/M	INJ	U	04Nov2010-04Nov2010	06Nov2010	U/2 Days	Hypotonic-hypore sponsive episode	R
#B0713426A	Poland	MD,RA	2 Months/U	INJ	U	1 Days	12Mar2011	U/Unknown	Hypotonic-hypore sponsive episode	U

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#B0725461A	Spain	MD,RA	4 Months/F	INJ	U	20Apr2011-20Apr2011	20Apr2011	U/0 Days	Hypotonic-hypore sponsive episode	R
#R0014955A	Czech Republic	C	3 Months/M	INJ	U	08Dec2010-08Dec2010	08Dec2010	U/7 Hours	Hypotonic-hypore sponsive episode*	R
#B0686455A	Poland	MD,RA	2 Months/U	INJ	U	04Nov2010-04Nov2010	07Nov2010	U/3 Days	Hypotonic-hypore sponsive episode, Abdominal pain, Vaccination complication, Restlessness, Crying, Somnolence	U
#B0714363A	Netherlands	HP,RA	2 Months/M	INJ	U	01Mar2011-01Mar2011	01Mar2011	U/8 Hours	Hypotonic-hypore sponsive episode, Anaemia, Hypotonia, Pallor, Dyspnoea, Bradycardia, Hypopnoea, Staring	R
#D0070026A	Germany	RA	9 Weeks/F	INJ	.5ML	22Dec2010-22Dec2010	22Dec2010	U/0 Days	Hypotonic-hypore sponsive episode*, Apathy*	R

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#D0071099A	Germany	MD,RA	11 Weeks/F	INJ	U	06Apr2011-06Apr2011	06Apr2011	U/0 Days	Hypotonic-hypore sponsive episode, Body temperature increased, Crying, Asthenia, Pallor, Depressed level of consciousness, Pallor, Pharyngeal erythema	R
#D0071446A	Germany	OM,MD,RA	8 Weeks/M	INJ	U	15Apr2011-15Apr2011	15Apr2011	U/6 Hours	Hypotonic-hypore sponsive episode, Circulatory collapse, Apathy, Pallor	R
#B0732350B	Netherlands	CO,RA	6 Months/M	INJ	U	17Aug2011-17Aug2011	17Aug2011	U/3 Hours	Hypotonic-hypore sponsive episode, Crying, Pallor, Hypotonia, Somnolence, Unresponsive to stimuli	R
#B0693275A	Poland	MD,RA	4 Months/U	INJ	U	20Apr2010-20Apr2010	20Apr2010	U/0 Days	Hypotonic-hypore sponsive episode, Cyanosis	R
#B0706016A	Poland	MD,RA	2 Months/F	INJ	U	27Jan2011-27Jan2011	27Jan2011	U/3 Hours	Hypotonic-hypore sponsive episode, Cyanosis, Somnolence, Crying, Restlessness, Pyrexia, Hypotonia,	R

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									Anxiety, Lividity	
#B0709632A	Poland	MD,RA	4 Months/U	INJ	U	20Jan2011-20Jan2011	21Jan2011	U/1 Days	Hypotonic-hypore sponsive episode, Decreased activity, Hypotonia, Decreased appetite	R
#D0072088A	Germany	MD,RA	8 Weeks/F	INJ	U	15Jun2011-15Jun2011	15Jun2011	U/7 Hours	Hypotonic-hypore sponsive episode, Dyspnoea, Vomiting, Hypotonia, Apathy, Vaccination complication	R
#D0071728A	Germany	RA	3 Months/F	INJ	.5ML	30Mar2011-30Mar2011, 18May2011-18May2011	18May2011	U/0 Days, U/U	Hypotonic-hypore sponsive episode*, Eye movement disorder*, Convulsion*, Gaze palsy*, Opisthotonus*, Crying*	R
#B0690071A	Czech Republic	MD,RA	3 Months/M	INJ	U	08Dec2010-08Dec2010	08Dec2010	U/8 Hours	Hypotonic-hypore sponsive episode, Gaze palsy, Opisthotonus, Pallor, Apathy, Fear, Agitation, Hypotonia, Crying	U

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#B0742512A	Switzerland	RA	2 Months/M	INJ	.5ML	28Jun2011-28Jun2011	28Jun2011	U/Immediate	Hypotonic-hypore sponsive episode, Hypersensitivity, Pallor, Eye movement disorder, Dyspnoea, Crying, Hypotonia, Eye disorder	R
#B0724391A	Spain	HP,RA	2 Months/F	INJ	U	23May2011-23May2011	23May2011	U/Immediate	Hypotonic-hypore sponsive episode, Hypotonia	R
#B0701374A	Switzerland	MD,RA,RP	2 Months/M	INJ, INJ	U, U	11Feb2011-11Feb2011, 29Apr2011-29Apr2011	11Feb2011	U/0 Days, U/3 Hours	Hypotonic-hypore sponsive episode, Loss of consciousness, Depressed level of consciousness, Unresponsive to stimuli, Cyanosis, Cough, Ill-defined disorder, Fatigue, Adverse event, Vomiting, Eyelid disorder, Crying, Somnolence, Crying	R
#B0741462A	Poland	MD,RA	3 Months/U	INJ	U	29Jun2011-29Jun2011	29Jun2011	U/Immediate	Hypotonic-hypore sponsive episode, Loss of consciousness, Somnolence, Pallor, Hypotonia,	R

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									Crying	
#B0722375A	Poland	MD,RA	22 Months/U	INJ	U	27Apr2011-27Apr2011	27Apr2011	U/Hours	Hypotonic-hypore sponsive episode, Pain in extremity, Gait disturbance, Body temperature increased, Somnolence	R
#B0727152A	Italy	MD,RA	2 Months/M	INJ	U	03Jun2011-03Jun2011	03Jun2011	U/6 Hours	Hypotonic-hypore sponsive episode, Pallor	R
#B0712205A	Switzerland	MD,RA	70 Days/M	INJ	.5ML	20Dec2010-20Dec2010	20Dec2010	U/5 Hours	Hypotonic-hypore sponsive episode, Pallor	R
#B0686517A	Greece	MD,RA	4 Months/F	INJ	U	15Sep2010-15Sep2010	15Sep2010	U/5 Hours	Hypotonic-hypore sponsive episode*, Pallor*	R

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#B0727181A	Sweden	HP,RA	3 Months/F	INJ	U	02May2011-02May2011	02May2011	U/0 Days	Hypotonic-hypore sponsive episode, Pallor, Ill-defined disorder, Nasopharyngitis	R
#B0727465A	Poland	MD,RA	1 Months/U	INJ	U	24May2011-24May2011	24May2011	U/0 Days	Hypotonic-hypore sponsive episode, Pallor, Lividity, Cyanosis	R
#D0070873A	Germany	RA	2 Months/F	INJ	U	25Jan2011-25Jan2011	25Jan2011	U/0 Days	Hypotonic-hypore sponsive episode, Pallor, Somnolence	R
D0070860A	Germany	MD	2 Months/M	INJ, INJ	U, U	01Mar2011-01Mar2011, 01Feb2011-01Feb2011	01Feb2011	U/0 Days, U/6 Hours	Hypotonic-hypore sponsive episode, Pyrexia	R
#B0741329A	Poland	MD,RA	2 Months/U	INJ	U	20Jul2011-20Jul2011	20Jul2011	U/0 Days	Hypotonic-hypore sponsive episode, Pyrexia	R
#B0720694A	Poland	MD,RA	19 Months/U	INJ	U	01Mar2011-01Mar2011	01Mar2011	U/0 Days	Hypotonic-hypore sponsive episode, Pyrexia, Crying, Somnolence	R

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#D0070819A	Germany	MD	4 Months/F	INJ	U	10Mar2011-10Mar2011	10Mar2011	U/0 Days	Hypotonic-hypore sponsive episode, Pyrexia, Vomiting, Loss of consciousness, Restlessness, Hyperhidrosis, Abnormal faeces, Hypotonia, Eye movement disorder, Fatigue, Abdominal distension, Abnormal faeces, Pharyngeal erythema	R
#B0710929A	Netherlands	HP,RA	2 Months/F	INJ	U	11Mar2011-11Mar2011	11Mar2011	U/Minutes	Hypotonic-hypore sponsive episode, Respiratory arrest, Crying	R
#B0686677A	Poland	MD,RA	4 Months/M	INJ	U	06Oct2010-06Oct2010	06Oct2010	U/0 Days	Hypotonic-hypore sponsive episode*, Screaming*, Apathy*, Unresponsive to stimuli*, Sleep disorder*, Muscle tightness*, Abdominal pain*, Decreased activity*, Hypertonia*, Ill-defined disorder*,	R

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									Hypotonia*, Developmental delay*, Muscle spasms*, Restlessness*, Crying*	
#B0734272A	Poland	MD,RA	1 Months/F	INJ	U	25May2011-25May2011	28May2011	U/0 Days	Hypotonic-hypore sponsive episode, Somnolence, Hypotonia, Body temperature decreased	R
#B0702562A	France	MD,RA	10 Weeks/M	INJ	U	23Feb2011-23Feb2011	24Feb2011	U/18 Hours	Hypotonic-hypore sponsive episode, Somnolence, Pallor, Incorrect route of drug administration, Neurological examination abnormal	R
#D0069604A	Germany	MD	6 Months/F	INJ	.5ML	23Nov2010-23Nov2010	23Nov2010	U/Immediate	Hypotonic-hypore sponsive episode*, Syncope*, Skin discolouration*, Pallor*, Crying*, Unresponsive to stimuli*, Cardiovascular disorder*	R
#B0700353A	Spain	CO,MD	2 Months/F	INJ	U	10Feb2011-10Feb2011	10Feb2011	U/Hours	Hypotonic-hypore sponsive episode, Unresponsive to stimuli, Respiration abnormal,	R

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									Hypotonia, Pyrexia, Hypotonia	
#B0733152A	Italy	MD,RA	2 Months/F	INJ	U	27Jun2011-27Jun2011	28Jun2011	U/1 Days	Hypotonic-hypore sponsive episode, Vomiting, Diarrhoea, Decreased appetite	I
#B0684471A	Italy	MD	7 Months/F	INJ	U	02Dec2003-02Dec2003, 29Sep2003-29Sep2003	01Feb2004	U/2 Months, U/U	Infantile spasms	N
#D0069378A	Germany	HP,RA	5 Months/F	INJ, INJ	U, U	14Jun2010-14Jun2010, 19May2010-19May2010	29Jul2010	U/45 Days, U/71 Days	Infantile spasms, Cerebral disorder	N
#D0070024A	Germany	HP	4 Months/F	INJ, INJ	U, U	08May2009-08May2009, 05Jun2009-05Jun2009, 17Jul2009-17Jul2009	05Jun2009	U/0 Days, U/7 Days, U/Unknown	Infantile spasms, Developmental delay, Posture abnormal, Restlessness, Crying, Hypotonia, Microcephaly, Infantile spasms, Cerebral atrophy, Bone marrow failure, Vomiting, Dehydration,	U

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									Hypokalaemia, Pancytopenia	
#B0695552A	Italy	MD,RA	2 Months/M	INJ	.5ML	13Jan2011-13Jan2011	13Jan2011	U/Hours	Infantile spasms, Slow response to stimuli, Hypertonia, Staring, Tremor, Clonus, Muscle spasms, Joint hyperextension, Adenovirus test positive, Pyrexia, Crying	U
#D0071516A	Germany	MD,RA	3 Months/F	INJ	.5ML	20Oct2010-20Oct2010	20Oct2010	U/30 Minutes	Loss of consciousness	R
#B0717794A	Netherlands	HP,MD,RA	2 Months/F	INJ	U	21Sep2010-21Sep2010	01Sep2010	U/36 Hours	Loss of consciousness, Apnoea, Depressed level of consciousness, Gaze palsy, Pallor, Cyanosis, Hypotonia, Peripheral coldness, Pyrexia	R

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#B0732350A	Netherlands	MD,RA	3 Months/M	INJ	.5ML	09Jun2011-09Jun2011	09Jun2011	U/4 Hours	Loss of consciousness, Apnoea, Hypotonic-hypore sponsive episode, Pallor, Hypotonia	R
#B0722809A	Czech Republic	MD,RA	3 Months/F	INJ	U	29Nov2010-29Nov2010	29Nov2010	U/0 Days	Loss of consciousness, Convulsion, Cyanosis, Somnolence, Body temperature increased, Crying	R
#B0712712A	Netherlands	HP,RA	13 Months/M	INJ	U	10Aug2010-10Aug2010	10Aug2010	U/Hours	Loss of consciousness, Depressed level of consciousness, Convulsion, Gaze palsy, Respiration abnormal, Pallor, Hypotonia, Drooling, Cyanosis, Pyrexia, Vomiting	R
#B0687865A	Italy	MD,RA	11 Months/M	INJ	U	11Jun2010-11Jun2010	13Jun2010	U/2 Days	Loss of consciousness, Gaze palsy, Pallor, Hypotonia	R
#B0757269A	France	MD,RP	2 Months/U	INJ	U	01Oct2011-01Oct2011	01Oct2011	U/10 Minutes	Loss of consciousness, Hypotonia, Somnolence	R

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#B0716724A	Poland	MD,RA	2 Months/F	INJ	U	15Mar2011-15Mar2011	15Mar2011	U/0 Days	Loss of consciousness, Hypotonic-hypore sponsive episode, Hypotonia, Diarrhoea	R
#B0744808A	Italy	MD,RA	5 Months/M	INJ	U	27Jan2011-27Jan2011	15Feb2011	U/19 Days	Loss of consciousness, Nystagmus, Opisthotonus, Eye movement disorder, Pyrexia, Vomiting	R
#B0695521A	Netherlands	HP,RA	2 Months/M	INJ	U	23Jun2010-23Jun2010	01Jun2010	U/8 Hours	Loss of consciousness, Pallor, Hypotonia, Feeling cold, Somnolence	R
#B0709247A	Netherlands	HP,RA	6 Months/M	INJ	U	13Mar2009-13Mar2009	13Mar2009	U/1 Hours	Loss of consciousness, Pallor, Hypotonia, Hypotonic-hypore sponsive episode, Vomiting	R
#B0709210A	Italy	MD,RA	2 Months/M	INJ	U	31Jan2011-31Jan2011	31Jan2011	U/8 Hours	Loss of consciousness, Pallor, Pyrexia	R

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#B0702744A	Italy	MD,RA	2 Months/M	INJ	U	16Nov2009-16Nov2009	17Nov2009	U/1 Days	Loss of consciousness, Pyrexia	R
#B0724363A	Italy	MD,RA	4 Months/M	INJ	U	12Nov2010-12Nov2010	12Nov2010	U/0 Days	Loss of consciousness, Pyrexia, Pallor, Arrhythmia	R
#B0712309A	Ireland	MD,RA	9 Months/F	INJ	U	18Jan2011-18Jan2011	25Jan2011	U/7 Days	Myelitis transverse, Muscular weakness, Mobility decreased, Hypotonia	N
B0732338A	Mexico	MD,RP	Infant/U	INJ	U	08Apr2011-08Apr2011	09Apr2011	U/1 Days	Myoclonus	I
D0069372A	Germany	MD,RA	5 Months/F	INJ	U	07Oct2010-07Oct2010	08Oct2010	U/1 Days	Neuropathy peripheral, Infection	N

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#D0073031A	Germany	HP	U/U	INJ	U	13Nov2003-13Nov2003		U/Unknown	Paresis	U
#B0713436A	Italy	MD,RA	5 Months/F	INJ	U	30Mar2011-30Mar2011	31Mar2011	U/1 Days	Petit mal epilepsy, Blepharospasm, Dyskinesia	R
#D0070286A	Germany	CO,PH,MD, RP	1 Years/F	INJ	U	02Sep2010-02Sep2010	08Sep2010	U/6 Days	Petit mal epilepsy, Staring, Dyskinesia	U
#B0705098A	France	MD	2 Months/F	INJ	U	22Dec2010-22Dec2010	22Dec2010	U/Immediate	Presyncope, Bradycardia, Hypotonia, Injection site pain, Loss of consciousness, Cyanosis	R
#B0750040A	Netherlands	MD,RA	2 Months/F	INJ	U	11Jul2011-11Jul2011	11Jul2011	U/7 Hours	Presyncope, Febrile convulsion, Depressed level of consciousness, Hypertonia, Myoclonus, Pallor, Pyrexia, Musculoskeletal stiffness	R

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#B0683333A	Netherlands	HP,RA	3 Months/M	INJ	U	23Sep2010-23Sep2010, 26Aug2010-26Aug2010	01Sep2010	U/Hours, U/U	Presyncope, Loss of consciousness, Depressed level of consciousness, Staring, Hypotonia, Pallor, Crying, Pyrexia, Pain, Mental impairment, Vomiting, Muscle contractions involuntary, Myoclonus, Abdominal abscess, Irritability, Hypotonic-hypore sponsive episode	R
#B0756838A	Netherlands	HP,MD,RA	2 Months/M	INJ	.5ML	03Oct2011-03Oct2011	03Oct2011	U/2 Minutes	Presyncope, Pallor, Hyperhidrosis, Feeling cold, Heart rate increased	R
#B0733860A	Italy	RA	5 Months/F	INJ	U	25May2011-25May2011	25May2011	U/0 Days	Presyncope, Syncope, Pallor, Hypotonia, Vomiting	R
#B0691520A	United Arab Emirates	MD	2 Months/F	INJ	U	10Oct2010-10Oct2010	10Oct2010	U/0 Days	Seizure like phenomena	R

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#B0690039A	Greece	CO,MD	8 Months/F	INJ	U	17Nov2010-17Nov2010	18Nov2010	U/1 Days	Seizure like phenomena, Oedema peripheral, Immobile	I
#B0738735A	Italy	RA	3 Months/M	INJ	U	01Aug2011-01Aug2011	02Aug2011	U/1 Days	Slow response to stimuli, Hypotonia	R
#B0693450A	Italy	RA	5 Months/M	INJ	U	16Mar2010-16Mar2010	16Mar2010	U/0 Days	Slow response to stimuli, Hypotonia, Pyrexia	R
#B0709033A	Italy	MD,RA	2 Months/M	INJ	U	14Mar2011-14Mar2011	14Mar2011	U/10 Minutes	Slow response to stimuli, Hypotonia, Rash macular, Petechiae, Ecchymosis, Conjunctival haemorrhage, Rash, Joint hyperextension	R
#B0696267A	Italy	RA	2 Months/M	INJ	U	24Jan2011-24Jan2011	24Jan2011	U/0 Days	Slow response to stimuli, Pallor	I

#D0072337B	Germany	MD	7 Months/M	INJ	U	04Aug2011-04Aug2011	01Aug2011	U/8 Hours	Slow response to stimuli, Pallor, Vomiting	R
#D0072337A	Germany	MD	5 Months/M	INJ	U	28Jun2011-28Jun2011	01Jan2011	U/8 Hours	Slow response to stimuli, Pallor, Vomiting, Rash	R
#B0747384A	Italy	MD,RA	2 Months/M	INJ	U	01Jul2011-01Jul2011	01Jul2011	U/0 Days	Slow response to stimuli, Pyrexia, Decreased appetite, Crying, Hypotonia, Opisthotonus	R
#B0720136A	Italy	RA	3 Months/F	INJ	U	14Jan2011-14Jan2011	14Jan2011	U/0 Days	Slow response to stimuli, Tremor, Respiratory disorder, Pyrexia	R
#B0712001A	Poland	CO,MD	7 Weeks/F	INJ	U	30Mar2011-30Mar2011	31Mar2011	U/1 Days	Somnolence, Injection site reaction	R
#B0710868A	Netherlands	HP,RA	11 Months/F	INJ	U	12Feb2010-12Feb2010	12Feb2010	U/0 Days	Status epilepticus, Loss of consciousness, Apnoea, Convulsion, Vomiting, Skin	R

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									warm, Staring, Hypotonia, Nerve stimulation test abnormal, Crying, Erythema, Upper respiratory tract infection, Pyrexia, Hypertonia, Postictal state, Malaise, Listless	
#B0687818A	Italy	MD,RA	11 Months/F	INJ	U	02Dec2010-02Dec2010, 23Mar2010-23Mar2010, 25May2010-25May2010	02Dec2010	U/0 Days, U/U, U/U	Syncope	R
#D0072433A	Germany	RA	6 Months/F	INJ	.5ML	09Aug2011-09Aug2011, 30Apr2011-30Apr2011, 28May2011-28May2011	09Aug2011	U/0 Days, U/U, U/U	Syncope*, Cyanosis*, Restlessness*, Pallor*, Vomiting*, Hypotonia*, Unresponsive to stimuli*	R
#B0692220A	Italy	MD,RA	11 Months/M	INJ, INJ, INJ	U, U, U	20Dec2010-20Dec2010, 01Jan2010-01Jan2010, 01Jan2010-01Jan2010		U/Unknown, U/Unknown, U/1 Days	Syncope, Loss of consciousness, Febrile convulsion, Eye movement disorder, Opisthotonus, Pallor, Pyrexia, Pyrexia, Pyrexia	R

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#B0716232A	Italy	MD,RA	3 Months/M	INJ	U	14Feb2011-14Feb2011	14Feb2011	U/0 Days	Syncope, Loss of consciousness, Pallor	R
#D0071075A	Germany	MD,RA	3 Months/M	INJ	U	24Mar2011-24Mar2011	25Mar2011	U/1 Days	Thalamus haemorrhage, Convulsion, Facial paresis, Hemiparesis, Hypophagia, Restlessness, Pyrexia, Screaming, Somnolence, Pallor, Hyperaesthesia, Eyelid oedema, Abdominal distension, Hypotonia, Gaze palsy, Apnoea	U
#B0711562A	Italy	RA	14 Months/M	INJ	U	21Mar2011-21Mar2011	21Mar2011	U/0 Days	Tongue paralysis, Clonus	I
#B0702721A	France	MD,RP	7 Weeks/M	INJ	U	26Feb2011-26Feb2011	27Feb2011	U/0 Days	Tonic convulsion, Apnoeic attack, Pyrexia, Hypertonia, Pallor, Hypotonia, Staring, Opisthotonus,	R

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									Drug administration error	
#B0737089A	Poland	MD,RA	18 Months/F	INJ	U	21Jun2011-21Jun2011	22Jun2011	U/1 Days	Tremor, Gait disturbance, Oropharyngeal pain, Injection site reaction, Tonsillar disorder, White blood cells urine positive, Bacterial test positive, Anxiety, Upper respiratory tract congestion, Crying, Restlessness	R
#B0684621A	Italy	MD,RA	4 Months/M	INJ	U	10Nov2010-10Nov2010	10Nov2010	U/0 Days	Tremor, Pallor, Pyrexia	I
#B0735253A	Italy	RA	2 Months/M	INJ	U	27Jun2011-27Jun2011	27Jun2011	U/0 Days	Unresponsive to stimuli, Hypotonia, Pallor, Pyrexia	R

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#B0721081A	Poland	MD,RA	2 Months/U	INJ	U	30Mar2011-30Mar2011	01Apr2011	U/2 Days	Unresponsive to stimuli, Loss of consciousness, Hypotonic-hypore sponsive episode, Apathy, Restlessness, Somnolence, Crying	R
#B0699467A	Italy	RA	3 Months/M	INJ	U	04Jan2011-04Jan2011	05Jan2011	U/1 Days	Unresponsive to stimuli, Muscle contractions involuntary, Eye movement disorder, Pyrexia, Restlessness, Crying	R
#B0699755A	Ireland	MD,RA	2 Months/M	INJ	U	04Jan2011-04Jan2011	04Jan2011	U/0 Days	Unresponsive to stimuli, Syncope, Pallor	R
#D0071922A	Germany	MD,RP	4 Months/M	INJ	.5ML	22Mar2011-22Mar2011, 18Jan2011-18Jan2011, 22Feb2011-22Feb2011	22Mar2011	U/0 Days, U/U, U/U	VIIth nerve paralysis*, Facial paresis*	N
#B0728966A	France	MD,RP	23 Months/M	INJ	U	19May2011-19May2011	20May2011	U/1 Days	VIIth nerve paralysis, Pain in extremity, Mobility decreased, Oedema peripheral, Erythema, Pyrexia, Facial	U

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									asymmetry	
#B0681066A	Belgium	HP	15 Months/M	INJ	U	13Sep2010-13Sep2010	05Oct2010	U/22 Days	VIth nerve paralysis, Strabismus	N
Psychiatric disorders										
#B0713438A	Ukraine	MD	9 Months/F	INJ	.5ML	25Mar2011-25Mar2011	26Mar2011	U/1 Days	Agitation, Hyperthermia, Crying	R
#B0756774A	Ukraine	MD	3 Months/F	INJ	.5ML	04Oct2011-04Oct2011	04Oct2011	U/0 Days	Agitation, Hyperthermia, Crying, Asthenia	R
#B0740599A	Poland	RA	3 Months/F	INJ, INJ	U, U	01Jan2011-01Jan2011, 19Jul2011-19Jul2011		U/0 Days, U/0 Days	Anxiety, Crying, Apathy, Body temperature increased, Anxiety	U

D0070801A	Germany	MD,RP	3 Months/M	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/0 Days	Apathy, Pallor	U
#B0719542A	Poland	RA	1 Months/M	INJ	U	24Feb2011-24Feb2011	24Feb2011	U/0 Days	Decreased activity, Hypotonia, Somnolence	U
#B0720709A	Poland	MD,RA	23 Months/F	INJ	U	12Apr2011-12Apr2011	12Apr2011	U/6 Hours	Insomnia, Gait disturbance, Hypotonic-hypore sponsive episode	U
B0712015A	Netherlands	HP,RA	11 Months/M	INJ	U	19May2010-19May2010	01May2010	U/Days	Insomnia, Rash, Malaise, Crying	R
#B0708195A	Austria	MD,RA	Infant/F	INJ	U	1 Days		U/Unknown	Insomnia, Restlessness, Circadian rhythm sleep disorder	R
B0695605A	Netherlands	MD,RA	3 Months/F	INJ, INJ, INJ, INJ	U, U, U, U	14Apr2010-14Apr2010, 19May2010-19May2010, 05Jan2011-05Jan2011, 16Jun2010-16Jun2010	01Jan2010	U/0 Months, U/0 Months, U/Unknown, U/10 Hours	Listless, Rash, Listless, Rash, Listless, Rash, Rash morbilliform, Pyrexia, Pyrexia, Pyrexia, Pyrexia	R

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D0069283A	Germany	MD,RP	4 Months/M	INJ	U	21Sep2010-21Sep2010	21Sep2010	U/0 Days	Personality change, Restlessness, Sleep disorder	R
#D0072565A	Germany	MD,RA	3 Months/M	INJ	U	19Aug2011-19Aug2011	19Aug2011	U/0 Days	Phonological disorder, Respiration abnormal, Screaming, Sleep disorder, Pyrexia, Fatigue, Crying, Middle insomnia	N
#B0750036A	Poland	MD,RA	7 Months/U	INJ	U	06Sep2011-06Sep2011	06Sep2011	U/2 Hours	Restlessness, Body temperature increased, Crying, Asthenia	R
D0069714A	Germany	PH	2 Months/M	INJ, INJ	U, U	28Sep2010-28Sep2010, 09Nov2010-09Nov2010	29Sep2010	U/1 Days, U/0 Days	Restlessness, Middle insomnia, Middle insomnia, Restlessness, Crying, Pyrexia, Sleep disorder	U
D0070495A	Germany	HP,RA	3 Months/M	INJ	U	27Oct2010-27Oct2010	29Oct2010	U/2 Days	Restlessness, Muscle spasms, Insomnia, Crying	N

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#D0070862A	Germany	MD,RP	2 Months/F	INJ	U	24Mar2011-24Mar2011	24Mar2011	U/0 Days	Restlessness, Pallor, Hypophagia, Food aversion, Nasopharyngitis, Flatulence, Flatulence, Viral infection, Abnormal faeces, Screaming, Abnormal behaviour, Body temperature increased	U
D0072455A	Germany	MD	6 Months/M	INJ	U	15Jul2011-15Jul2011	15Jul2011	U/0 Days	Restlessness, Pyrexia, Insomnia, Decreased appetite, Muscle spasms, Crying, Agitation, Fatigue, Rash, Vaccination complication, Herpes virus infection, Exanthema subitum	N
D0069449A	Germany	MD	U/U	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/Unknown	Screaming	U

#B0693315A	Poland	MD,RA	2 Months/M	INJ	U	27Dec2010-27Dec2010	27Dec2010	U/1 Hours	Screaming, Crying	R
#B0684919A	Latvia	HP,RA	4 Months/M	INJ	U	17Aug2010-17Aug2010	17Aug2010	U/15 Minutes	Screaming, Crying, Oedema peripheral, Rash, Crying, Screaming, Rash, Oedema peripheral	R
D0069663A	Germany	MD,RA	2 Months/F	INJ	U	05Nov2010-05Nov2010	05Nov2010	U/0 Minutes	Screaming, Food aversion, Agitation, Crying	R
Respiratory, thoracic and mediastinal disorders										
#D0071220A	Germany	MD,RA	12 Weeks/M	INJ	U	18Apr2011-18Apr2011	18Apr2011	U/0 Days	Apnoea, Bradycardia	N
#B0691130A	France	RA	2 Months/M	INJ	U	15Dec2010-15Dec2010	15Dec2010	U/5 Hours	Apnoea, Bradycardia, Oxygen saturation decreased, Blood pressure decreased, Apparent life threatening event, Urine output	R

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									decreased, Cholinergic syndrome, Eye movement disorder, Gastrooesophageal reflux disease, Aspiration	
#A0901400A	Canada	PH	67 Days/F	INJ	.5ML	13Dec2010-13Dec2010	14Dec2010	U/Hours	Apnoea, Bradycardia, Oxygen saturation decreased, Wrong technique in drug usage process	I
#B0754941A	Belgium	CO,MD	2 Months/F	INJ	U	03Oct2011-03Oct2011	03Oct2011	U/Minutes	Apnoea, Bradycardia, Pallor, Foaming at mouth	R
#B0706228A	Italy	MD,RA	5 Months/M	INJ	U	27Jan2011-27Jan2011	27Jan2011	U/0 Days	Apnoea, Cyanosis, Hypertonia, Pyrexia	R
#D0071156A	Germany	RA	8 Weeks/M	INJ	U	07Mar2011-07Mar2011	07Mar2011	U/6 Hours	Apnoea, Cyanosis, Oxygen saturation decreased	R

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#B0699372A	Sweden	HP,RA	5 Months/F	INJ	U	13Sep2010-13Sep2010	13Sep2010	U/0 Days	Apnoea, Febrile convulsion, Mastication disorder, Skin discolouration	R
#B0690024A	Netherlands	HP,RA	2 Months/M	INJ	U	01Jun2010-01Jun2010	01Jun2010	U/1 Minutes	Apnoea, Hypotonia, Pallor, Staring, Crying	R
#B0755056A	France	RA	2 Months/F	INJ	U	18May2011-18May2011	18May2011	U/Same day	Apnoea, Hypoxia, Bradycardia, Malaise, Inflammation, Respiratory disorder	R
#B0691167A	Italy	RA	3 Months/M	INJ	U	09Jun2010-09Jun2010	09Jun2010	U/0 Days	Apnoea*, Loss of consciousness*, Erythema*, Hypertonia*	R
#B0731112A	Brazil	CO,MD	2 Months/M	INJ	U	26Oct2010-26Oct2010	26Oct2010	U/0 Days	Apnoea, Skin discolouration, Pallor, Rash macular, Erythema, Fatigue, Pyrexia, Vomiting, Cough, Crying*, Erythema, Petechiae, Hyperhidrosis, Hypersensitivity, Hypotonic-hypore	U

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									sponsive episode, General physical health deterioration, Pallor	
#D0071181A	Germany	RA	4 Months/M	INJ	U	25Feb2011-25Feb2011	25Feb2011	U/6 Hours	Apnoeic attack, Cyanosis, Upper respiratory tract infection, Body temperature increased	R
#B0707044A	Netherlands	HP,RA	2 Months/M	INJ	U	28Feb2011-28Feb2011	01Mar2011	U/8 Hours	Apparent life threatening event	I
#D0071421A	Germany	MD,RA	4 Months/M	INJ	U	29Mar2011-29Mar2011	02Apr2011	U/4 Days	Apparent life threatening event, Altered state of consciousness, Hypothyroidism, Neutropenia, Staring, Hypotonia, Pallor, Respiratory arrest, Crying	N
#D0071146A	Germany	OM,MD	12 Weeks/F	INJ	.5ML	13Apr2011-13Apr2011	13Apr2011	U/2 Hours	Apparent life threatening event, Pallor, Loss of consciousness, Erythema, Respiratory arrest, Somnolence	R

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D0070592A	Germany	HP,RA	4 Months/M	INJ	U	20Jan2011-20Jan2011	25Jan2011	U/5 Days	Bronchitis chronic, Bronchitis, Eye movement disorder, Pyrexia, Rash, Restlessness	N
B0707093A	Netherlands	MD,RA	11 Months/F	INJ	U	16Nov2010-16Nov2010		U/Unknown	Cough, Inflammation, Pain, Crying, Pyrexia, Vomiting	R
#D0072854A	Germany	HP,RA	7 Years/F	INJ, INJ, INJ, INJ	U, U, U, U	12Nov2004-12Nov2004, 10Dec2004-10Dec2004, 25Jan2005-25Jan2005, 03Mar2006-03Mar2006	01Sep2011	U/7 Years, U/7 Years, U/6 Years, U/5 Years	Cough, Vaccination failure	U
#B0682864A	France	RA	2 Years/F	INJ	U	12Oct2010-12Oct2010	12Oct2010	U/Same day	Dyspnoea, Pallor, Erythema, Pruritus	R
#B0749418A	Italy	MD,RA	3 Months/F	INJ	U	01Sep2011-01Sep2011	01Sep2011	U/0 Days	Dyspnoea, Pallor, Pyrexia, Hypotonia	R

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#B0731155A	Italy	OT,MD,RA	2 Months/F	INJ	U	17May2011-17May2011	17May2011	U/0 Days	Dyspnoea, Unresponsive to stimuli, Apnoeic attack, Irritability, Decreased appetite, Pallor	U
#D0071143A	Germany	MD,RA	6 Months/F	INJ, INJ, INJ	U, U, U	02Mar2011-02Mar2011, 08Jun2010-08Jun2010, 13Apr2010-13Apr2010, 19Jul2010-19Jul2010	08Jun2010	U/0 Days, U/0 Weeks, U/1 Days, U/U	Febrile convulsion*, Gaze palsy*, Altered state of consciousness*, Convulsion*, Pyrexia*, Dyspnoea*, Infection*, Erythema*, Swelling*, Hypokinesia*, Pain*, Apnoea*, Cyanosis*, Body temperature increased, Breath holding*, Moaning*	U
#B0748225A	Czech Republic	MD,RA	6 Months/F	INJ	U	01Aug2010-01Aug2010, 01Jun2010-01Jun2010, 01Jul2010-01Jul2010	01Sep2010	U/1 Months, U/U, U/U	Increased upper airway secretion, Sputum purulent, Cough	R
#D0072026A	Germany	MD,RA	4 Months/M	INJ, INJ	U, U	03Mar2011-03Mar2011, 05Apr2011-05Apr2011	05Mar2011	U/3 Days, U/2 Days	Obstructive airways disorder, Obstructive airways disorder	N

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B0719361A	Netherlands	HP,RA	2 Months/M	INJ	U	13Sep2010-13Sep2010	13Sep2010	U/90 Minutes	Respiration abnormal, Eczema, Pain, Pyrexia, Crying	R
B0717816A	Netherlands	MD,RA	4 Months/U	INJ	U	23Aug2010-23Aug2010	23Aug2010	U/13 Hours	Respiration abnormal, Oligodipsia, Skin discolouration, Chills, Somnolence, Pyrexia, Injection site pain	R
#B0741007A	Netherlands	MD,RA	10 Months/F	INJ	.5ML	09Aug2011-09Aug2011	09Aug2011	U/Immediate	Respiratory arrest, Depressed level of consciousness, Breath holding, Crying, Eye movement disorder, Skin discolouration, Pallor	N
#D0070339A	Germany	RA	3 Months/M	INJ	.5ML	05Nov2010-05Nov2010	05Nov2010	U/1 Minutes	Respiratory depression*	R
#B0707349A	Italy	MD,RA	14 Months/F	INJ, INJ, INJ	U, U, U	11Jan2011-11Jan2011, 09May2010-09May2010, 09Feb2010-09Feb2010		U/7 Days, U/7 Days, U/48 Hours	Respiratory failure, Cyanosis, Bronchospasm, Bronchospasm, Respiratory disorder, Respiratory	U

									disorder	
B0709886A	South Africa	HP	21 Months/M	INJ	U	23Mar2011-23Mar2011	23Mar2011	U/Hours	Rhinorrhoea, Pyrexia, Irritability	N
#B0756155A	Italy	MD,RA	3 Months/M	INJ	U	05Oct2011-05Oct2011	05Oct2011	U/0 Days	Sleep apnoea syndrome, Loss of consciousness, Cyanosis, Neutropenia, Salivary hypersecretion, Hyperpyrexia	R
#B0741792A	Netherlands	MD,RA	2 Months/F	INJ	U	04Jul2011-04Jul2011	04Jul2011	U/10 Hours	Stridor, Febrile convulsion, Cyanosis, Myoclonus, Pyrexia, Dysphagia, Choking	U
Skin and subcutaneous tissue disorders										
#B0743733A	Argentina	OT,MD	7 Months/M	INJ	U	20Aug2011-20Aug2011	21Aug2011	U/1 Days	Acute haemorrhagic oedema of infancy, Malaise, Tachycardia, Purpura, Pyrexia, Rash, Toxic skin eruption	I

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#B0741876A	Italy	RA	11 Months/F	INJ	U	17Aug2011-17Aug2011	17Aug2011	U/0 Days	Angioedema	I
#B0691862A	Italy	RA	5 Months/F	INJ	.5ML	17Dec2010-17Dec2010	17Dec2010	U/0 Days	Angioedema*	R
#B0749275A	Italy	RA	5 Months/F	INJ	U	18Aug2011-18Aug2011, 20Jun2011-20Jun2011	18Aug2011	U/0 Days, U/U	Angioedema, Hyperaemia, Pyrexia	R
#B0730009A	Italy	RA	13 Months/F	INJ	U	04May2011-04May2011	04May2011	U/0 Days	Angioedema, Urticaria	U
#D0069340A	Germany	MD	11 Months/M	INJ	U	21Jul2010-21Jul2010	22Jul2010	U/24 Hours	Blister, Injection site erythema, Skin lesion, Skin exfoliation	R
#D0070018A	Germany	RA	9 Weeks/M	INJ	U	02Nov2010-02Nov2010	02Nov2010	U/2 Hours	Dermatitis allergic	R

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B0727148A	Czech Republic	MD	4 Months/M	INJ	U	22Sep2010-22Sep2010	25Sep2010	U/3 Days	Dermatitis atopic	N
B0730499A	Switzerland	MD	4 Months/F	INJ	.5ML	11Apr2011-11Apr2011, 11Feb2011-11Feb2011	12Apr2011	U/1 Days, U/U	Dermatitis atopic, Erythema, Dry skin	I
D0069826A	Germany	MD,RP	U/U	INJ, INJ, INJ	U, U, U	1 Days, 1 Days, 1 Days		U/Unknown, U/Unknown, U/Unknown	Eczema, Eczema, Eczema	U
B0711288A	Netherlands	HP,RA	2 Months/F	INJ	U	03Jun2010-03Jun2010	03Jun2010	U/0 Days	Eczema, Eczema, Inflammation, Crying	R
B0690459A	Netherlands	HP,RA	3 Months/M	INJ	U	10May2010-10May2010		U/Hours	Eczema, Milk allergy, Rash, Impetigo, Pyrexia	R
D0071785A	Germany	HP,RA	3 Months/M	INJ	U	08Apr2011-08Apr2011	16Apr2011	U/8 Days	Eczema, Personality change, Immobile	N

B0728834A	Netherlands	CO,HP,RA	12 Months/M	INJ	U	11Jan2011-11Jan2011	11Jan2011	U/0 Days	Eczema, Pruritus, Pyrexia, Restlessness	N
D0069510A	Germany	PH	2 Months/F	INJ	U	05Nov2010-05Nov2010	06Nov2010	U/1 Days	Erythema	I
#B0703950A	Italy	MD,RA	3 Months/F	INJ	U	15Feb2011-15Feb2011	15Feb2011	U/15 Minutes	Erythema	I
B0708066A	France	MD	2 Months/F	INJ	U	11Feb2011-11Feb2011	11Feb2011	U/1 Hours	Erythema, Crying, Cyanosis, Hyperaesthesia	R
#B0705317A	France	PH,MD	16 Months/F	INJ	U	03Mar2011-03Mar2011	04Mar2011	U/12 Hours	Erythema, Hyperthermia, Injection site erythema, Injection site oedema, Injection site induration, Injection site pain	R

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D0070503A	Germany	MD	3 Months/M	INJ	U	13Dec2010-13Dec2010	13Dec2010	U/0 Days	Erythema*, Injection site cyst*	R
#D0069303A	Germany	MD	9 Months/U	INJ	U	01Jan2010-01Jan2010		U/1 Days	Erythema multiforme	U
#D0072847A	Germany	MD	2 Months/M	INJ, INJ, INJ	U, U, U	15Jul2011-15Jul2011, 12Aug2011-12Aug2011, 20Sep2011-20Sep2011	01Jan2011	U/28 Days, U/0 Days, U/0 Days	Erythema multiforme, Urticaria, Arthropod bite, Swelling, Erythema, Pyrexia, Hypertonia, Herpes simplex, General physical health deterioration, Urticaria, Urticaria, Pyrexia, Rash	R
#D0071461A	Germany	HP,RA	19 Months/F	INJ	U	21Apr2011-21Apr2011	22Apr2011	U/1 Days	Erythema, Myosclerosis	R

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#B0715209A	Netherlands	HP,RA	13 Months/F	INJ	.5ML	08Feb2011-08Feb2011	13Feb2011	U/5 Days	Erythema nodosum, Arthralgia, Petechiae	R
B0734938A	France	MD	2 Months/U	INJ	U	01Jun2011-01Jun2011	01Jun2011	U/Immediate	Erythema, Oedema peripheral, Pain in extremity, Crying, Skin discolouration, Product quality issue	N
D0071643A	Germany	MD	3 Months/M	INJ	U	06Jun2011-06Jun2011	06Jun2011	U/0 Days	Erythema, Oedema peripheral, Skin warm, Crying, Restlessness	R
B0687425A	France	MD,RP	Infant/U	INJ	U	1 Days		U/Unknown	Erythema, Rash macular, Rash	U
B0727462A	France	MD	2 Months/U	INJ	U	01Jun2011-01Jun2011	01Jun2011	U/Seconds	Erythema, Skin warm, Oedema peripheral, Malaise	R

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D0070840A	Germany	HP,RA	6 Months/F	INJ	U	20Dec2010-20Dec2010	20Dec2010	U/0 Days	Erythema, Swelling, Body temperature increased, Rash pustular, Swelling face	R
D0073090A	Germany	MD	3 Years/M	U	U	U		U/U	Erythema, Swelling, Feeling hot	U
D0070150A	Germany	HP,RA	28 Months/M	INJ	.5ML	11Jan2011-11Jan2011	12Jan2011	U/1 Days	Erythema*, Swelling*, Feeling hot*, Pain*	N
#B0734041A	France	RA	2 Months/F	INJ	U	26Apr2011-26Apr2011	26Apr2011	U/12 Hours	Erythrosis, Pallor, Cyanosis, Hypotonia, Eye disorder, Crying	R
B0715665A	France	CO,MD	2 Months/F	INJ	U	07Feb2011-07Feb2011	01Jan2011	U/Same day	Generalised erythema, Hypersensitivity, Skin erosion, Eczema, Skin depigmentation, Pruritus	S

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#D0070216A	Germany	MD,RP	9 Months/M	INJ	U	01Apr2010-01Apr2010	01Apr2010	U/28 Days	Henoch-Schonlein purpura, Thrombocytopenia, Petechiae, Pyrexia, Upper respiratory tract infection, Anaemia	R
B0726309A	Poland	MD,RA	2 Months/U	INJ	U	07Jan2011-07Jan2011	07Feb2011	U/31 Days	Keloid scar, Lividity	I
#D0072895A	Germany	MD	U/F	INJ	U	1 Days		U/Unknown	Lipoatrophy	U
#B0728714A	Poland	MD,RA	6 Months/M	INJ	U	11May2011-11May2011	11May2011	U/3 Hours	Lividity, Ecchymosis, Anxiety, Petechiae, Erythema, Crying, Body temperature increased, Hypersensitivity, Restlessness	R
#D0070291A	Germany	HP,MD,RA	11 Weeks/F	INJ	U	23Nov2010-23Nov2010	10Dec2010	U/17 Days	Neurodermatitis	S

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D0071186A	Germany	HP,RA	2 Months/F	INJ	U	25Feb2011-25Feb2011	28Feb2011	U/3 Days	Neurodermatitis, Staphylococcal infection	N	
#B0729166A	Spain	LI	3 Months/F	INJ	U	U		U/3 Weeks	Pemphigoid, Leukocytosis, Thrombocytosis, Blister, Scab, Skin lesion, Pruritus, Eosinophilia, Urticaria	R	M. Valdivioelso-Ramos et al, Infantile bullous pemphigoid developing after hexavalent, meningococcal and pneumococcal vaccinations, anales de pediatria, Elsevier, 2011.
D0072699A	Germany	MD,RA	5 Months/F	INJ	U	1 Days	21Mar2011	U/Unknown	Petechiae, Oedema peripheral	R	
#B0705315A	France	PH,MD	18 Months/F	INJ	U	03Mar2011-03Mar2011	01Mar2011	U/12 Hours	Purpura, Pyrexia, Injection site erythema, Injection site oedema, Injection site induration, Rash macular	R	
B0682750A	Argentina	MD	2 Months/M	INJ	U	1 Days		U/Unknown	Rash	U	

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B0682883A	Argentina	MD	Child/M	INJ	U	1 Days		U/Unknown	Rash	U
#B0748229A	Czech Republic	MD,RA	12 Months/F	INJ	U	01Dec2010-01Dec2010	01Dec2010	U/0 Months	Rash	N
#B0714550A	Ireland	HP,RA	2 Months/M	INJ	U	06Apr2011-06Apr2011	06Apr2011	U/15 Minutes	Rash	R
#D0071682A	Germany	MD,RA	15 Months/F	INJ	U	24May2011-24May2011	26May2011	U/2 Days	Rash generalised, Pyrexia	N
B0731182A	Sweden	HP	5 Months/F	INJ	U	20Jun2011-20Jun2011	01Jun2011	U/Days	Rash generalised, Pyrexia, Pain	U
B0711011A	France	MD	2 Months/M	INJ	U	01Mar2011-01Mar2011	01Mar2011	U/Same day	Rash maculo-papular, Pyrexia, Hypersensitivity	R

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#B0686640A	Italy	MD,RA	2 Months/M	INJ	U	03Nov2010-03Nov2010	03Nov2010	U/0 Days	Rash papular, Pyrexia	R
#D0070018B	Germany	RA	4 Months/M	INJ	U	12Jan2011-12Jan2011	12Jan2011	U/8 Hours	Rash, Pyrexia	R
#B0743128A	France	RA	14 Months/M	INJ	U	27Jun2011-27Jun2011	27Jun2011	U/0 Days	Rash, Pyrexia, Eyelid oedema, Eosinophilia, Rash morbilliform, Cheilitis, Blister, Fatigue, Pain, Diarrhoea, Vomiting	R
B0690425A	France	MD	2 Months/U	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/12 Hours	Rash, Pyrexia, Hypersensitivity	R
D0071081A	Germany	MD	3 Months/F	INJ	U	15Apr2011-15Apr2011	15Apr2011	U/3 Minutes	Rash, Skin warm, Restlessness	R

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B0690447A	Netherlands	HP,RA	3 Months/F	INJ	U	27May2010-27May2010		U/0 Weeks	Skin depigmentation, Macule	R
B0717275A	Netherlands	HP,RA	11 Months/M	INJ	U	14Feb2011-14Feb2011	15Feb2011	U/Hours	Skin discolouration, Erythema, Oedema peripheral, Crying	R
B0733567A	Netherlands	MD,RA	4 Months/F	INJ	.5ML	17May2011-17May2011	17May2011	U/4 Hours	Skin discolouration, Pallor, Pyrexia, Erythema	R
B0727162A	Netherlands	CO,MD,RA	2 Months/F	INJ, INJ	U, U	26May2011-26May2011, 30Jun2011-30Jun2011	26May2011	U/6 Hours, U/Immediate	Skin discolouration, Screaming, Oedema peripheral, Skin tightness, Oedema genital, Petechiae, Pyrexia, Crying, Injection site pain, Screaming, Skin discolouration, Crying, Oedema peripheral, Petechiae	R

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D0072634A	Germany	MD,RA	2 Months/F	INJ	U	15Aug2011-15Aug2011	01Aug2011	U/0 Weeks	Skin disorder, Fatigue, Screaming, Pain, Feeling hot, Swelling, Erythema, Injection site induration, Nasopharyngitis, Immune system disorder, Skin reaction	U
B0707675A	France	MD,RP	18 Months/M	INJ	U	14Mar2011-14Mar2011	14Mar2011	U/12 Hours	Skin lesion, Injection site induration	R
#B0732862A	Belgium	MD,RP	2 Months/F	INJ	U	27Jun2011-27Jun2011	27Jun2011	U/3 Minutes	Skin warm, Urticaria papular, Erythema, Urticaria	R
#B0700364A	Australia	HP	18 Months/F	INJ	U	08Feb2011-08Feb2011	10Feb2011	U/2 Days	Stevens-Johnson syndrome, Eye swelling, Erythema, Conjunctivitis, Lethargy, Eating disorder, Rash, Tachypnoea, Skin exfoliation, Ill-defined disorder, Blister, Increased upper airway secretion,	N

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									Measles, Mucosal inflammation, Irritability	
B0745076A	France	MD	4 Months/M	INJ, INJ	U, U	04Jan2011-04Jan2011, 09Nov2010-09Nov2010	01Jan2011	U/3 Weeks, U/2 Months	Subcutaneous nodule, Injection site pruritus, Injection site eczema, Injection site induration, Injection site nodule	I
B0682576A	France	MD	10 Weeks/F	INJ	U	27Oct2010-27Oct2010	28Oct2010	U/1 Days	Swelling face, Local swelling, Hypersensitivity	R
#B0757243A	France	RA	2 Months/F	INJ	U	23Aug2011-23Aug2011	23Aug2011	U/0 Days	Urticaria	U
#D0070154A	Germany	MD,RA	U/M	INJ	U	1 Days	15Oct2010	U/Unknown	Urticaria	U

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#D0070854A	Germany	PH,MD	3 Months/M	INJ	U	12Jan2011-12Jan2011	01Jan2011	U/8 Hours	Urticaria	R
#D0071462A	Germany	HP,RA	10 Months/F	INJ	U	09May2011-09May2011	11May2011	U/2 Days	Urticaria	R
D0069610A	Germany	MD	1 Years/F	INJ	U	28Oct2010-28Oct2010		U/0 Years	Urticaria, Granuloma, Injection site swelling, Injection site erythema, Injection site induration, Pyrexia	N
B0726556A	Poland	MD,RA	2 Months/M	INJ	U	04Apr2011-04Apr2011	05Apr2011	U/1 Days	Urticaria, Rash	R
#B0737088A	France	MD	2 Months/M	INJ	U	04Jul2011-04Jul2011	05Jul2011	U/24 Hours	Urticaria, Rash macular, Hypersensitivity	R

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#D0071406A	Germany	MD,RA,RP	6 Months/M	INJ	.5ML	28Apr2011-28Apr2011, 15Feb2011-15Feb2011, 15Mar2011-15Mar2011	28Apr2011	U/1 Hours, U/U, U/U	Urticaria, Rash, Rash erythematous, Blister, Restlessness, Cough, Skin reaction	R
#D0072586A	Germany	MD	U/M	INJ	U	16Jul2010-16Jul2010	19Aug2010	U/34 Days	Urticaria thermal	N
#B0731863A	Ireland	HP,RA	6 Months/M	INJ	U	08Dec2010-08Dec2010	09Dec2010	U/1 Days	Urticaria, Tonsillitis	R
#B0712007A	Netherlands	RA	3 Months/M	INJ	U	02Sep2010-02Sep2010	02Sep2010	U/5 Hours	Yellow skin, Crying, Malaise	R
Surgical and medical procedures										
B0680977A	France	MD	6 Weeks/M	INJ	U	27Sep2010-27Sep2010	27Sep2010	U/See text	Off label use	X

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B0680979A	France	MD	1 Months/F	INJ	U	17Sep2010-17Sep2010		U/See text	Off label use	X
B0680980A	France	MD	5 Weeks/U	INJ	U	1 Days		U/See text	Off label use	X
B0682278A	France	MD	1 Months/U	INJ	U	1 Days		U/See text	Off label use	X
B0698936A	France	MD	3 Years/U	INJ	U	01Nov2010-01Nov2010	01Nov2010	U/See text	Off label use	X
D0070180A	Germany	MD	17 Years/M	INJ	U	01Feb2011-01Feb2011	01Feb2011	U/0 Days	Off label use	X
D0072603A	Germany	MD	5 Years/F	INJ	U	06Sep2011-06Sep2011	06Sep2011	U/During	Off label use	X

D0070247A	Germany	MD	3 Years/F	INJ, INJ	U, U	01Nov2008-01Nov2008, 01Jul2010-01Jul2010	01Nov2008	U/During, U/During	Off label use, Off label use	X
Vascular disorders										
#D0069460A	Germany	OM,MD,RP	3 Months/M	INJ	U	14Oct2010-14Oct2010	14Oct2010	U/Minutes	Circulatory collapse, Apathy*, Pallor*, Asthenia*, Heart rate decreased*, Screaming*, Staring*	R
#D0069341A	Germany	MD	3 Months/M	INJ	U	05Nov2010-05Nov2010	05Nov2010	U/0 Hours	Circulatory collapse, Apnoea, Loss of consciousness, Pallor, Bradycardia, Salivary hypersecretion, Cyanosis, Epilepsy, Partial seizures, Foaming at mouth, Hypotonia, Cardiac arrest, Vomiting, Dyskinesia, Eye movement disorder, Productive cough, Depressed level of consciousness, Hypokinesia,	R

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									Epilepsy, Bronchitis	
#B0713106A	Netherlands	MD,RA	12 Months/M	INJ	U	04Nov2010-04Nov2010	04Nov2010	U/22 Hours	Circulatory collapse, Cyanosis, Pallor	R
#D0070901A	Germany	MD,RA	12 Weeks/M	INJ	U	22Mar2011-22Mar2011	22Mar2011	U/7 Hours	Circulatory collapse, Respiratory arrest, Cyanosis, Hypotonic-hypore sponsive episode, Screaming, Agitation, Hypotonia, Peripheral coldness, Ill-defined disorder, Fatigue, Pyrexia	R
#D0072852A	Germany	HP,MD,RA, RP	5 Months/M	INJ	U	20Sep2011-20Sep2011	20Sep2011	U/1 Days	Circulatory collapse, Sepsis, Shock, Crying, Pallor	F

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D0071906A	Germany	MD	3 Months/M	INJ	.5ML	29Jun2011-29Jun2011	29Jun2011	U/5 Minutes	Flushing*	R
#D0071144A	Germany	HP,RA	5 Months/F	INJ	U	06Apr2011-06Apr2011	07Apr2011	U/0 Days	Haematoma, Injection site erythema, Vaccination complication	R
#D0071621A	Germany	MD,RA	12 Months/M	INJ, INJ	U, U	06May2011-06May2011, 02Nov2010-02Nov2010	09May2011	U/3 Days, U/Unknown	Kawasaki's disease*, Meningitis*, Leukocytosis*, Pericarditis*, Mitral valve incompetence*, Pyrexia*, Fluid intake reduced*, General physical health deterioration*, Rash maculo-papular*, Fungal skin infection*, Cheilitis*, Chapped lips*, Palmar erythema*, Lymphadenopathy*, Infection*, Pyrexia*	N

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#D0070921A	Germany	MD,RA	2 Months/F	INJ	U	28Feb2011-28Feb2011	28Feb2011	U/0 Days	Kawasaki's disease*, Pyelonephritis*, Pyrexia*, Infection*, Somnolence*, Fluid intake reduced*, General physical health deterioration*, Pallor*, Ill-defined disorder*, Rash*, Conjunctivitis*, Erythema*, Enanthema*, Chapped lips*, Hypertrophy of tongue papillae*	R
#B0691861A	Italy	RA	2 Months/M	INJ	U	11Nov2010-11Nov2010	13Nov2010	U/2 Days	Kawasaki's disease*, Rash maculo-papular*, Diarrhoea*, Pyrexia*, Cheilitis*, Skin exfoliation*, Oedema peripheral*, Erythema*	U
#B0706959A	Austria	RA	4 Months/M	INJ	U	25Jan2011-25Jan2011	25Jan2011	U/3 Minutes	Pallor, Hyperhidrosis, Screaming, Rash, Crying, Rash erythematous	R

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B0689223A	France	MD	10 Weeks/U	INJ	U	01Dec2010-01Dec2010	01Dec2010	U/Immediate	Pallor, Somnolence, Injection site erythema, Injection site oedema, Injection site inflammation	U
#D0072908A	Germany	RA	3 Months/M	INJ	U	22Sep2011-22Sep2011	22Sep2011	U/2 Hours	Shock, Pallor, Vomiting, Hypophagia	I
#B0706503A	Thailand	MD	2 Months/F	INJ	.5ML	09Mar2011-09Mar2011	10Mar2011	U/1 Days	Shock, Respiratory arrest, Cardiac arrest, Pyrexia, Somnolence, Hypotonia, Vomiting, Crying, Apnoea	F
B0703972A	France	PH	11 Weeks/M	INJ	U	17Feb2011-17Feb2011	26Feb2011	U/8 Days	Vasodilatation, Petechiae, Erythema, Skin warm	R

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APPENDIX 3B : All serious attributable clinical trial cases which were received prior to the period of this PSUR but unblinded during the reporting period (no such case was received during the period)

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APPENDIX 3C : All non-serious listed cases (excluding consumer and regulatory authority reports)

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Appendix 3C: Individual Case Histories of Non-Serious Listed Cases Received in Time Period of PSUR for:

Infanrix hexa

Case No.	Country	Report Source	Age/Sex	Form'n or Route	TDD	Treatment Dates†	Event Onset	TTO / TTOSLD	Events	Outcome	Comments
Blood and lymphatic system disorders											
D0072958A	Germany	MD	U/U	INJ	U	U		U/U	Lymphadenopathy	U	
Gastrointestinal disorders											
B0712444A	France	MD	2 Months/F	INJ, INJ	U, U	01Dec2010-01Dec2010, 01Mar2011-01Mar2011		U/48 Hours, U/48 Hours	Diarrhoea	R	
D0071537A	Germany	MD,RP	2 Months/F	INJ	U	02May2011-02May2011	06May2011	U/4 Days	Diarrhoea	I	

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B0682692A	Hong Kong	MD	5 Weeks/M	INJ	U	27Oct2010-27Oct2010		U/0 Days	Vomiting	R
B0683077A	Poland	MD,RA	2 Months/U	INJ	U	20May2010-20May2010	20May2010	U/0 Days	Vomiting	R
General disorders and administration site conditions										
B0734921A	Austria	MD	U/U	INJ	U	U		U/Hours	Pyrexia	U
B0706692A	Belgium	MD,RP	18 Months/U	INJ	U	1 Days		U/Unknown	Pyrexia	R
B0687293A	France	MD	18 Months/F	INJ	U	30Nov2010-30Nov2010	01Dec2010	U/0 Weeks	Injection site oedema, Injection site erythema	N

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B0704749A	France	MD	2 Years/M	INJ, INJ, INJ	U, U, U	01Apr2009-01Apr2009, 08Jun2009-08Jun2009, 01Jun2010-01Jun2010		U/Unknown, U/Unknown, U/Unknown	No therapeutic response	X
B0705102A	France	MD	Infant/U	INJ	U	1 Days		U/Immediate	Injection site pain	U
B0715647A	France	MD	2 Years/U	INJ	U	01Feb2011-01Feb2011	01Feb2011	U/48 Hours	Extensive swelling of vaccinated limb, Pyrexia	R
B0716266A	France	PH	Infant/M	INJ	U	01Jan2011-01Jan2011	01Jan2001	U/Unknown	Injection site erythema, Pyrexia	U
B0755889A	France	MD	15 Months/U	INJ	U	10Oct2011-10Oct2011	10Oct2011	U/Same day	Pyrexia	N
D0069558A	Germany	HP,RA	19 Months/F	INJ	U	04Nov2010-04Nov2010	06Nov2010	U/2 Days	Injection site erythema, Injection site swelling	R

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D0070056A	Germany	MD,RA	4 Months/M	INJ	U	13Dec2010-13Dec2010	13Dec2010	U/0 Days	Pyrexia	R
D0070070A	Germany	HP,RA	15 Months/F	INJ	U	07Dec2010-07Dec2010	08Dec2010	U/1 Days	Pyrexia	R
D0070269A	Germany	MD,RP	Child/U	INJ	U	1 Days		U/Unknown	No therapeutic response	X
D0070393A	Germany	MD	2 Months/M	INJ, INJ	U, U	03Jan2011-03Jan2011, 03Feb2011-03Feb2011	01Jan2011	U/0 Months, U/0 Months	Pyrexia, Restlessness, Pyrexia, Restlessness	R
D0070527A	Germany	OM,MD,RA	U/F	INJ, INJ	U, U	1 Days, 1 Days		U/Unknown, U/Unknown	Pyrexia, Pyrexia	U
D0071619A	Germany	MD,RA	33 Months/M	INJ	U	21Apr2011-21Apr2011	22Apr2011	U/1 Days	Pyrexia, Injection site swelling	R

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D0072122A	Germany	MD	U/F	INJ	U	1 Days		U/0 Days	Pyrexia, Pyrexia, Rash, Pyrexia	I
D0072481A	Germany	MD,RP	11 Years/M	INJ	U	1 Days		U/Unknown	Injection site swelling, Injection site erythema, Injection site pain	U
D0072494B	Germany	MD,RP	9 Weeks/M	INJ	.5ML	09Jun2011-09Jun2011	09Jun2011	U/12 Hours	Pyrexia*	R
D0072506A	Germany	MD	Infant/M	INJ, INJ	U, U	01Jan2011-01Jan2011, 01Jan2011-01Jan2011	01Jan2011	U/0 Years, U/0 Years	Pyrexia, Crying, Pyrexia, Crying	U
D0072890A	Germany	MD	2 Months/F	INJ	U	24Aug2011-24Aug2011	01Aug2011	U/6 Hours	Pyrexia, Rash	R
B0701433A	Netherlands	MD,RA	6 Months/M	INJ	U	30Dec2010-30Dec2010	30Dec2010	U/1 Hours	Pyrexia	R

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B0709029A	Netherlands	HP,RA	3 Months/M	INJ	U	19Mar2009-19Mar2009	01Mar2009	U/1 Days	Pyrexia, Urticaria	R
B0726092A	Netherlands	MD,RA	11 Months/F	INJ	U	17Nov2010-17Nov2010	17Nov2010	U/8 Hours	Pyrexia	R
B0727154A	Netherlands	HP,RA	6 Months/M	INJ	U	08Apr2011-08Apr2011	08Apr2011	U/5 Hours	Pyrexia	R
B0742965A	Netherlands	HP,RA	3 Months/F	INJ	U	28Jul2009-28Jul2009	28Jul2009	U/0 Days	Pyrexia	R
B0755900A	Netherlands	MD,RA	2 Months/F	INJ	.5ML	25Jul2011-25Jul2011	25Jul2011	U/0 Days	Pyrexia	R
B0708546A	Peru	MD	2 Years/M	INJ	U	11Feb2011-11Feb2011	11Feb2011	U/Hours	Injection site erythema, Injection site oedema, Injection site pain, Injection site swelling	R

B0683070A	Poland	MD,RA	27 Months/U	INJ	U	10Jun2010-10Jun2010	11Jun2010	U/1 Days	Injection site oedema, Body temperature increased	R
B0683696A	Poland	MD,RA	19 Months/U	INJ	U	23Jun2010-23Jun2010	24Jun2010	U/1 Days	Injection site erythema, Injection site oedema	R
B0688156A	Poland	MD,RA	20 Months/U	INJ	U	22Jun2010-22Jun2010	23Jun2010	U/24 Hours	Injection site erythema, Injection site oedema	U
B0692009A	Poland	MD,RA	26 Months/U	INJ	U	15Sep2010-15Sep2010	16Sep2010	U/1 Days	Injection site oedema, Injection site erythema, Injection site pain, Body temperature increased, Extensive swelling of vaccinated limb	R
B0726137A	Poland	MD,RA	5 Months/U	INJ	U	12Apr2011-12Apr2011	13Apr2011	U/1 Days	Injection site oedema, Injection site erythema	R

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B0727348A	Poland	MD,RA	20 Months/M	INJ	U	14Apr2011-14Apr2011	15Apr2011	U/1 Days	Injection site oedema, Injection site pain	R
B0730870A	Poland	MD,RA	18 Months/U	INJ	U	25May2011-25May2011	25May2011	U/Hours	Injection site oedema, Injection site erythema, Injection site pain, Pyrexia, Extensive swelling of vaccinated limb	R
B0731114A	Poland	MD,RA	8 Months/U	INJ	U	13Apr2011-13Apr2011	14Apr2011	U/1 Days	Injection site oedema, Injection site erythema, Extensive swelling of vaccinated limb	R
B0716355A	Romania	MD,RP	2 Months/U	INJ	U	05Jan2011-05Jan2011	05Jan2011	U/0 Days	Pyrexia, Diarrhoea	R
B0733647A	Romania	MD	2 Months/F	INJ	U	17Jun2011-17Jun2011		U/0 Months	Pyrexia	R
B0684776A	South Africa	HP	19 Months/M	INJ	U	15Nov2010-15Nov2010	16Nov2010	U/1 Days	Injection site swelling	U

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B0695402A	South Africa	HP	18 Months/F	INJ	U	18Jan2011-18Jan2011	18Jan2011	U/Hours	Injection site erythema, Pyrexia	U
B0705537A	Viet Nam	MD,RP	16 Months/M	INJ	.5ML	05Mar2011-05Mar2011	06Mar2011	U/1 Days	Injection site swelling	U
B0730568A	Viet Nam	MD,RP	20 Months/F	INJ	U	12Jun2011-12Jun2011	12Jun2011	U/0 Days	Injection site erythema, Injection site swelling	N
Investigations										
B0698656A	Poland	MD,RA	23 Months/U	INJ	U	08Oct2010-08Oct2010	09Oct2010	U/1 Days	Body temperature increased, Injection site oedema, Injection site erythema	R
Nervous system disorders										
B0743970A	France	PH	2 Months/F	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/4 Hours	Crying	R

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B0727692A	Netherlands	MD,RA	3 Months/F	INJ	U	15Sep2010-15Sep2010	15Sep2010	U/3 Hours	Crying	R
B0732813A	Netherlands	HP,RA	12 Weeks/F	INJ, INJ	U, U	21Apr2011-21Apr2011, 01Jan2011-U	21Apr2011	U/2 Hours, U/Hours	Crying, Crying, Pyrexia	U
B0737130A	Netherlands	MD,RA	11 Months/F	INJ, INJ	U, .5ML	20Jul2011-20Jul2011, U		U/Unknown, U/Hours	Crying, Pyrexia, Crying, Pyrexia	R
B0705793A	Peru	MD	2 Months/F	INJ	U	09Mar2011-09Mar2011	09Mar2011	U/0 Days	Crying	R
B0708789A	Poland	MD	2 Months/M	INJ	U	05Jan2011-05Jan2011	05Jan2011	U/30 Minutes	Crying, Somnolence, Decreased appetite	R
B0741965A	Romania	CO,MD	6 Months/M	INJ	U	28Jun2011-28Jun2011	28Jun2011	U/45 Minutes	Somnolence	R

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Skin and subcutaneous tissue disorders

B0741520A	Belgium	MD	U/U	INJ	U	16Aug2011-16Aug2011	17Aug2011	U/1 Days	Rash	U
B0741521A	Belgium	MD	U/U	INJ	U	16Aug2011-16Aug2011	17Aug2011	U/1 Days	Rash	U
B0687294A	France	MD	16 Months/F	INJ	U	01Aug2010-01Aug2010	01Jan2010	U/1 Days	Urticaria	U
B0692425A	France	MD	3 Months/F	INJ, INJ	U, U	23Oct2010-23Oct2010, 21Dec2010-21Dec2010	01Oct2010	U/0 Weeks, U/2 Days	Urticaria	R
B0729681A	France	MD	16 Months/F	INJ	U	27Jun2011-27Jun2011	27Jun2011	U/4 Hours	Urticaria, Pyrexia, Diarrhoea	U

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B0742850A	France	MD	2 Months/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/1 Days	Urticaria	R
B0751893A	France	MD	14 Months/U	INJ	U	01Jan2011-01Jan2011	01Jan2011	U/48 Hours	Eczema, Hypersensitivity	I
D0069348A	Germany	HP,RA	4 Months/F	INJ	U	28Sep2010-28Sep2010, 31Aug2010-31Aug2010	29Sep2010	U/1 Days, U/U	Urticaria	R
D0069457A	Germany	MD,RG,RA	27 Months/F	INJ	U	26Aug2010-26Aug2010	26Aug2010	U/0 Days	Urticaria	R
D0070920A	Germany	MD,RP	3 Months/M	INJ	U	04Mar2011-04Mar2011	05Mar2011	U/1 Days	Urticaria	R
D0071119A	Germany	MD,RP	U/U	INJ	U	1 Days		U/4 Hours	Urticaria	U

D0072418A	Germany	MD	7 Months/F	INJ	U	09Aug2011-09Aug2011	01Aug2011	U/1 Weeks	Rash generalised	U
D0072419A	Germany	MD	U/F	INJ, INJ, INJ	U, U, U	1 Days, 1 Days, 1 Days		U/Unknown, U/Unknown, U/Unknown	Pruritus, Pruritus, Pruritus	U
B0739776A	Singapore	MD,RP	2 Months/F	INJ	.5ML	U, 25May2011-25May2011	26May2011	U/1 Days, U/U	Rash morbilliform	R

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APPENDIX 3D : All non-medically verified cases

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Appendix 3D: Individual Case Histories of Non-Medically Verified Cases Received in Time Period of PSUR for:

Infanrix hexa

Case No.	Country	Report Source	Age/Sex	Form'n or Route	TDD	Treatment Dates†	Event Onset	TTO / TTOSLD	Events	Outcome	Comments
Gastrointestinal disorders											
B0723208A	Australia	CO	4 Months/M	SUS	U	U		U/Unknown	Infrequent bowel movements, Abnormal faeces	U	
General disorders and administration site conditions											
D0071893A	Germany	CO	2 Months/F	INJ, INJ	U, U	1 Days, 1 Days		U/Unknown, U/Unknown	Adverse event, Off label use	U	
#B0735723A	Australia	CO	6 Weeks/M	INJ	U	20Jul2011-20Jul2011	21Jul2011	U/14 Hours	Death	F	

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B0735472A	France	CO,CN	Infant/F	INJ, INJ	U, U	26Jul2011-26Jul2011, 1 Days		U/0 Days, U/Unknown	Extensive swelling of vaccinated limb, Injection site reaction, Injection site nodule, Injection site erythema, Injection site warmth, Injection site induration, Injection site pruritus, Hypersensitivity	N
B0741549A	Czech Republic	CO	3 Months/F	INJ	U	09Aug2011-09Aug2011	09Aug2011	U/0 Days	Fatigue, Rash	N
B0695090A	France	CO	3 Months/M	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/See text	Incorrect product storage	X
B0715826A	France	CO	2 Months/F	INJ	U	22Feb2011-22Feb2011	22Feb2011	U/See text	Incorrect product storage	X
B0734427A	France	CO,CN	2 Months/U	INJ	U	20Jul2011-20Jul2011	20Jul2011	U/See text	Incorrect product storage	X

B0690208A	Italy	CO	5 Years/M	INJ	U	1 Days		U/Unknown	Injection site anaesthesia, Injection site pain	I
B0734758A	Italy	CO	10 Months/M	INJ	U	U	24Jun2011	U/Unknown	Injection site erythema, Extensive swelling of vaccinated limb, Injection site induration	N
B0756909A	Australia	CO	4 Months/M	INJ	U	U		U/Unknown	Injection site erythema, Injection site swelling, Irritability	R
B0711440A	Brazil	CO	6 Months/M	INJ	U	04Mar2011-04Mar2011	04Mar2011	U/0 Days	Injection site induration, Injection site reaction, Pyrexia, Irritability	R
D0070074A	Germany	CO	15 Months/M	INJ	U	24Jan2011-24Jan2011	24Jan2011	U/0 Days	Injection site irritation, Underdose	U
D0072541A	Germany	CO	40 Years/F	INJ	U	U		U/0 Days	Injection site pain, Wrong drug administered	U

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D0069937A	Germany	CO	13 Months/F	INJ	U	1 Days		U/1 Days	Injection site swelling, Injection site erythema, Injection site swelling	R
B0696960A	Poland	CO	19 Months/M	INJ	U	19Jan2011-19Jan2011	27Jan2011	U/8 Days	Oedema peripheral, Rash	U
B0684619A	Austria	CO	Child/F	INJ	U	09Nov2010-09Nov2010	09Nov2010	U/Hours	Pyrexia	R
B0684560A	France	CO	Infant/F	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/Unknown	Pyrexia	R
D0070214A	Germany	CO	15 Months/M	INJ	U	04Feb2011-04Feb2011	05Feb2011	U/1 Days	Pyrexia	U
D0072188A	Germany	CO	2 Years/M	INJ	U	1 Days		U/10 Days	Pyrexia, Erythema, Pharyngitis, Malaise, Photophobia, White blood cell count increased, Bacterial	U

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									infection, Rash, Pyrexia, Rash, Pharyngeal erythema, Pyrexia	
B0684559A	France	CO	2 Months/U	INJ	U	01Nov2010-01Nov2010	01Nov2010	U/Same day	Pyrexia, Incorrect product storage	R
D0071039A	Germany	CO	10 Years/F	INJ	U	1 Days		U/Unknown	Pyrexia*, Pain*	U
D0069525A	Germany	CO	4 Years/M	INJ	U	18Nov2010-18Nov2010	19Nov2010	U/1 Days	Pyrexia, Pain, Vomiting	R
B0684422A	Croatia	CO	5 Months/F	INJ, INJ	U, .5ML	31Aug2010-31Aug2010, 10Nov2010-10Nov2010, 24Jun2010-24Jun2010	01Jan2010	U/Unknown, U/8 Hours, U/U	Pyrexia, Pyrexia	R

Infections and infestations

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#D0069806A	Germany	CO	Infant/U	INJ	.5ML	1 Days		U/Unknown	Injection site abscess*	U
#B0737601A	South Africa	CO	18 Months/F	INJ	U	1 Days		U/Unknown	Pertussis	U
D0069959A	Germany	CO	24 Months/M	INJ	U	14Nov2010-14Nov2010	15Nov2010	U/1 Days	Rash pustular, Injection site erythema, Injection site warmth, Injection site induration, Pyrexia, Lymphadenopathy, Erythema	U
Injury, poisoning and procedural complications										
B0704430A	South Africa	CO	3 Months/U	INJ	U	04Mar2011-04Mar2011	04Mar2011	U/During	Accidental overdose	X
B0696711A	Brazil	CO	2 Months/F	INJ	.5ML	20Jan2011-20Jan2011	20Jan2011	U/See text	Expired drug administered	X

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D0072542A	Germany	CO	28 Years/M	INJ	U	U		U/0 Days	Wrong drug administered	X
B0684758A	Sweden	CO,NP	2 Years/M	INJ	U	1 Days		U/During	Wrong drug administered	X
B0691614A	France	CO	3 Months/F	INJ, INJ	U, U	01Jan2010-01Jan2010, 01Jan2010-01Jan2010, 01Jan2010-01Jan2010, 01Jan2010-01Jan2010	01Jan2010	U/See text, U/See text, U/U, U/U	Wrong drug administered, Incorrect dose administered	X
B0683346A	Australia	CO	4 Months/M	INJ	U	01Nov2010-01Nov2010	01Nov2010	U/24 Hours	Wrong drug administered, Overdose, Somnolence, Irritability	U
B0716836A	Argentina	CO	6 Months/M	INJ	U	12Apr2011-12Apr2011	12Apr2011	U/During	Wrong technique in drug usage process	X
B0733404A	Poland	OT	18 Months/M	INJ	U	12Jul2011-12Jul2011	12Jul2011	U/During	Wrong technique in drug usage process, Oedema peripheral, Insomnia, Anxiety, Erythema	R

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Musculoskeletal and connective tissue disorders										
D0072247A	Germany	CO	26 Months/M	INJ	U	29Jul2011-29Jul2011	29Jul2011	U/0 Days	Pain in extremity	U
D0072372A	Germany	CO	U/F	INJ	U	1 Days		U/0 Days	Pain in extremity, Gait disturbance, Crying	U
Nervous system disorders										
D0069784A	Germany	CO,OT	12 Weeks/M	INJ	.5ML	03Dec2010-03Dec2010	03Dec2010	U/0 Days	Crying*, Respiratory disorder*, Presyncope*, Pyrexia*, Fatigue*, Apathy*, Crying*, Dyskinesia*, Inappropriate affect*, Fatigue*, Decreased interest*, Initial insomnia*, Diarrhoea*	R
D0072114A	Germany	CO	4 Months/F	INJ	U	15Jul2011-15Jul2011	18Jul2011	U/3 Days	Hypersomnia, Hypophagia	U

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B0703207A	Poland	CO	2 Years/M	INJ	U	24Feb2011-24Feb2011	24Feb2011	U/0 Days	Lethargy, Face oedema, Sluggishness, Pain in extremity, Pyrexia	N
B0705201A	Romania	CO	2 Months/M	INJ	U	15Feb2011-15Feb2011	15Feb2011	U/0 Days	Somnolence, Urticaria, Acne	R
#B0722633A	Kenya	CO,RP	6 Weeks/F	INJ	U	01Apr2011-01Apr2011	01Apr2011	U/0 Days	Tremor, Pyrexia	R
Respiratory, thoracic and mediastinal disorders										
#B0703891A	Kenya	CO	2 Months/F	INJ	U	18Feb2011-18Feb2011	20Feb2011	U/2 Days	Cough, Dyspnoea, Wheezing	N
Skin and subcutaneous tissue disorders										
#B0720037A	Poland	CO	1 Years/M	INJ	U	1 Days		U/Unknown	Dermatitis allergic	R

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B0692908A	France	CO	3 Months/M	INJ	U	06Dec2010-06Dec2010	01Dec2010	U/See text	Eczema	N
B0744392A	France	CO,CN	U/M	INJ	U	1 Days		U/See text	Eczema	U
#B0713508A	France	CO	3 Months/U	INJ, INJ	U, U	1 Seconds, 1 Days		U/Hours, U/Hours	Eczema, Hypersensitivity	R
B0755697A	Ecuador	CO	6 Months/F	INJ	.5ML	28Sep2011-28Sep2011, U, U	29Sep2011	U/1 Days, U/U, U/U	Erythema, Pruritus	N
#B0710915A	France	CO,CN	5 Months/F	INJ	U	22Mar2011-22Mar2011	27Mar2011	U/5 Days	Henoch-Schonlein purpura, Contusion	I
#D0072611A	Germany	CO	3 Months/M	INJ	.5ML	25Aug2011-25Aug2011	25Aug2011	U/5 Hours	Petechiae*, Haematoma*	R

D0071437A	Germany	CO	4 Months/F	INJ	U	17May2011-17May2011	17May2011	U/0 Days	Petechiae, Skin discolouration	U
B0740880A	South Africa	CO	8 Weeks/F	INJ	U	12Aug2011-12Aug2011	12Aug2011	U/0 Days	Pigmentation disorder	R
B0726374A	Italy	CO	6 Months/F	INJ	U	18Apr2011-18Apr2011	18Apr2011	U/0 Days	Rash morbilliform, Pyrexia	R
B0687729A	Poland	CO	6 Weeks/F	INJ	U	03Dec2010-03Dec2010	03Dec2010	U/0 Days	Skin striae	U

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APPENDIX 3E : Cases from a previous period not included in previous PSUR

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Infanrix Hexa: line listing of cases from a previous period and not included in a previous PSUR

Case No.	Country	Report Source	Age/Sex	Form'n or Route	TDD	Treatment Dates*	Event Onset	TTO	Events	Outcome	Comments
General disorders and administration site conditions											
D0061162A	Germany	RA	4M / F	INJ	U	10Dec2008 - 10Dec2008	10Dec2008	0D	Pyrexia; Pyrexia;	Resolved	-
				INJ	U	27Feb2009 - 27Feb2009	10Dec2008	0D			
B0637096A	Italy	RA	4M / F	INJ	U	23Oct2009 - 23Oct2009	23Oct2009	0D	Injection site nodule, Injection site erythema;	Resolved	-
Infections and infestations											
D0063259A	Germany	RA	3M / M	INJ	0.5ml	15Sep2009 - 15Sep2009	29Sep2009	14D	Bronchitis, Wheezing, Cough;	Unresolved	-
D0060830A	Germany	RA	8M / M	INJ	U	29Jan2008 - 29Jan2008	2008	U	Rhinitis, Vaccination complication;	Resolved	-
				INJ	U	1Days	2008	U			
Nervous system disorders											
#B0591710A	Netherlands	RA	2M / F	INJ	U	18May2009 - 18May2009	May2009	6H	Loss of consciousness, Hypotonia, Vomiting, Pallor, Cyanosis, Drooling;	Resolved	-
B0647987A	France	MD	7W / F	INJ	U	15Feb2010 - 15Feb2010	15Feb2010	30D	Crying, Pyrexia, Drug administered to patient of inappropriate age;	Resolved	-
#B0674885A	Italy	RA MD	13M / F	INJ	U	01Sep2010 - 01Sep2010	02Sep2010	1D	Febrile convulsion, Pyrexia;	Resolved	-
#B0631888A	Sweden	RA	11M / M	INJ	U	16Sep2009 - 16Sep2009	17Sep2009	1D	Febrile convulsion, Ill-defined disorder, Muscle twitching, Muscle twitching, Crying;	Resolved	-
Skin and subcutaneous tissue disorders											
D0066216A	Germany	RA	11M / M	INJ	U	16Sep2009 - 16Sep2009	23Sep2009	7D	Rash vesicular, Open wound, Rash pruritic, Bacterial infection;	Unresolved	-
D0066224A	Germany	RA	4M / F	INJ	U	27Jul2009 - 27Jul2009	30Jul2009	3D	Urticaria;	Resolved	-

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APPENDIX 4A : All reported AEs for cases included in APPENDIX 3A

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Appendix 4A: Summary Tabulation of Adverse Events Included in the Line Listing for:

Infanrix hexa

N.B. Events are only considered serious if they fulfil GSK medically serious criteria. GSK medically serious criteria are applied automatically only to events from spontaneous, post-marketing or literature case reports. Events arising from Clinical trial cases are not run against the list of GSK medically serious terms. For this reason events may appear as both serious and non-serious. For full explanation see section 6.2.2.

MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Anaemia	No	6	0	6
		Bone marrow failure	No	1	0	1
		Hypochromic anaemia	No	1	0	1
		Pancytopenia	No	1	0	1
	Coagulopathies and bleeding diatheses (excl thrombocytopenic)	Haemorrhagic diathesis	No	2	0	2
	Haemolyses and related conditions	Anaemia haemolytic autoimmune	No	1	0	1
	Platelet disorders	Idiopathic thrombocytopenic purpura	No	5	0	5
		Thrombocytopenia	Yes	9	0	9
		Thrombocytopenic purpura	No	4	0	4
		Thrombocytosis	No	2	0	2
	Spleen, lymphatic and reticuloendothelial system disorders	Lymphadenopathy	Yes	0	12	12
		Splenomegaly	No	2	0	2
	White blood cell disorders	Agranulocytosis	No	1	0	1
		Eosinophilia	No	0	2	2

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Leukocytosis	No	4	0	4
		Leukopenia	No	1	0	1
		Neutropenia	No	2	0	2
Cardiac disorders	Cardiac arrhythmias	Arrhythmia	No	0	1	1
		Atrial tachycardia	No	1	0	1
		Bradycardia	No	0	11	11
		Cardiac arrest	No	3	0	3
		Cardio-respiratory arrest	No	1	0	1
		Supraventricular tachycardia	No	1	0	1
		Tachycardia	No	0	4	4
	Cardiac disorder signs and symptoms	Cardiovascular disorder	No	0	4	4
		Cardiovascular insufficiency	Yes	1	0	1
		Cyanosis	No	49	7	56
	Cardiac valve disorders	Mitral valve incompetence	No	1	0	1
	Heart failures	Cardiac failure	No	1	0	1
		Cardiogenic shock	No	1	0	1
		Cardiopulmonary failure	No	1	0	1
	Myocardial disorders	Cardiomyopathy	No	1	0	1
		Congestive cardiomyopathy	No	1	0	1

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
	Pericardial disorders	Pericarditis	No	1	0	1
Congenital, familial and genetic disorders	Musculoskeletal and connective tissue disorders congenital	Macrocephaly	No	1	0	1
		Microcephaly	No	1	0	1
		Talipes	No	1	0	1
	Neurological disorders congenital	Congenital neuropathy	No	1	0	1
	Reproductive tract and breast disorders congenital	Hydrocele	No	1	0	1
Ear and labyrinth disorders	External ear disorders (excl congenital)	Cerumen impaction	No	0	1	1
	Middle ear disorders (excl congenital)	Tympanic membrane disorder	No	0	1	1
		Tympanic membrane hyperaemia	No	0	1	1
		Tympanic membrane perforation	No	0	2	2
Endocrine disorders	Thyroid gland disorders	Hypothyroidism	No	2	0	2
Eye disorders	Eye disorders NEC	Eye disorder	No	0	6	6
		Eyelid disorder	No	0	1	1
		Eye oedema	No	0	1	1
		Eye swelling	No	0	1	1
	Ocular haemorrhages and vascular disorders NEC	Conjunctival haemorrhage	No	0	1	1
	Ocular infections, irritations and inflammations	Conjunctivitis	No	0	4	4
		Eyelid oedema	Yes	0	4	4
	Ocular neuromuscular disorders	Blepharospasm	No	0	1	1

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Eye movement disorder	No	0	17	17
		Gaze palsy	No	18	0	18
		Oculogyric crisis	No	2	0	2
		Pupils unequal	No	0	1	1
		Strabismus	No	0	2	2
	Vision disorders	Visual acuity reduced	No	0	1	1
Gastrointestinal disorders	Dental and gingival conditions	Gingival bleeding	No	0	2	2
	Gastrointestinal conditions NEC	Gastrointestinal disorder	No	0	2	2
	Gastrointestinal haemorrhages NEC	Haematochezia	No	3	0	3
		Rectal haemorrhage	No	1	0	1
	Gastrointestinal inflammatory conditions	Colitis	No	1	0	1
		Gastrointestinal inflammation	No	0	1	1
	Gastrointestinal motility and defaecation conditions	Constipation	No	0	1	1
		Diarrhoea	Yes	0	27	27
		Diarrhoea haemorrhagic	No	2	0	2
		Frequent bowel movements	Yes	0	1	1
		Gastrooesophageal reflux disease	No	1	2	3
		Ileus paralytic	No	1	0	1
	Gastrointestinal signs and symptoms	Abdominal distension	No	0	4	4

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Abdominal pain	No	0	7	7
		Abnormal faeces	No	0	3	3
		Dyspepsia	No	0	1	1
		Dysphagia	No	0	1	1
		Faeces discoloured	No	0	2	2
		Flatulence	No	0	3	3
		Gastrointestinal pain	No	0	2	2
		Nausea	No	0	1	1
		Post-tussive vomiting	No	0	1	1
		Regurgitation	No	0	1	1
		Vomiting	Yes	0	53	53
	Gastrointestinal stenosis and obstruction	Intussusception	No	1	0	1
	Oral soft tissue conditions	Chapped lips	No	0	2	2
		Cheilitis	No	0	4	4
		Lip haematoma	No	0	1	1
		Lip swelling	Yes	0	2	2
		Mouth haemorrhage	No	1	1	1
	Peritoneal and retroperitoneal conditions	Ascites	No	1	0	1
	Salivary gland conditions	Lip dry	No	0	1	1

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Salivary hypersecretion	No	0	6	6
	Tongue conditions	Glossoptosis	No	0	1	1
		Hypertrophy of tongue papillae	No	0	1	1
		Swollen tongue	Yes	0	1	1
General disorders and administration site conditions	Administration site reactions	Injected limb mobility decreased	No	0	3	3
		Injection site abscess sterile	No	0	1	1
		Injection site cyst	No	0	2	2
		Injection site dermatitis	Yes	0	1	1
		Injection site discolouration	No	0	19	19
		Injection site eczema	No	0	1	1
		Injection site erythema	Yes	0	89	89
		Injection site extravasation	No	0	6	6
		Injection site haematoma	No	0	8	8
		Injection site haemorrhage	No	0	2	2
		Injection site induration	Yes	0	40	40
		Injection site inflammation	No	0	31	31
		Injection site nodule	No	0	17	17
		Injection site oedema	Yes	0	21	21
		Injection site pain	Yes	0	37	37

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Injection site papule	No	0	1	1
		Injection site pruritus	No	0	16	16
		Injection site rash	Yes	0	3	3
		Injection site reaction	No	0	20	20
		Injection site scar	No	0	1	1
		Injection site swelling	Yes	0	57	57
		Injection site urticaria	No	0	1	1
		Injection site vesicles	Yes	0	3	3
		Injection site warmth	No	0	39	39
		Vaccination site induration	Yes	0	1	1
	Body temperature conditions	Hyperpyrexia	No	0	6	6
		Hyperthermia	No	0	4	4
		Hypothermia	No	0	2	2
		Pyrexia	Yes	1	284	285
	Fatal outcomes	Death	No	4	0	4
		Sudden death	No	1	0	1
		Sudden infant death syndrome	No	3	0	3
	General system disorders NEC	Abasia	No	0	1	1
		Abscess sterile	No	6	0	6

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Asthenia	No	0	6	6
		Chills	No	0	5	5
		Condition aggravated	No	0	1	1
		Developmental delay	No	0	8	8
		Discomfort	No	0	1	1
		Enanthema	No	0	1	1
		Extensive swelling of vaccinated limb	Yes	0	18	18
		Face oedema	Yes	0	1	1
		Fatigue	No	0	16	16
		Feeling abnormal	No	0	1	1
		Feeling cold	No	0	2	2
		Feeling hot	No	0	7	7
		Foaming at mouth	No	0	3	3
		Foreign body reaction	No	0	3	3
		Gait disturbance	No	0	11	11
		Generalised oedema	No	0	1	1
		General physical health deterioration	No	0	7	7
		Granuloma	No	0	3	3
		Ill-defined disorder	No	0	32	32

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Induration	No	0	6	6
		Inflammation	No	0	16	16
		Irritability	Yes	0	21	21
		Localised oedema	No	0	1	1
		Local reaction	No	0	1	1
		Local swelling	No	0	2	2
		Malaise	No	0	23	23
		Mucosal inflammation	No	0	1	1
		Mucous membrane disorder	No	0	1	1
		Multi-organ failure	No	1	0	1
		Oedema	No	0	5	5
		Oedema peripheral	No	0	26	26
		Pain	No	0	21	21
		Swelling	No	0	10	10
		Tenderness	No	0	1	1
		Thirst decreased	No	0	1	1
	Product quality issues	Incorrect product storage	No	0	43	43
		Product quality issue	No	0	18	18
	Therapeutic and nontherapeutic effects (excl toxicity)	Adverse event	No	0	2	2

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Drug ineffective	Yes	0	1	1
		No therapeutic response	Yes	0	5	5
		Therapeutic response decreased	Yes	0	1	1
	Tissue disorders NEC	Cyst	No	0	1	1
		Fibrosis	No	0	4	4
		Nodule	No	0	2	2
Hepatobiliary disorders	Gallbladder disorders	Cholecystitis	No	1	0	1
	Hepatic and hepatobiliary disorders	Hepatic function abnormal	No	0	1	1
		Hepatomegaly	No	0	1	1
		Hepatosplenomegaly	No	0	1	1
		Hepatotoxicity	No	1	0	1
		Hypertransaminasaemia	No	1	0	1
		Jaundice	No	1	0	1
Immune system disorders	Allergic conditions	Allergy to metals	No	0	1	1
		Allergy to vaccine	Yes	0	1	1
		Anaphylactic reaction	Yes	3	0	3
		Anaphylactic shock	Yes	3	0	3
		Anaphylactoid reaction	Yes	1	0	1
		Drug hypersensitivity	Yes	0	1	1

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Hypersensitivity	Yes	0	18	18
		Milk allergy	No	0	1	1
	Immune disorders NEC	Immune system disorder	No	0	1	1
Infections and infestations	Ancillary infectious topics	Transmission of an infectious agent via a medicinal product	No	1	0	1
	Bacterial infectious disorders	Bacterial infection	No	0	1	1
		Cellulitis	No	2	0	2
		Erysipelas	No	0	1	1
		Escherichia infection	No	0	2	2
		Escherichia urinary tract infection	No	0	1	1
		Gastroenteritis Escherichia coli	No	1	0	1
		Gastroenteritis staphylococcal	No	1	0	1
		Haemophilus infection	No	0	3	3
		Injection site cellulitis	No	0	1	1
		Meningitis haemophilus	No	4	0	4
		Meningitis pneumococcal	No	2	0	2
		Pertussis	No	0	40	40
		Pneumococcal infection	No	0	1	1
		Pneumococcal sepsis	No	0	1	1
		Salmonella sepsis	No	1	0	1

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Salmonellosis	No	0	1	1
		Staphylococcal abscess	No	0	3	3
		Staphylococcal infection	No	0	1	1
		Streptococcal abscess	No	0	2	2
		Streptococcal bacteraemia	No	0	1	1
	Fungal infectious disorders	Fungal skin infection	Yes	0	1	1
	Infections - pathogen unspecified	Abdominal abscess	No	0	1	1
		Abscess	No	0	8	8
		Abscess limb	No	0	1	1
		Bacteraemia	No	2	0	2
		Bone abscess	No	1	0	1
		Bronchitis	Yes	0	5	5
		Bronchopneumonia	No	1	0	1
		Ear infection	No	0	3	3
		Encephalitic infection	No	1	0	1
		Gastroenteritis	No	2	0	2
		Groin abscess	No	0	1	1
		Impetigo	No	0	3	3
		Incision site abscess	No	0	2	2

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Infection	No	0	7	7
		Injection site abscess	No	0	11	11
		Injection site infection	No	0	2	2
		Injection site pustule	No	0	1	1
		Labyrinthitis	No	0	1	1
		Lung infection	No	0	1	1
		Meningitis	Yes	3	0	3
		Meningitis aseptic	Yes	1	0	1
		Nasopharyngitis	Yes	0	9	9
		Osteomyelitis	No	1	0	1
		Otitis media	No	0	5	5
		Otitis media acute	No	0	1	1
		Pharyngitis	Yes	0	2	2
		Pneumonia primary atypical	No	1	0	1
		Purulence	No	0	1	1
		Purulent discharge	No	0	1	1
		Pyelonephritis	No	2	0	2
		Rash pustular	Yes	0	2	2
		Respiratory tract infection	Yes	0	5	5

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Rhinitis	Yes	0	7	7
		Sepsis	No	4	0	4
		Septic shock	No	1	0	1
		Soft tissue infection	No	0	1	1
		Sputum purulent	No	0	1	1
		Subdural empyema	No	0	1	1
		Tonsillitis	Yes	0	3	3
		Upper respiratory tract infection	Yes	0	10	10
		Urinary tract infection	No	1	1	2
	Viral infectious disorders	Exanthema subitum	No	0	1	1
		Gastroenteritis astroviral	No	1	0	1
		Gastroenteritis rotavirus	No	7	0	7
		H1N1 influenza	No	0	1	1
		Herpes simplex	No	0	1	1
		Herpes virus infection	No	0	1	1
		Herpes zoster	Yes	0	2	2
		Measles	No	0	1	1
		Meningitis viral	Yes	1	0	1
		Respiratory syncytial virus infection	No	0	2	2

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Varicella	No	0	1	1
		Vestibular neuronitis	No	0	1	1
		Viral infection	No	0	3	3
		Viral rash	Yes	0	3	3
Injury, poisoning and procedural complications	Chemical injury and poisoning	Maternal exposure during pregnancy	No	0	1	1
	Injuries NEC	Arthropod bite	No	0	1	1
		Contusion	No	0	2	2
		Fall	No	0	4	4
	Medication errors	Accidental exposure	No	0	1	1
		Accidental overdose	No	0	6	6
		Drug administered to patient of inappropriate age	No	0	6	6
		Drug administration error	No	0	22	22
		Drug prescribing error	No	0	1	1
		Expired drug administered	No	0	9	9
		Inappropriate schedule of drug administration	No	0	28	28
		Incorrect dose administered	No	0	22	22
		Incorrect route of drug administration	No	0	18	18
		Incorrect storage of drug	No	0	18	18
		Medication error	No	0	1	1

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Overdose	No	0	22	22
		Underdose	No	0	18	18
		Wrong drug administered	No	0	26	26
		Wrong technique in drug usage process	No	0	82	82
	Procedural related injuries and complications NEC	Vaccination complication	No	0	10	10
		Vaccination failure	Yes	48	0	48
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Blood pressure decreased	Yes	0	2	2
		Cardiac murmur	No	0	1	1
		Heart rate decreased	No	0	1	1
		Heart rate increased	No	0	3	3
		Pulse absent	No	1	0	1
		Pulse pressure decreased	No	0	1	1
	Enzyme investigations NEC	Blood lactate dehydrogenase increased	No	0	1	1
	Haematology investigations (incl blood groups)	Platelet count decreased	Yes	0	2	2
	Hepatobiliary investigations	Alanine aminotransferase increased	No	1	0	1
		Aspartate aminotransferase increased	No	2	0	2
		Transaminases increased	No	5	0	5
	Immunology and allergy investigations	Autoantibody positive	No	0	1	1
		Immunology test abnormal	No	0	1	1

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
	Metabolic, nutritional and blood gas investigations	Oxygen saturation decreased	No	0	8	8
	Microbiology and serology investigations	Adenovirus test positive	No	0	1	1
		Bacterial test positive	No	0	1	1
		Bordetella test negative	No	0	1	1
		Bordetella test positive	No	0	2	2
		Clostridium test	No	0	1	1
		Clostridium test negative	No	0	3	3
		Corynebacterium test negative	No	0	3	3
		Cytomegalovirus test positive	No	0	1	1
		Hepatitis B antibody negative	No	0	3	3
		Hepatitis B antibody positive	No	0	1	1
	Neurological, special senses and psychiatric investigations	Electroencephalogram abnormal	No	0	1	1
		Nerve stimulation test abnormal	No	0	1	1
		Reflex test normal	No	0	1	1
	Physical examination topics	Body temperature	No	0	1	1
		Body temperature decreased	No	0	1	1
		Body temperature fluctuation	No	0	1	1
		Body temperature increased	Yes	0	20	20
		Lymph node palpable	No	0	1	1

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Neurological examination abnormal	No	0	1	1
		Respiratory rate decreased	No	0	1	1
		Weight decreased	No	0	4	4
	Protein and chemistry analyses NEC	C-reactive protein increased	No	0	6	6
		Inflammatory marker increased	No	0	2	2
	Renal and urinary tract investigations and urinalyses	Urine output decreased	No	0	1	1
		White blood cells urine positive	No	0	1	1
Metabolism and nutrition disorders	Acid-base disorders	Acidosis	No	2	0	2
		Ketosis	No	0	1	1
		Lactic acidosis	No	1	0	1
	Appetite and general nutritional disorders	Decreased appetite	Yes	0	19	19
		Feeding disorder neonatal	No	0	1	1
		Hypophagia	Yes	0	3	3
		Increased appetite	No	0	1	1
		Weight gain poor	No	0	2	2
	Diabetic complications	Diabetic ketoacidosis	No	1	0	1
	Electrolyte and fluid balance conditions	Dehydration	No	0	4	4
		Fluid intake reduced	No	0	6	6
		Hypokalaemia	No	2	0	2

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Oligodipsia	No	0	7	7
		Polydipsia	No	0	1	1
	Food intolerance syndromes	Cow's milk intolerance	No	0	1	1
	Glucose metabolism disorders (incl diabetes mellitus)	Hyperglycaemia	No	0	1	1
		Type 1 diabetes mellitus	No	1	0	1
	Iron and trace metal metabolism disorders	Iodine deficiency	No	0	1	1
		Iron deficiency	No	0	1	1
Musculoskeletal and connective tissue disorders	Joint disorders	Arthralgia	No	0	2	2
		Arthritis	Yes	0	1	1
		Joint hyperextension	No	0	3	3
		Joint swelling	No	0	1	1
	Muscle disorders	Muscle rigidity	No	0	1	1
		Muscle spasms	No	0	8	8
		Muscle tightness	No	0	1	1
		Muscle twitching	No	0	9	9
		Muscular weakness	Yes	0	2	2
		Myosclerosis	No	0	1	1
		Nuchal rigidity	No	0	2	2

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
	Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)	Facial asymmetry	No	0	1	1
		Foot deformity	No	0	1	1
		Hip deformity	No	0	1	1
	Musculoskeletal and connective tissue disorders NEC	Mastication disorder	No	0	1	1
		Mobility decreased	No	0	2	2
		Muscle contracture	No	0	1	1
		Musculoskeletal stiffness	No	0	8	8
		Pain in extremity	No	0	10	10
		Posture abnormal	No	0	3	3
		Soft tissue necrosis	No	1	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Skin neoplasms malignant and unspecified	Neoplasm skin	No	1	0	1
Nervous system disorders	Central nervous system infections and inflammations	Central nervous system inflammation	No	0	1	1
		Encephalitis	Yes	3	0	3
		Myelitis transverse	No	1	0	1
	Central nervous system vascular disorders	Cerebral ischaemia	No	2	0	2
		Thalamus haemorrhage	No	1	0	1
	Cranial nerve disorders (excl neoplasms)	Facial paresis	Yes	3	0	3

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Tongue paralysis	Yes	1	0	1
		VIIth nerve paralysis	Yes	2	0	2
		VIth nerve paralysis	Yes	1	0	1
	Demyelinating disorders	Demyelination	No	1	0	1
	Encephalopathies	Encephalopathy	Yes	1	0	1
	Headaches	Headache	No	0	2	2
	Increased intracranial pressure and hydrocephalus	Hydrocephalus	No	1	0	1
	Mental impairment disorders	Mental impairment	No	0	1	1
	Movement disorders (incl parkinsonism)	Dyskinesia	No	0	16	16
		Extrapyramidal disorder	No	1	0	1
		Hemiparesis	Yes	1	0	1
		Hypokinesia	No	0	3	3
		Motor developmental delay	No	0	1	1
		Movement disorder	No	0	1	1
		Opisthotonus	No	0	7	7
		Paresis	Yes	1	0	1
		Psychomotor hyperactivity	No	0	3	3
		Tremor	No	0	13	13
	Neurological disorders NEC	Altered state of consciousness	No	3	0	3

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Areflexia	No	0	1	1
		Ataxia	No	0	1	1
		Balance disorder	No	0	7	7
		Cerebellar ataxia	No	0	2	2
		Cerebral disorder	No	0	1	1
		Clonus	No	0	7	7
		Crying	Yes	0	126	126
		Depressed level of consciousness	No	24	0	24
		Dizziness	No	0	1	1
		Drooling	No	0	1	1
		Dysstasia	No	0	1	1
		Fontanelle bulging	No	0	1	1
		Hyperaesthesia	No	0	4	4
		Hypoaesthesia	Yes	0	1	1
		Hyporeflexia	No	0	1	1
		Lethargy	No	0	3	3
		Loss of consciousness	No	35	0	35
		Motor dysfunction	No	0	2	2
		Myoclonus	No	0	10	10

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Neurological symptom	No	0	1	1
		Nystagmus	No	0	2	2
		Postictal state	No	0	2	2
		Presyncope	No	5	0	5
		Slow response to stimuli	No	12	0	12
		Somnolence	Yes	0	43	43
		Speech disorder	No	0	1	1
		Stupor	Yes	0	1	1
		Syncope	No	8	0	8
		Unresponsive to stimuli	No	15	0	15
	Neuromuscular disorders	Autonomic nervous system imbalance	No	0	1	1
		Cholinergic syndrome	No	0	1	1
		Hypertonia	No	0	19	19
		Hypotonia	No	0	79	79
		Hypotonic-hyporesponsive episode	Yes	2	61	63
		Muscle contractions involuntary	No	0	2	2
	Peripheral neuropathies	Demyelinating polyneuropathy	No	1	0	1
		Guillain-Barre syndrome	Yes	2	0	2
		Neuropathy peripheral	Yes	0	2	2

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
	Seizures (incl subtypes)	Clonic convulsion	Yes	4	0	4
		Complex partial seizures	Yes	1	0	1
		Convulsion	Yes	53	0	53
		Epilepsy	Yes	8	0	8
		Febrile convulsion	Yes	42	0	42
		Grand mal convulsion	Yes	15	0	15
		Infantile spasms	Yes	6	0	6
		Lennox-Gastaut syndrome	No	1	0	1
		Partial seizures	Yes	3	0	3
		Petit mal epilepsy	Yes	3	0	3
		Seizure like phenomena	No	2	0	2
		Status epilepticus	No	2	0	2
		Tonic clonic movements	Yes	0	1	1
		Tonic convulsion	Yes	1	0	1
	Sleep disturbances (incl subtypes)	Circadian rhythm sleep disorder	No	0	1	1
		Hypersomnia	No	0	2	2
	Structural brain disorders	Cerebral atrophy	No	1	0	1
		Subdural hygroma	No	0	1	1
Psychiatric disorders	Anxiety disorders and symptoms	Agitation	No	0	9	9

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Anxiety	No	0	5	5
		Fear	No	0	1	1
	Changes in physical activity	Decreased activity	No	0	3	3
		Restlessness	Yes	0	50	50
		Stereotypy	No	0	1	1
	Communication disorders and disturbances	Phonological disorder	No	0	1	1
		Screaming	No	0	21	21
	Depressed mood disorders and disturbances	Tearfulness	Yes	0	1	1
	Eating disorders and disturbances	Eating disorder	No	0	2	2
		Food aversion	Yes	0	3	3
	Mood disorders and disturbances NEC	Apathy	No	0	13	13
		Listless	No	0	3	3
		Moaning	No	0	2	2
	Personality disorders and disturbances in behaviour	Personality change	No	0	2	2
	Psychiatric and behavioural symptoms NEC	Abnormal behaviour	No	0	4	4
		Breath holding	No	0	2	2
		Staring	No	0	26	26
	Schizophrenia and other psychotic disorders	Psychotic disorder	No	1	0	1
	Sleep disorders and disturbances	Insomnia	No	0	12	12

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Middle insomnia	No	0	3	3
		Sleep disorder	No	0	8	8
Renal and urinary disorders	Renal disorders (excl nephropathies)	Oliguria	No	0	1	1
		Pyelocaliectasis	No	0	1	1
		Renal impairment	No	0	2	2
	Ureteric disorders	Ureteric stenosis	No	0	1	1
	Urinary tract signs and symptoms	Polyuria	No	0	1	1
Reproductive system and breast disorders	Reproductive tract disorders NEC	Oedema genital	No	0	1	1
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Asthma	No	1	0	1
		Bronchial hyperreactivity	No	1	0	1
		Bronchitis chronic	Yes	0	1	1
		Bronchospasm	No	0	2	2
		Obstructive airways disorder	No	1	0	1
	Lower respiratory tract disorders (excl obstruction and infection)	Emphysema	No	0	1	1
		Pneumonia aspiration	No	1	0	1
	Neonatal respiratory disorders	Apparent life threatening event	No	4	0	4
	Respiratory disorders NEC	Acute respiratory failure	No	1	0	1
		Apnoea	Yes	25	0	25

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Apnoeic attack	Yes	0	3	3
		Asphyxia	No	1	0	1
		Aspiration	No	0	1	1
		Choking	No	2	0	2
		Cough	Yes	0	19	19
		Dysphonia	No	0	1	1
		Dyspnoea	No	0	15	15
		Hypopnoea	Yes	0	1	1
		Hypoventilation	Yes	2	0	2
		Hypoxia	No	1	0	1
		Increased upper airway secretion	No	0	3	3
		Lung disorder	No	0	1	1
		Oropharyngeal pain	No	0	1	1
		Productive cough	Yes	0	1	1
		Respiration abnormal	No	0	10	10
		Respiratory arrest	Yes	7	0	7
		Respiratory depression	Yes	1	0	1
		Respiratory disorder	No	0	6	6
		Respiratory failure	No	1	0	1

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Respiratory tract congestion	No	0	1	1
		Respiratory tract inflammation	No	0	1	1
		Rhinorrhoea	No	0	3	3
		Sleep apnoea syndrome	No	0	1	1
		Sneezing	No	0	1	1
		Snoring	No	0	1	1
		Tachypnoea	No	0	3	3
		Upper respiratory tract congestion	No	0	1	1
		Upper respiratory tract inflammation	No	0	1	1
	Upper respiratory tract disorders (excl infections)	Epistaxis	No	0	2	2
		Nasal congestion	No	0	1	1
		Pharyngeal erythema	No	0	7	7
		Stridor	No	2	0	2
		Tonsillar disorder	No	0	1	1
		Tonsillar hypertrophy	No	0	1	1
Skin and subcutaneous tissue disorders	Angioedema and urticaria	Angioedema	Yes	4	0	4
		Urticaria	Yes	0	20	20
		Urticaria papular	No	0	2	2
		Urticaria thermal	No	0	1	1

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
	Cornification and dystrophic skin disorders	Keloid scar	No	0	1	1
	Cutaneous neoplasms benign	Dermal cyst	No	0	1	1
	Epidermal and dermal conditions	Blister	No	0	5	5
		Decubitus ulcer	No	0	1	1
		Dermatitis	Yes	0	1	1
		Dermatitis allergic	Yes	0	1	1
		Dermatitis atopic	Yes	0	2	2
		Dermatitis diaper	Yes	0	1	1
		Dry skin	No	0	1	1
		Eczema	Yes	0	10	10
		Erythema	Yes	0	57	57
		Erythema multiforme	Yes	2	0	2
		Erythrosis	No	0	1	1
		Generalised erythema	Yes	0	2	2
		Granuloma skin	No	0	1	1
		Macule	Yes	0	1	1
		Neurodermatitis	Yes	0	2	2
		Palmar erythema	Yes	0	1	1
		Papule	Yes	0	3	3

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Pemphigoid	No	1	0	1
		Pruritus	Yes	0	5	5
		Rash	Yes	0	35	35
		Rash erythematous	Yes	0	4	4
		Rash generalised	Yes	0	7	7
		Rash macular	Yes	0	10	10
		Rash maculo-papular	Yes	0	5	5
		Rash morbilliform	Yes	0	5	5
		Rash papular	Yes	0	2	2
		Rash pruritic	Yes	0	1	1
		Rash vesicular	Yes	0	2	2
		Scab	No	0	3	3
		Scar	No	0	3	3
		Seborrhoeic dermatitis	Yes	0	1	1
		Skin discolouration	No	0	16	16
		Skin disorder	No	0	1	1
		Skin exfoliation	Yes	0	3	3
		Skin induration	No	0	1	1
		Skin lesion	No	0	3	3

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Skin reaction	No	0	2	2
		Skin tightness	No	0	1	1
		Skin warm	No	0	9	9
		Stevens-Johnson syndrome	Yes	1	0	1
		Swelling face	Yes	0	2	2
		Toxic skin eruption	Yes	0	1	1
		Yellow skin	No	2	0	2
	Pigmentation disorders	Skin depigmentation	No	0	2	2
	Skin and subcutaneous tissue disorders NEC	Erythema nodosum	No	0	1	1
		Lipoatrophy	No	1	0	1
		Skin erosion	No	0	1	1
		Skin ulcer	No	0	1	1
		Subcutaneous nodule	No	0	2	2
	Skin appendage conditions	Acne	Yes	0	1	1
		Cold sweat	No	0	1	1
		Hyperhidrosis	No	0	9	9
		Hypertrichosis	No	0	2	2
	Skin vascular abnormalities	Acute haemorrhagic oedema of infancy	No	1	0	1
		Ecchymosis	No	0	3	3

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Henoch-Schonlein purpura	No	1	0	1
		Increased tendency to bruise	No	0	1	1
		Lividity	No	0	5	5
		Petechiae	No	0	23	23
		Purpura	No	0	2	2
Social circumstances	Lifestyle issues	Disability	No	1	0	1
		Immobile	No	0	3	3
Surgical and medical procedures	Nervous system, skull and spine therapeutic procedures	Neurosurgery	No	0	1	1
	Respiratory tract therapeutic procedures	Endotracheal intubation	No	0	1	1
	Therapeutic procedures and supportive care NEC	Abscess drainage	No	0	1	1
		Debridement	No	0	1	1
		Off label use	No	0	11	11
		Surgery	No	0	1	1
Vascular disorders	Arteriosclerosis, stenosis, vascular insufficiency and necrosis	Peripheral coldness	Yes	0	5	5
	Decreased and nonspecific blood pressure disorders and shock	Circulatory collapse	Yes	7	0	7
		Shock	Yes	4	0	4
	Vascular disorders NEC	Flushing	No	0	3	3
		Hyperaemia	No	0	7	7

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MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
		Pallor	No	0	88	88
		Vasodilatation	No	0	1	1
	Vascular haemorrhagic disorders	Haematoma	No	0	10	10
		Haemorrhage	No	1	0	1
	Vascular hypertensive disorders	Hypertension	No	0	1	1
	Vascular inflammations	Kawasaki's disease	No	0	3	3

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APPENDIX 4B : All reported AEs for cases included in APPENDIX 3C

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Appendix 4B: Summary Tabulation of Adverse Events for Non-Serious Listed Cases for:

Infanrix hexa

N.B. Events are considered non serious against GSK list of medically serious terms (see section 6.3.)

MedDRA SOC	HLGT	Event PT	Non-serious
Blood and lymphatic system disorders	Spleen, lymphatic and reticuloendothelial system disorders	Lymphadenopathy	1
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Diarrhoea	4
	Gastrointestinal signs and symptoms	Vomiting	2
General disorders and administration site conditions	Administration site reactions	Injection site erythema	14
		Injection site oedema	11
		Injection site pain	6
		Injection site swelling	7
	Body temperature conditions	Pyrexia	27
	General system disorders NEC	Extensive swelling of vaccinated limb	4
	Therapeutic and nontherapeutic effects (excl toxicity)	No therapeutic response	2
Immune system disorders	Allergic conditions	Hypersensitivity	1
Investigations	Physical examination topics	Body temperature increased	3
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Decreased appetite	1
Nervous system disorders	Neurological disorders NEC	Crying	7
		Somnolence	2
Psychiatric disorders	Changes in physical activity	Restlessness	1
Skin and subcutaneous tissue disorders	Angioedema and urticaria	Urticaria	9
	Epidermal and dermal conditions	Eczema	1
		Pruritus	1
		Rash	4
		Rash generalised	1
		Rash morbilliform	1

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APPENDIX 4C : All reported AEs from non-medically verified serious cases and non-serious unlisted cases (no such case was received during the period)

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APPENDIX 4D : All reported AEs from non-medically verified non-serious listed cases

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Appendix 4D: Summary Tabulation of Adverse Events from Non-Medically Verified, Non-Serious Listed Cases for:

Infanrix hexa

N.B. Events are considered non serious against GSK list of medically serious terms (see section 6.3.)

MedDRA SOC	HLGT	Event (PT)	Non-serious
General disorders and administration site conditions	Administration site reactions	Injection site erythema	3
		Injection site induration	1
		Injection site swelling	2
	Body temperature conditions	Pyrexia	4
	General system disorders NEC	Extensive swelling of vaccinated limb	1
		Irritability	1
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Eczema	1
		Erythema	1
		Pruritus	1

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APPENDIX 4E : Cumulative tabulation of all unlisted events from serious unlisted spontaneous reports and all serious unlisted reactions from clinical trial cases reported since launch

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Cumulative count
23oct2000 to 22oct2011
Drug PTT decode : IGA182
Date of Refresh : 07Nov2011

MedDRA SOC	MedDRA HLGT	MedDRA PT	Number of AEs	Event level Seriousness
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Anaemia	1	No
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Anaemia	31	Yes
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Aplastic anaemia	1	Yes
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Bicytopenia	1	Yes
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Bone marrow failure	1	Yes
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Haemorrhagic anaemia	3	Yes
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Hypochromic anaemia	4	Yes
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Iron deficiency anaemia	4	Yes
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Microcytic anaemia	3	Yes
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Pancytopenia	4	Yes
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Protein deficiency anaemia	1	Yes
Blood and lymphatic system disorders	Coagulopathies and bleeding diatheses (excl thrombocytopenic)	Coagulopathy	3	Yes
Blood and lymphatic system disorders	Coagulopathies and bleeding diatheses (excl thrombocytopenic)	Disseminated intravascular coagulation	5	Yes
Blood and lymphatic system disorders	Coagulopathies and bleeding diatheses (excl thrombocytopenic)	Haemorrhagic diathesis	4	Yes
Blood and lymphatic system disorders	Haematological disorders NEC	Hypergammaglobulinaemia	1	Yes
Blood and lymphatic system disorders	Haemolyses and related conditions	Anaemia haemolytic autoimmune	4	Yes
Blood and lymphatic system disorders	Haemolyses and related conditions	Haemolysis	4	Yes
Blood and lymphatic system disorders	Haemolyses and related conditions	Haemolytic anaemia	3	Yes
Blood and lymphatic system disorders	Haemolyses and related conditions	Haemolytic uraemic syndrome	1	Yes
Blood and lymphatic system disorders	Haemolyses and related conditions	Jaundice acholuric	1	Yes
Blood and lymphatic system disorders	Haemolyses and related conditions	Warm type haemolytic anaemia	1	Yes
Blood and lymphatic system disorders	Platelet disorders	Autoimmune thrombocytopenia	7	Yes

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Blood and lymphatic system disorders	Platelet disorders	Idiopathic thrombocytopenic purpura	26	Yes
Blood and lymphatic system disorders	Platelet disorders	Thrombocytopenia	1	No
Blood and lymphatic system disorders	Platelet disorders	Thrombocytopenia	41	Yes
Blood and lymphatic system disorders	Platelet disorders	Thrombocytopenic purpura	12	Yes
Blood and lymphatic system disorders	Platelet disorders	Thrombocytosis	10	Yes
Blood and lymphatic system disorders	Red blood cell disorders	Hypochromasia	1	Yes
Blood and lymphatic system disorders	Red blood cell disorders	Microcytosis	2	Yes
Blood and lymphatic system disorders	Spleen, lymphatic and reticuloendothelial system disorders	Lymphadenitis	5	No
Blood and lymphatic system disorders	Spleen, lymphatic and reticuloendothelial system disorders	Lymphadenitis	1	Yes
Blood and lymphatic system disorders	Spleen, lymphatic and reticuloendothelial system disorders	Lymphadenopathy	25	No
Blood and lymphatic system disorders	Spleen, lymphatic and reticuloendothelial system disorders	Lymphadenopathy	2	Yes
Blood and lymphatic system disorders	Spleen, lymphatic and reticuloendothelial system disorders	Lymphatic disorder	1	Yes
Blood and lymphatic system disorders	Spleen, lymphatic and reticuloendothelial system disorders	Lymph node pain	1	No
Blood and lymphatic system disorders	Spleen, lymphatic and reticuloendothelial system disorders	Splenitis	1	Yes
Blood and lymphatic system disorders	Spleen, lymphatic and reticuloendothelial system disorders	Splenomegaly	6	Yes
Blood and lymphatic system disorders	White blood cell disorders	Agranulocytosis	3	Yes
Blood and lymphatic system disorders	White blood cell disorders	Autoimmune neutropenia	1	Yes
Blood and lymphatic system disorders	White blood cell disorders	Eosinophilia	7	No
Blood and lymphatic system disorders	White blood cell disorders	Febrile neutropenia	1	Yes
Blood and lymphatic system disorders	White blood cell disorders	Granulocytopenia	5	Yes
Blood and lymphatic system disorders	White blood cell disorders	Leukocytosis	1	No
Blood and lymphatic system disorders	White blood cell disorders	Leukocytosis	32	Yes
Blood and lymphatic system disorders	White blood cell disorders	Leukopenia	5	Yes
Blood and lymphatic system disorders	White blood cell disorders	Lymphocytic infiltration	1	No
Blood and lymphatic system disorders	White blood cell disorders	Lymphocytosis	7	Yes
Blood and lymphatic system disorders	White blood cell disorders	Lymphopenia	2	Yes

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Blood and lymphatic system disorders	White blood cell disorders	Monocytosis	2	Yes
Blood and lymphatic system disorders	White blood cell disorders	Neutropenia	16	Yes
Blood and lymphatic system disorders	White blood cell disorders	Neutrophilia	1	Yes
Blood and lymphatic system disorders	White blood cell disorders	White blood cell disorder	1	Yes
Cardiac disorders	Cardiac arrhythmias	Arrhythmia	4	No
Cardiac disorders	Cardiac arrhythmias	Atrial tachycardia	1	Yes
Cardiac disorders	Cardiac arrhythmias	Atrioventricular block	1	Yes
Cardiac disorders	Cardiac arrhythmias	Bradycardia	43	No
Cardiac disorders	Cardiac arrhythmias	Cardiac arrest	12	Yes
Cardiac disorders	Cardiac arrhythmias	Cardio-respiratory arrest	6	Yes
Cardiac disorders	Cardiac arrhythmias	Extrasystoles	1	No
Cardiac disorders	Cardiac arrhythmias	Sinus arrhythmia	1	No
Cardiac disorders	Cardiac arrhythmias	Sinus bradycardia	1	Yes
Cardiac disorders	Cardiac arrhythmias	Sinus tachycardia	1	No
Cardiac disorders	Cardiac arrhythmias	Supraventricular tachycardia	1	Yes
Cardiac disorders	Cardiac arrhythmias	Tachycardia	30	No
Cardiac disorders	Cardiac arrhythmias	Tachycardia	1	Yes
Cardiac disorders	Cardiac arrhythmias	Ventricular asystole	1	Yes
Cardiac disorders	Cardiac arrhythmias	Ventricular flutter	1	Yes
Cardiac disorders	Cardiac arrhythmias	Ventricular tachycardia	1	Yes
Cardiac disorders	Cardiac arrhythmias	Wolff-Parkinson-White syndrome	2	Yes
Cardiac disorders	Cardiac disorder signs and symptoms	Cardiovascular disorder	12	No
Cardiac disorders	Cardiac disorder signs and symptoms	Cardiovascular disorder	1	Yes
Cardiac disorders	Cardiac disorder signs and symptoms	Cardiovascular insufficiency	1	Yes
Cardiac disorders	Cardiac disorder signs and symptoms	Cyanosis	38	No
Cardiac disorders	Cardiac disorder signs and symptoms	Cyanosis	234	Yes
Cardiac disorders	Cardiac valve disorders	Aortic valve incompetence	1	Yes
Cardiac disorders	Cardiac valve disorders	Mitral valve disease	2	No
Cardiac disorders	Cardiac valve disorders	Mitral valve incompetence	1	Yes
Cardiac disorders	Cardiac valve disorders	Pulmonary valve stenosis	1	Yes
Cardiac disorders	Cardiac valve disorders	Supravalvular aortic stenosis	1	No
Cardiac disorders	Coronary artery disorders	Arteritis coronary	2	Yes

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Cardiac disorders	Coronary artery disorders	Coronary artery aneurysm	1	Yes
Cardiac disorders	Coronary artery disorders	Coronary artery dilatation	2	No
Cardiac disorders	Coronary artery disorders	Coronary artery disease	1	No
Cardiac disorders	Coronary artery disorders	Myocardial infarction	3	Yes
Cardiac disorders	Endocardial disorders	Endocardial fibrosis	1	No
Cardiac disorders	Heart failures	Cardiac failure	6	Yes
Cardiac disorders	Heart failures	Cardiac failure acute	1	Yes
Cardiac disorders	Heart failures	Cardiogenic shock	1	Yes
Cardiac disorders	Heart failures	Cardiopulmonary failure	4	Yes
Cardiac disorders	Myocardial disorders	Atrial septal defect acquired	1	No
Cardiac disorders	Myocardial disorders	Cardiomegaly	2	No
Cardiac disorders	Myocardial disorders	Cardiomyopathy	1	Yes
Cardiac disorders	Myocardial disorders	Congestive cardiomyopathy	3	Yes
Cardiac disorders	Myocardial disorders	Hypertrophic cardiomyopathy	1	Yes
Cardiac disorders	Myocardial disorders	Myocarditis	3	Yes
Cardiac disorders	Pericardial disorders	Pericardial effusion	4	Yes
Cardiac disorders	Pericardial disorders	Pericarditis	1	Yes
Congenital, familial and genetic disorders	Blood and lymphatic system disorders congenital	Haemophilia	1	Yes
Congenital, familial and genetic disorders	Blood and lymphatic system disorders congenital	Infantile genetic agranulocytosis	2	Yes
Congenital, familial and genetic disorders	Cardiac and vascular disorders congenital	Atrial septal defect	5	Yes
Congenital, familial and genetic disorders	Chromosomal abnormalities and abnormal gene carriers	Cytogenetic abnormality	1	Yes
Congenital, familial and genetic disorders	Congenital and hereditary disorders NEC	Familial mediterranean fever	1	Yes
Congenital, familial and genetic disorders	Cytoplasmic disorders congenital	Mitochondrial encephalomyopathy	1	Yes
Congenital, familial and genetic disorders	Gastrointestinal tract disorders congenital	Pyloric stenosis	1	No
Congenital, familial and genetic disorders	Immune system disorders congenital	Thymus hypoplasia	1	Yes
Congenital, familial and genetic disorders	Metabolic and nutritional disorders congenital	Glycogen storage disorder	1	Yes
Congenital, familial and genetic disorders	Metabolic and nutritional disorders congenital	Leukodystrophy	2	Yes

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Congenital, familial and genetic disorders	Metabolic and nutritional disorders congenital	Methylmalonic aciduria	1	Yes
Congenital, familial and genetic disorders	Metabolic and nutritional disorders congenital	Rett's disorder	1	Yes
Congenital, familial and genetic disorders	Musculoskeletal and connective tissue disorders congenital	Dysmorphism	1	Yes
Congenital, familial and genetic disorders	Musculoskeletal and connective tissue disorders congenital	Macrocephaly	1	Yes
Congenital, familial and genetic disorders	Musculoskeletal and connective tissue disorders congenital	Microcephaly	4	Yes
Congenital, familial and genetic disorders	Musculoskeletal and connective tissue disorders congenital	Plagiocephaly	2	Yes
Congenital, familial and genetic disorders	Musculoskeletal and connective tissue disorders congenital	Skull malformation	1	No
Congenital, familial and genetic disorders	Musculoskeletal and connective tissue disorders congenital	Talipes	1	Yes
Congenital, familial and genetic disorders	Neurological disorders congenital	Aicardi's syndrome	1	Yes
Congenital, familial and genetic disorders	Neurological disorders congenital	Benign familial neonatal convulsions	1	Yes
Congenital, familial and genetic disorders	Neurological disorders congenital	Cerebral palsy	4	Yes
Congenital, familial and genetic disorders	Neurological disorders congenital	Congenital neuropathy	1	Yes
Congenital, familial and genetic disorders	Neurological disorders congenital	Lissencephaly	1	Yes
Congenital, familial and genetic disorders	Neurological disorders congenital	Microencephaly	1	Yes
Congenital, familial and genetic disorders	Neurological disorders congenital	Tuberous sclerosis	2	Yes
Congenital, familial and genetic disorders	Renal and urinary tract disorders congenital	Renal hypoplasia	1	Yes
Congenital, familial and genetic disorders	Reproductive tract and breast disorders congenital	Hydrocele	2	No
Congenital, familial and genetic disorders	Reproductive tract and breast disorders congenital	Hydrocele	2	Yes
Congenital, familial and genetic disorders	Reproductive tract and breast disorders congenital	Phimosis	1	Yes
Ear and labyrinth disorders	Aural disorders NEC	Ear pain	1	No
Ear and labyrinth disorders	Aural disorders NEC	Ear pain	1	Yes

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Ear and labyrinth disorders	External ear disorders (excl congenital)	Auricular perichondritis	1	No
Ear and labyrinth disorders	External ear disorders (excl congenital)	Auricular swelling	1	No
Ear and labyrinth disorders	External ear disorders (excl congenital)	Auricular swelling	1	Yes
Ear and labyrinth disorders	External ear disorders (excl congenital)	Cerumen impaction	1	No
Ear and labyrinth disorders	Hearing disorders	Deafness	2	Yes
Ear and labyrinth disorders	Hearing disorders	Deafness neurosensory	1	Yes
Ear and labyrinth disorders	Hearing disorders	Hyperacusis	1	No
Ear and labyrinth disorders	Inner ear and VIIIth cranial nerve disorders	Vertigo	1	No
Ear and labyrinth disorders	Middle ear disorders (excl congenital)	Otosalpingitis	1	No
Ear and labyrinth disorders	Middle ear disorders (excl congenital)	Tympanic membrane disorder	1	No
Ear and labyrinth disorders	Middle ear disorders (excl congenital)	Tympanic membrane hyperaemia	6	No
Ear and labyrinth disorders	Middle ear disorders (excl congenital)	Tympanic membrane perforation	2	No
Endocrine disorders	Endocrine and glandular disorders NEC	Endocrine pancreatic disorder	1	No
Endocrine disorders	Thyroid gland disorders	Hypothyroidism	5	Yes
Eye disorders	Eye disorders NEC	Eye disorder	22	No
Eye disorders	Eye disorders NEC	Eyelid disorder	7	No
Eye disorders	Eye disorders NEC	Eye oedema	1	No
Eye disorders	Eye disorders NEC	Eye swelling	2	No
Eye disorders	Eye disorders NEC	Lacrimation increased	4	No
Eye disorders	Eye disorders NEC	Periorbital oedema	1	No
Eye disorders	Ocular haemorrhages and vascular disorders NEC	Conjunctival haemorrhage	3	No
Eye disorders	Ocular haemorrhages and vascular disorders NEC	Corneal bleeding	1	Yes
Eye disorders	Ocular infections, irritations and inflammations	Conjunctival hyperaemia	3	No
Eye disorders	Ocular infections, irritations and inflammations	Conjunctivitis	16	No
Eye disorders	Ocular infections, irritations and inflammations	Eye discharge	1	No
Eye disorders	Ocular infections, irritations and inflammations	Eyelid oedema	9	No
Eye disorders	Ocular infections, irritations and inflammations	Ocular hyperaemia	1	No
Eye disorders	Ocular neuromuscular disorders	Binocular eye movement disorder	2	No
Eye disorders	Ocular neuromuscular disorders	Blepharospasm	3	No
Eye disorders	Ocular neuromuscular disorders	Excessive eye blinking	1	No

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Eye disorders	Ocular neuromuscular disorders	Eyelid function disorder	1	No
Eye disorders	Ocular neuromuscular disorders	Eyelid ptosis	3	No
Eye disorders	Ocular neuromuscular disorders	Eye movement disorder	87	No
Eye disorders	Ocular neuromuscular disorders	Eye movement disorder	3	Yes
Eye disorders	Ocular neuromuscular disorders	Gaze palsy	68	Yes
Eye disorders	Ocular neuromuscular disorders	Mydriasis	1	No
Eye disorders	Ocular neuromuscular disorders	Oculogyric crisis	3	Yes
Eye disorders	Ocular neuromuscular disorders	Ophthalmoplegia	3	Yes
Eye disorders	Ocular neuromuscular disorders	Opsoclonus myoclonus	2	No
Eye disorders	Ocular neuromuscular disorders	Pupil fixed	1	No
Eye disorders	Ocular neuromuscular disorders	Pupillary reflex impaired	1	No
Eye disorders	Ocular neuromuscular disorders	Pupils unequal	1	No
Eye disorders	Ocular neuromuscular disorders	Saccadic eye movement	1	No
Eye disorders	Ocular neuromuscular disorders	Strabismus	18	No
Eye disorders	Ocular sensory symptoms NEC	Asthenopia	1	No
Eye disorders	Ocular sensory symptoms NEC	Photophobia	2	No
Eye disorders	Retina, choroid and vitreous haemorrhages and vascular disorders	Retinal haemorrhage	4	Yes
Eye disorders	Vision disorders	Anisometropia	1	No
Eye disorders	Vision disorders	Astigmatism	1	No
Eye disorders	Vision disorders	Diplopia	1	No
Eye disorders	Vision disorders	Hypermetropia	2	No
Eye disorders	Vision disorders	Vision blurred	2	No
Eye disorders	Vision disorders	Visual acuity reduced	1	No
Eye disorders	Vision disorders	Visual impairment	4	No
Gastrointestinal disorders	Abdominal hernias and other abdominal wall conditions	Inguinal hernia	2	No
Gastrointestinal disorders	Abdominal hernias and other abdominal wall conditions	Umbilical hernia	1	No
Gastrointestinal disorders	Dental and gingival conditions	Gingival bleeding	2	No
Gastrointestinal disorders	Gastrointestinal conditions NEC	Anal fistula	1	No
Gastrointestinal disorders	Gastrointestinal conditions NEC	Disbacteriosis	1	No
Gastrointestinal disorders	Gastrointestinal conditions NEC	Gastrointestinal disorder	2	No
Gastrointestinal disorders	Gastrointestinal conditions NEC	Hyperchlorhydria	1	No
Gastrointestinal disorders	Gastrointestinal conditions NEC	Intestinal mucosal hypertrophy	1	No

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Gastrointestinal disorders	Gastrointestinal haemorrhages NEC	Gastrointestinal haemorrhage	2	Yes
Gastrointestinal disorders	Gastrointestinal haemorrhages NEC	Haematochezia	7	No
Gastrointestinal disorders	Gastrointestinal haemorrhages NEC	Haematochezia	9	Yes
Gastrointestinal disorders	Gastrointestinal haemorrhages NEC	Melaena	2	Yes
Gastrointestinal disorders	Gastrointestinal haemorrhages NEC	Rectal haemorrhage	4	Yes
Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Colitis	4	Yes
Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Duodenitis	2	No
Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Enteritis	8	Yes
Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Enterocolitis	1	Yes
Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Eosinophilic colitis	1	Yes
Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Gastritis	2	No
Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Gastroenteritis eosinophilic	2	Yes
Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Gastrointestinal inflammation	2	No
Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Oesophagitis	2	No
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Constipation	11	No
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Diarrhoea	1	No
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Diarrhoea haemorrhagic	12	Yes
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Dyskinesia oesophageal	1	No
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Gastrointestinal hypomotility	1	No
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Gastrointestinal motility disorder	1	Yes
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Gastrooesophageal reflux disease	17	No
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Gastrooesophageal reflux disease	1	Yes
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Ileus paralytic	3	Yes
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Intestinal dilatation	2	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Abdominal discomfort	1	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Abdominal distension	8	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Abdominal pain	14	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Abdominal pain	1	Yes
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Abdominal pain upper	1	No

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Gastrointestinal disorders	Gastrointestinal signs and symptoms	Abdominal rigidity	1	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Abnormal faeces	13	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Abnormal faeces	1	Yes
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Acute abdomen	1	Yes
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Aphagia	1	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Dyspepsia	3	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Dysphagia	6	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Faecal incontinence	1	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Faecal incontinence	1	Yes
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Faeces discoloured	11	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Flatulence	7	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Gastrointestinal pain	2	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Gastrointestinal sounds abnormal	1	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Mucous stools	5	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Nausea	7	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Nausea	1	Yes
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Post-tussive vomiting	1	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Regurgitation	6	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Vomiting	1	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Vomiting	1	Yes
Gastrointestinal disorders	Gastrointestinal stenosis and obstruction	Intestinal obstruction	1	Yes
Gastrointestinal disorders	Gastrointestinal stenosis and obstruction	Intussusception	9	Yes
Gastrointestinal disorders	Gastrointestinal stenosis and obstruction	Subileus	1	Yes
Gastrointestinal disorders	Malabsorption conditions	Malabsorption	1	No
Gastrointestinal disorders	Malabsorption conditions	Steatorrhoea	1	No
Gastrointestinal disorders	Oral soft tissue conditions	Aphthous stomatitis	6	No
Gastrointestinal disorders	Oral soft tissue conditions	Chapped lips	4	No
Gastrointestinal disorders	Oral soft tissue conditions	Cheilitis	7	No
Gastrointestinal disorders	Oral soft tissue conditions	Lip disorder	2	No

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Gastrointestinal disorders	Oral soft tissue conditions	Lip haematoma	1	No
Gastrointestinal disorders	Oral soft tissue conditions	Lip oedema	3	No
Gastrointestinal disorders	Oral soft tissue conditions	Lip swelling	3	No
Gastrointestinal disorders	Oral soft tissue conditions	Mouth haemorrhage	6	No
Gastrointestinal disorders	Oral soft tissue conditions	Mouth haemorrhage	1	Yes
Gastrointestinal disorders	Oral soft tissue conditions	Oral discharge	1	No
Gastrointestinal disorders	Oral soft tissue conditions	Oral mucosal erythema	1	Yes
Gastrointestinal disorders	Oral soft tissue conditions	Stomatitis	3	No
Gastrointestinal disorders	Oral soft tissue conditions	Stomatitis haemorrhagic	1	Yes
Gastrointestinal disorders	Peritoneal and retroperitoneal conditions	Ascites	5	Yes
Gastrointestinal disorders	Peritoneal and retroperitoneal conditions	Peritoneal disorder	1	No
Gastrointestinal disorders	Salivary gland conditions	Lip dry	1	No
Gastrointestinal disorders	Salivary gland conditions	Salivary hypersecretion	36	No
Gastrointestinal disorders	Tongue conditions	Glossoptosis	1	No
Gastrointestinal disorders	Tongue conditions	Hypertrophy of tongue papillae	1	No
Gastrointestinal disorders	Tongue conditions	Protrusion tongue	2	No
Gastrointestinal disorders	Tongue conditions	Swollen tongue	1	No
Gastrointestinal disorders	Tongue conditions	Tongue discolouration	1	No
General disorders and administration site conditions	Administration site reactions	Application site discolouration	1	No
General disorders and administration site conditions	Administration site reactions	Application site rash	1	No
General disorders and administration site conditions	Administration site reactions	Embolia cutis medicamentosa	4	Yes
General disorders and administration site conditions	Administration site reactions	Injected limb mobility decreased	6	No
General disorders and administration site conditions	Administration site reactions	Injection site abscess sterile	7	No
General disorders and administration site conditions	Administration site reactions	Injection site abscess sterile	1	Yes
General disorders and administration site conditions	Administration site reactions	Injection site atrophy	1	Yes
General disorders and administration site conditions	Administration site reactions	Injection site dermatitis	1	No

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General disorders and administration site conditions	Administration site reactions	Injection site discolouration	9	No
General disorders and administration site conditions	Administration site reactions	Injection site erythema	1	No
General disorders and administration site conditions	Administration site reactions	Injection site extravasation	14	No
General disorders and administration site conditions	Administration site reactions	Injection site haematoma	14	No
General disorders and administration site conditions	Administration site reactions	Injection site haemorrhage	4	No
General disorders and administration site conditions	Administration site reactions	Injection site induration	72	No
General disorders and administration site conditions	Administration site reactions	Injection site induration	3	Yes
General disorders and administration site conditions	Administration site reactions	Injection site inflammation	17	No
General disorders and administration site conditions	Administration site reactions	Injection site mass	1	No
General disorders and administration site conditions	Administration site reactions	Injection site necrosis	6	Yes
General disorders and administration site conditions	Administration site reactions	Injection site nodule	27	No
General disorders and administration site conditions	Administration site reactions	Injection site nodule	3	Yes
General disorders and administration site conditions	Administration site reactions	Injection site pain	1	No
General disorders and administration site conditions	Administration site reactions	Injection site pallor	1	No
General disorders and administration site conditions	Administration site reactions	Injection site pruritus	5	No
General disorders and administration site conditions	Administration site reactions	Injection site rash	6	No
General disorders and administration site conditions	Administration site reactions	Injection site reaction	55	No
General disorders and administration site conditions	Administration site reactions	Injection site scab	1	No
General disorders and administration site conditions	Administration site reactions	Injection site scar	1	No
General disorders and administration site conditions	Administration site reactions	Injection site swelling	1	No
General disorders and administration site conditions	Administration site reactions	Injection site swelling	1	Yes

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General disorders and administration site conditions	Administration site reactions	Injection site urticaria	4	No
General disorders and administration site conditions	Administration site reactions	Injection site vesicles	9	No
General disorders and administration site conditions	Administration site reactions	Injection site warmth	41	No
General disorders and administration site conditions	Administration site reactions	Injection site warmth	1	Yes
General disorders and administration site conditions	Administration site reactions	Vaccination site abscess sterile	1	Yes
General disorders and administration site conditions	Body temperature conditions	Hyperpyrexia	29	No
General disorders and administration site conditions	Body temperature conditions	Hyperpyrexia	2	Yes
General disorders and administration site conditions	Body temperature conditions	Hyperthermia	10	No
General disorders and administration site conditions	Body temperature conditions	Hyperthermia	1	Yes
General disorders and administration site conditions	Body temperature conditions	Hypothermia	9	No
General disorders and administration site conditions	Body temperature conditions	Pyrexia	4	No
General disorders and administration site conditions	Device issues	Device dislocation	1	No
General disorders and administration site conditions	Fatal outcomes	Brain death	2	Yes
General disorders and administration site conditions	Fatal outcomes	Death	20	Yes
General disorders and administration site conditions	Fatal outcomes	Sudden cardiac death	1	Yes
General disorders and administration site conditions	Fatal outcomes	Sudden death	9	Yes
General disorders and administration site conditions	Fatal outcomes	Sudden infant death syndrome	72	Yes
General disorders and administration site conditions	General system disorders NEC	Abasia	2	No
General disorders and administration site conditions	General system disorders NEC	Abscess sterile	22	Yes
General disorders and administration site conditions	General system disorders NEC	Asthenia	51	No
General disorders and administration site conditions	General system disorders NEC	Asthenia	2	Yes

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General disorders and administration site conditions	General system disorders NEC	Chest discomfort	1	No
General disorders and administration site conditions	General system disorders NEC	Chest pain	1	No
General disorders and administration site conditions	General system disorders NEC	Chills	21	No
General disorders and administration site conditions	General system disorders NEC	Condition aggravated	4	No
General disorders and administration site conditions	General system disorders NEC	Developmental delay	39	No
General disorders and administration site conditions	General system disorders NEC	Developmental delay	3	Yes
General disorders and administration site conditions	General system disorders NEC	Discomfort	4	No
General disorders and administration site conditions	General system disorders NEC	Disease recurrence	1	No
General disorders and administration site conditions	General system disorders NEC	Enanthema	1	No
General disorders and administration site conditions	General system disorders NEC	Face oedema	3	No
General disorders and administration site conditions	General system disorders NEC	Fatigue	67	No
General disorders and administration site conditions	General system disorders NEC	Fatigue	1	Yes
General disorders and administration site conditions	General system disorders NEC	Feeling abnormal	5	No
General disorders and administration site conditions	General system disorders NEC	Feeling cold	4	No
General disorders and administration site conditions	General system disorders NEC	Feeling hot	11	No
General disorders and administration site conditions	General system disorders NEC	Feeling of body temperature change	1	No
General disorders and administration site conditions	General system disorders NEC	Feeling of relaxation	3	No
General disorders and administration site conditions	General system disorders NEC	Feeling of relaxation	1	Yes
General disorders and administration site conditions	General system disorders NEC	Foaming at mouth	17	No
General disorders and administration site conditions	General system disorders NEC	Foreign body reaction	2	No
General disorders and administration site conditions	General system disorders NEC	Gait disturbance	23	No

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General disorders and administration site conditions	General system disorders NEC	Gait disturbance	1	Yes
General disorders and administration site conditions	General system disorders NEC	Generalised oedema	1	No
General disorders and administration site conditions	General system disorders NEC	Generalised oedema	1	Yes
General disorders and administration site conditions	General system disorders NEC	General physical health deterioration	53	No
General disorders and administration site conditions	General system disorders NEC	General physical health deterioration	3	Yes
General disorders and administration site conditions	General system disorders NEC	General symptom	1	No
General disorders and administration site conditions	General system disorders NEC	Granuloma	2	No
General disorders and administration site conditions	General system disorders NEC	Ill-defined disorder	58	No
General disorders and administration site conditions	General system disorders NEC	Ill-defined disorder	1	Yes
General disorders and administration site conditions	General system disorders NEC	Induration	11	No
General disorders and administration site conditions	General system disorders NEC	Induration	1	Yes
General disorders and administration site conditions	General system disorders NEC	Inflammation	31	No
General disorders and administration site conditions	General system disorders NEC	Influenza like illness	3	No
General disorders and administration site conditions	General system disorders NEC	Irritability	1	No
General disorders and administration site conditions	General system disorders NEC	Irritability	1	Yes
General disorders and administration site conditions	General system disorders NEC	Localised oedema	3	No
General disorders and administration site conditions	General system disorders NEC	Local reaction	11	No
General disorders and administration site conditions	General system disorders NEC	Local swelling	7	No
General disorders and administration site conditions	General system disorders NEC	Malaise	36	No
General disorders and administration site conditions	General system disorders NEC	Mucosal dryness	1	No
General disorders and administration site conditions	General system disorders NEC	Mucosal haemorrhage	1	Yes

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General disorders and administration site conditions	General system disorders NEC	Mucosal inflammation	1	No
General disorders and administration site conditions	General system disorders NEC	Mucous membrane disorder	1	No
General disorders and administration site conditions	General system disorders NEC	Multi-organ failure	7	Yes
General disorders and administration site conditions	General system disorders NEC	No adverse event	2	No
General disorders and administration site conditions	General system disorders NEC	Nonspecific reaction	2	No
General disorders and administration site conditions	General system disorders NEC	Oedema	9	No
General disorders and administration site conditions	General system disorders NEC	Oedema peripheral	82	No
General disorders and administration site conditions	General system disorders NEC	Oedema peripheral	9	Yes
General disorders and administration site conditions	General system disorders NEC	Pain	43	No
General disorders and administration site conditions	General system disorders NEC	Pneumatosis	1	No
General disorders and administration site conditions	General system disorders NEC	Sense of oppression	1	No
General disorders and administration site conditions	General system disorders NEC	Swelling	22	No
General disorders and administration site conditions	General system disorders NEC	Systemic inflammatory response syndrome	2	Yes
General disorders and administration site conditions	General system disorders NEC	Thirst decreased	2	No
General disorders and administration site conditions	Product quality issues	Product quality issue	28	No
General disorders and administration site conditions	Therapeutic and nontherapeutic effects (excl toxicity)	Adverse drug reaction	1	No
General disorders and administration site conditions	Therapeutic and nontherapeutic effects (excl toxicity)	Adverse event	2	No
General disorders and administration site conditions	Tissue disorders NEC	Atrophy	1	Yes
General disorders and administration site conditions	Tissue disorders NEC	Cyst	2	No
General disorders and administration site conditions	Tissue disorders NEC	Cyst	1	Yes

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General disorders and administration site conditions	Tissue disorders NEC	Dysplasia	2	No
General disorders and administration site conditions	Tissue disorders NEC	Hyperplasia	3	No
General disorders and administration site conditions	Tissue disorders NEC	Hypertrophy	1	No
General disorders and administration site conditions	Tissue disorders NEC	Mass	1	No
General disorders and administration site conditions	Tissue disorders NEC	Necrosis	4	Yes
General disorders and administration site conditions	Tissue disorders NEC	Nodule	4	No
General disorders and administration site conditions	Tissue disorders NEC	Ulcer	1	No
Hepatobiliary disorders	Gallbladder disorders	Cholecystitis	1	Yes
Hepatobiliary disorders	Gallbladder disorders	Cholelithiasis	1	No
Hepatobiliary disorders	Gallbladder disorders	Gallbladder disorder	1	No
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Acute hepatic failure	1	Yes
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Cholestasis	1	Yes
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Hepatic failure	2	Yes
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Hepatic function abnormal	3	No
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Hepatic steatosis	1	Yes
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Hepatitis acute	1	Yes
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Hepatitis neonatal	1	Yes
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Hepatomegaly	2	No
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Hepatosplenomegaly	2	No
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Hepatotoxicity	1	Yes
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Hypertransaminasaemia	1	Yes
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Jaundice	8	Yes
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Liver disorder	4	No
Immune system disorders	Allergic conditions	Allergy to metals	2	No
Immune system disorders	Allergic conditions	Anaphylactic reaction	1	Yes
Immune system disorders	Allergic conditions	Atopy	1	No

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Immune system disorders	Allergic conditions	Food allergy	3	No
Immune system disorders	Allergic conditions	Hypersensitivity	1	Yes
Immune system disorders	Allergic conditions	Milk allergy	2	No
Immune system disorders	Allergic conditions	Multiple allergies	1	No
Immune system disorders	Allergic conditions	Serum sickness	1	No
Immune system disorders	Allergic conditions	Type III immune complex mediated reaction	2	No
Immune system disorders	Immune disorders NEC	Decreased immune responsiveness	1	No
Immune system disorders	Immune disorders NEC	Immunisation reaction	1	No
Immune system disorders	Immune disorders NEC	Immunisation reaction	1	Yes
Immune system disorders	Immunodeficiency syndromes	Hypogammaglobulinaemia	1	No
Infections and infestations	Ancillary infectious topics	Transmission of an infectious agent via a medicinal product	1	Yes
Infections and infestations	Bacterial infectious disorders	Bacterial infection	5	No
Infections and infestations	Bacterial infectious disorders	Bacterial pyelonephritis	1	Yes
Infections and infestations	Bacterial infectious disorders	Bacterial tracheitis	1	Yes
Infections and infestations	Bacterial infectious disorders	Bronchitis bacterial	2	No
Infections and infestations	Bacterial infectious disorders	Cellulitis	28	Yes
Infections and infestations	Bacterial infectious disorders	Clostridial infection	1	No
Infections and infestations	Bacterial infectious disorders	Conjunctivitis bacterial	1	No
Infections and infestations	Bacterial infectious disorders	Erysipelas	7	No
Infections and infestations	Bacterial infectious disorders	Erysipelas	1	Yes
Infections and infestations	Bacterial infectious disorders	Erythema migrans	1	No
Infections and infestations	Bacterial infectious disorders	Escherichia infection	5	No
Infections and infestations	Bacterial infectious disorders	Escherichia urinary tract infection	3	No
Infections and infestations	Bacterial infectious disorders	Gastroenteritis bacterial	1	Yes
Infections and infestations	Bacterial infectious disorders	Gastroenteritis Escherichia coli	1	Yes
Infections and infestations	Bacterial infectious disorders	Gastroenteritis staphylococcal	1	Yes

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Infections and infestations	Bacterial infectious disorders	Haemophilus infection	11	No
Infections and infestations	Bacterial infectious disorders	Haemophilus sepsis	3	No
Infections and infestations	Bacterial infectious disorders	Injection site cellulitis	5	No
Infections and infestations	Bacterial infectious disorders	Injection site cellulitis	2	Yes
Infections and infestations	Bacterial infectious disorders	Meningitis bacterial	3	Yes
Infections and infestations	Bacterial infectious disorders	Meningitis haemophilus	11	Yes
Infections and infestations	Bacterial infectious disorders	Meningitis pneumococcal	6	Yes
Infections and infestations	Bacterial infectious disorders	Meningococcal sepsis	1	No
Infections and infestations	Bacterial infectious disorders	Meningoencephalitis bacterial	1	Yes
Infections and infestations	Bacterial infectious disorders	Necrotising ulcerative gingivostomatitis	1	Yes
Infections and infestations	Bacterial infectious disorders	Neuroborreliosis	1	Yes
Infections and infestations	Bacterial infectious disorders	Pertussis	98	No
Infections and infestations	Bacterial infectious disorders	Pertussis	1	Yes
Infections and infestations	Bacterial infectious disorders	Pharyngitis streptococcal	1	No
Infections and infestations	Bacterial infectious disorders	Pneumococcal infection	2	No
Infections and infestations	Bacterial infectious disorders	Pneumococcal sepsis	2	No
Infections and infestations	Bacterial infectious disorders	Pneumonia pneumococcal	1	Yes
Infections and infestations	Bacterial infectious disorders	Proteus infection	1	Yes
Infections and infestations	Bacterial infectious disorders	Salmonella sepsis	1	Yes
Infections and infestations	Bacterial infectious disorders	Scarlet fever	1	No
Infections and infestations	Bacterial infectious disorders	Staphylococcal abscess	4	No
Infections and infestations	Bacterial infectious disorders	Staphylococcal abscess	1	Yes
Infections and infestations	Bacterial infectious disorders	Staphylococcal infection	5	No
Infections and infestations	Bacterial infectious disorders	Staphylococcal infection	1	Yes
Infections and infestations	Bacterial infectious disorders	Staphylococcal scalded skin syndrome	1	No
Infections and infestations	Bacterial infectious disorders	Staphylococcal sepsis	2	Yes
Infections and infestations	Bacterial infectious disorders	Streptococcal abscess	2	No
Infections and infestations	Bacterial infectious disorders	Streptococcal bacteraemia	1	No

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Infections and infestations	Bacterial infectious disorders	Streptococcal infection	1	No
Infections and infestations	Bacterial infectious disorders	Superinfection bacterial	1	No
Infections and infestations	Bacterial infectious disorders	Waterhouse-Friderichsen syndrome	1	Yes
Infections and infestations	Fungal infectious disorders	Candida nappy rash	3	No
Infections and infestations	Fungal infectious disorders	Candidiasis	3	No
Infections and infestations	Fungal infectious disorders	Fungal skin infection	1	No
Infections and infestations	Fungal infectious disorders	Genital candidiasis	3	No
Infections and infestations	Fungal infectious disorders	Oral candidiasis	4	No
Infections and infestations	Infections - pathogen unspecified	Abdominal abscess	1	No
Infections and infestations	Infections - pathogen unspecified	Abscess	15	No
Infections and infestations	Infections - pathogen unspecified	Abscess	5	Yes
Infections and infestations	Infections - pathogen unspecified	Abscess limb	9	No
Infections and infestations	Infections - pathogen unspecified	Abscess soft tissue	1	No
Infections and infestations	Infections - pathogen unspecified	Acute tonsillitis	3	No
Infections and infestations	Infections - pathogen unspecified	Bacteraemia	3	Yes
Infections and infestations	Infections - pathogen unspecified	Bone abscess	1	Yes
Infections and infestations	Infections - pathogen unspecified	Bronchitis	22	No
Infections and infestations	Infections - pathogen unspecified	Bronchitis	2	Yes
Infections and infestations	Infections - pathogen unspecified	Bronchopneumonia	8	Yes
Infections and infestations	Infections - pathogen unspecified	Conjunctivitis infective	1	No
Infections and infestations	Infections - pathogen unspecified	Device related sepsis	1	Yes
Infections and infestations	Infections - pathogen unspecified	Ear infection	10	No
Infections and infestations	Infections - pathogen unspecified	Eczema infected	1	No
Infections and infestations	Infections - pathogen unspecified	Empyema	1	No
Infections and infestations	Infections - pathogen unspecified	Encephalitic infection	1	Yes
Infections and infestations	Infections - pathogen unspecified	Enteritis infectious	2	No
Infections and infestations	Infections - pathogen unspecified	Enteritis infectious	2	Yes
Infections and infestations	Infections - pathogen unspecified	Epiglottitis	1	Yes
Infections and infestations	Infections - pathogen unspecified	Febrile infection	13	No

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Infections and infestations	Infections - pathogen unspecified	Febrile infection	1	Yes
Infections and infestations	Infections - pathogen unspecified	Gastroenteritis	3	No
Infections and infestations	Infections - pathogen unspecified	Gastroenteritis	36	Yes
Infections and infestations	Infections - pathogen unspecified	Gastrointestinal infection	3	No
Infections and infestations	Infections - pathogen unspecified	Groin abscess	2	No
Infections and infestations	Infections - pathogen unspecified	Impetigo	1	No
Infections and infestations	Infections - pathogen unspecified	Incision site abscess	6	No
Infections and infestations	Infections - pathogen unspecified	Infection	21	No
Infections and infestations	Infections - pathogen unspecified	Infection	3	Yes
Infections and infestations	Infections - pathogen unspecified	Infectious peritonitis	1	Yes
Infections and infestations	Infections - pathogen unspecified	Injection site abscess	45	No
Infections and infestations	Infections - pathogen unspecified	Injection site abscess	10	Yes
Infections and infestations	Infections - pathogen unspecified	Injection site infection	4	No
Infections and infestations	Infections - pathogen unspecified	Laryngitis	2	No
Infections and infestations	Infections - pathogen unspecified	Localised infection	1	No
Infections and infestations	Infections - pathogen unspecified	Lung infection	1	No
Infections and infestations	Infections - pathogen unspecified	Lymph node abscess	1	No
Infections and infestations	Infections - pathogen unspecified	Mastoiditis	3	No
Infections and infestations	Infections - pathogen unspecified	Meningitis	14	Yes
Infections and infestations	Infections - pathogen unspecified	Meningitis aseptic	2	Yes
Infections and infestations	Infections - pathogen unspecified	Nasopharyngitis	21	No
Infections and infestations	Infections - pathogen unspecified	Nasopharyngitis	2	Yes
Infections and infestations	Infections - pathogen unspecified	Necrotising fasciitis	1	Yes
Infections and infestations	Infections - pathogen unspecified	Orchitis	1	No
Infections and infestations	Infections - pathogen unspecified	Osteomyelitis	4	Yes
Infections and infestations	Infections - pathogen unspecified	Otitis media	15	No
Infections and infestations	Infections - pathogen unspecified	Otitis media	1	Yes
Infections and infestations	Infections - pathogen unspecified	Otitis media acute	2	No
Infections and infestations	Infections - pathogen unspecified	Peritonsillar abscess	1	No
Infections and infestations	Infections - pathogen unspecified	Pharyngitis	13	No

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Infections and infestations	Infections - pathogen unspecified	Pharyngitis	1	Yes
Infections and infestations	Infections - pathogen unspecified	Pharyngotonsillitis	2	No
Infections and infestations	Infections - pathogen unspecified	Pneumonia	1	No
Infections and infestations	Infections - pathogen unspecified	Pneumonia	27	Yes
Infections and infestations	Infections - pathogen unspecified	Pneumonia primary atypical	1	Yes
Infections and infestations	Infections - pathogen unspecified	Pseudocroup	2	No
Infections and infestations	Infections - pathogen unspecified	Purulence	3	No
Infections and infestations	Infections - pathogen unspecified	Pyelonephritis	6	Yes
Infections and infestations	Infections - pathogen unspecified	Pyelonephritis acute	1	Yes
Infections and infestations	Infections - pathogen unspecified	Rash pustular	5	No
Infections and infestations	Infections - pathogen unspecified	Respiratory tract infection	13	No
Infections and infestations	Infections - pathogen unspecified	Rhinitis	37	No
Infections and infestations	Infections - pathogen unspecified	Sepsis	33	Yes
Infections and infestations	Infections - pathogen unspecified	Sepsis syndrome	2	No
Infections and infestations	Infections - pathogen unspecified	Septic shock	1	Yes
Infections and infestations	Infections - pathogen unspecified	Sinusitis	1	No
Infections and infestations	Infections - pathogen unspecified	Skin infection	1	No
Infections and infestations	Infections - pathogen unspecified	Soft tissue infection	6	No
Infections and infestations	Infections - pathogen unspecified	Soft tissue infection	1	Yes
Infections and infestations	Infections - pathogen unspecified	Sputum purulent	1	No
Infections and infestations	Infections - pathogen unspecified	Subcutaneous abscess	1	No
Infections and infestations	Infections - pathogen unspecified	Subdural empyema	1	No
Infections and infestations	Infections - pathogen unspecified	Superinfection	4	No
Infections and infestations	Infections - pathogen unspecified	Tonsillitis	7	No
Infections and infestations	Infections - pathogen unspecified	Tonsillitis	1	Yes
Infections and infestations	Infections - pathogen unspecified	Tracheitis	2	No
Infections and infestations	Infections - pathogen unspecified	Upper respiratory tract infection	35	No
Infections and infestations	Infections - pathogen unspecified	Upper respiratory tract infection	2	Yes
Infections and infestations	Infections - pathogen unspecified	Urinary tract infection	6	No

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Infections and infestations	Infections - pathogen unspecified	Urinary tract infection	1	Yes
Infections and infestations	Infections - pathogen unspecified	Vaccination site abscess	2	Yes
Infections and infestations	Infections - pathogen unspecified	Vaccination site infection	1	No
Infections and infestations	Infections - pathogen unspecified	Viraemia	1	Yes
Infections and infestations	Infections - pathogen unspecified	Wound infection	1	No
Infections and infestations	Viral infectious disorders	Adenovirus infection	1	No
Infections and infestations	Viral infectious disorders	Bronchiolitis	7	No
Infections and infestations	Viral infectious disorders	Coxsackie viral infection	1	No
Infections and infestations	Viral infectious disorders	Croup infectious	2	No
Infections and infestations	Viral infectious disorders	Cytomegalovirus infection	3	No
Infections and infestations	Viral infectious disorders	Cytomegalovirus infection	1	Yes
Infections and infestations	Viral infectious disorders	Eczema herpeticum	1	No
Infections and infestations	Viral infectious disorders	Encephalitis herpes	2	Yes
Infections and infestations	Viral infectious disorders	Encephalitis viral	1	Yes
Infections and infestations	Viral infectious disorders	Enterovirus infection	1	No
Infections and infestations	Viral infectious disorders	Epstein-Barr virus infection	1	No
Infections and infestations	Viral infectious disorders	Exanthema subitum	4	No
Infections and infestations	Viral infectious disorders	Exanthema subitum	3	Yes
Infections and infestations	Viral infectious disorders	Gastroenteritis adenovirus	3	Yes
Infections and infestations	Viral infectious disorders	Gastroenteritis astroviral	1	Yes
Infections and infestations	Viral infectious disorders	Gastroenteritis norovirus	6	Yes
Infections and infestations	Viral infectious disorders	Gastroenteritis rotavirus	20	Yes
Infections and infestations	Viral infectious disorders	Gastroenteritis viral	3	Yes
Infections and infestations	Viral infectious disorders	Gianotti-Crosti syndrome	3	No
Infections and infestations	Viral infectious disorders	Gianotti-Crosti syndrome	1	Yes
Infections and infestations	Viral infectious disorders	H1N1 influenza	1	No
Infections and infestations	Viral infectious disorders	Hepatitis B	1	No
Infections and infestations	Viral infectious disorders	Herpes ophthalmic	1	No
Infections and infestations	Viral infectious disorders	Herpes simplex	2	No
Infections and infestations	Viral infectious disorders	Herpes zoster	1	No

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Infections and infestations	Viral infectious disorders	Human herpesvirus 6 infection	2	No
Infections and infestations	Viral infectious disorders	Influenza	2	No
Infections and infestations	Viral infectious disorders	Measles	1	No
Infections and infestations	Viral infectious disorders	Meningitis viral	4	Yes
Infections and infestations	Viral infectious disorders	Pneumonia respiratory syncytial viral	1	Yes
Infections and infestations	Viral infectious disorders	Pneumonia viral	1	Yes
Infections and infestations	Viral infectious disorders	Respiratory syncytial virus bronchiolitis	2	No
Infections and infestations	Viral infectious disorders	Respiratory syncytial virus infection	8	No
Infections and infestations	Viral infectious disorders	Respiratory tract infection viral	1	Yes
Infections and infestations	Viral infectious disorders	Rotavirus infection	5	No
Infections and infestations	Viral infectious disorders	Varicella	2	No
Infections and infestations	Viral infectious disorders	Viral infection	28	No
Infections and infestations	Viral infectious disorders	Viral infection	2	Yes
Infections and infestations	Viral infectious disorders	Viral pharyngitis	1	No
Infections and infestations	Viral infectious disorders	Viral rash	3	No
Infections and infestations	Viral infectious disorders	Viral upper respiratory tract infection	1	No
Injury, poisoning and procedural complications	Bone and joint injuries	Forearm fracture	1	Yes
Injury, poisoning and procedural complications	Bone and joint injuries	Joint dislocation	2	Yes
Injury, poisoning and procedural complications	Bone and joint injuries	Limb injury	1	No
Injury, poisoning and procedural complications	Bone and joint injuries	Skull fracture	1	Yes
Injury, poisoning and procedural complications	Chemical injury and poisoning	Carbon monoxide poisoning	1	No
Injury, poisoning and procedural complications	Chemical injury and poisoning	Poisoning	1	No
Injury, poisoning and procedural complications	Chemical injury and poisoning	Toxicity to various agents	1	No
Injury, poisoning and procedural complications	Injuries NEC	Arthropod bite	1	No

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Injury, poisoning and procedural complications	Injuries NEC	Child maltreatment syndrome	2	No
Injury, poisoning and procedural complications	Injuries NEC	Concussion	1	Yes
Injury, poisoning and procedural complications	Injuries NEC	Contusion	7	No
Injury, poisoning and procedural complications	Injuries NEC	Craniocerebral injury	1	Yes
Injury, poisoning and procedural complications	Injuries NEC	Eschar	1	No
Injury, poisoning and procedural complications	Injuries NEC	Excoriation	1	No
Injury, poisoning and procedural complications	Injuries NEC	Fall	14	No
Injury, poisoning and procedural complications	Injuries NEC	Injury	1	No
Injury, poisoning and procedural complications	Injuries NEC	Subdural haematoma	2	Yes
Injury, poisoning and procedural complications	Medication errors	Drug administered to patient of inappropriate age	4	No
Injury, poisoning and procedural complications	Medication errors	Drug administration error	3	No
Injury, poisoning and procedural complications	Medication errors	Expired drug administered	1	No
Injury, poisoning and procedural complications	Medication errors	Inappropriate schedule of drug administration	9	No
Injury, poisoning and procedural complications	Medication errors	Incorrect route of drug administration	16	No
Injury, poisoning and procedural complications	Medication errors	Medication error	2	No
Injury, poisoning and procedural complications	Medication errors	Overdose	5	No
Injury, poisoning and procedural complications	Medication errors	Wrong drug administered	3	No
Injury, poisoning and procedural complications	Medication errors	Wrong technique in drug usage process	9	No
Injury, poisoning and procedural complications	Procedural related injuries and complications NEC	Seroma	1	No

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Injury, poisoning and procedural complications	Procedural related injuries and complications NEC	Vaccination complication	50	No
Injury, poisoning and procedural complications	Procedural related injuries and complications NEC	Vaccination complication	2	Yes
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Blood pressure decreased	2	No
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Blood pressure immeasurable	1	Yes
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Cardiac murmur	9	No
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Heart rate decreased	4	No
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Heart rate increased	9	No
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Heart sounds abnormal	1	No
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Peripheral pulse decreased	1	No
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Pulse absent	1	No
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Pulse absent	1	Yes
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Pulse pressure decreased	1	No
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Pulse pressure increased	1	No
Investigations	Enzyme investigations NEC	Blood alkaline phosphatase increased	1	No
Investigations	Enzyme investigations NEC	Blood creatine phosphokinase increased	1	No
Investigations	Enzyme investigations NEC	Blood lactate dehydrogenase increased	3	No
Investigations	Haematology investigations (incl blood groups)	Activated partial thromboplastin time prolonged	1	No
Investigations	Haematology investigations (incl blood groups)	Bleeding time prolonged	1	Yes
Investigations	Haematology investigations (incl blood groups)	Blood thromboplastin decreased	1	No
Investigations	Haematology investigations (incl blood groups)	Coombs test positive	1	No
Investigations	Haematology investigations (incl blood groups)	Haematocrit decreased	1	Yes

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Investigations	Haematology investigations (incl blood groups)	Haemoglobin decreased	4	No
Investigations	Haematology investigations (incl blood groups)	Haemoglobin decreased	1	Yes
Investigations	Haematology investigations (incl blood groups)	Lymphocyte count increased	1	No
Investigations	Haematology investigations (incl blood groups)	Neutrophil toxic granulation present	1	No
Investigations	Haematology investigations (incl blood groups)	Platelet count abnormal	2	No
Investigations	Haematology investigations (incl blood groups)	Platelet count decreased	5	No
Investigations	Haematology investigations (incl blood groups)	Platelet count increased	2	No
Investigations	Haematology investigations (incl blood groups)	Prothrombin time prolonged	1	No
Investigations	Haematology investigations (incl blood groups)	Red blood cell count increased	1	No
Investigations	Haematology investigations (incl blood groups)	Red blood cell sedimentation rate increased	2	No
Investigations	Haematology investigations (incl blood groups)	Shift to the left	1	No
Investigations	Haematology investigations (incl blood groups)	White blood cell count decreased	1	No
Investigations	Haematology investigations (incl blood groups)	White blood cell count increased	5	No
Investigations	Haematology investigations (incl blood groups)	White blood cell count increased	1	Yes
Investigations	Hepatobiliary investigations	Alanine aminotransferase increased	10	Yes
Investigations	Hepatobiliary investigations	Ammonia increased	2	No
Investigations	Hepatobiliary investigations	Aspartate aminotransferase increased	9	Yes
Investigations	Hepatobiliary investigations	Blood bilirubin increased	1	Yes
Investigations	Hepatobiliary investigations	Hepatic enzyme increased	5	Yes
Investigations	Hepatobiliary investigations	Liver function test abnormal	1	Yes
Investigations	Hepatobiliary investigations	Transaminases increased	17	Yes
Investigations	Immunology and allergy investigations	Autoantibody positive	1	No
Investigations	Immunology and allergy investigations	Blood immunoglobulin A increased	1	Yes
Investigations	Immunology and allergy investigations	Blood immunoglobulin E increased	1	No
Investigations	Immunology and allergy investigations	Blood immunoglobulin M increased	1	No

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Investigations	Immunology and allergy investigations	Blood immunoglobulin M increased	1	Yes
Investigations	Lipid analyses	Carnitine decreased	1	No
Investigations	Metabolic, nutritional and blood gas investigations	Blood glucose increased	1	No
Investigations	Metabolic, nutritional and blood gas investigations	Blood lactic acid increased	2	No
Investigations	Metabolic, nutritional and blood gas investigations	Blood pH decreased	1	No
Investigations	Metabolic, nutritional and blood gas investigations	Oxygen saturation decreased	34	No
Investigations	Microbiology and serology investigations	Adenovirus test positive	1	No
Investigations	Microbiology and serology investigations	Bacterial test positive	1	No
Investigations	Microbiology and serology investigations	Bordetella test negative	2	No
Investigations	Microbiology and serology investigations	Bordetella test positive	2	No
Investigations	Microbiology and serology investigations	Cytomegalovirus test positive	1	No
Investigations	Microbiology and serology investigations	Hepatitis B antibody negative	2	No
Investigations	Microbiology and serology investigations	Hepatitis B antibody positive	1	No
Investigations	Microbiology and serology investigations	Hepatitis B surface antigen positive	1	No
Investigations	Microbiology and serology investigations	Mycoplasma test positive	1	No
Investigations	Microbiology and serology investigations	Rotavirus test positive	3	No
Investigations	Microbiology and serology investigations	Staphylococcus test positive	1	No
Investigations	Microbiology and serology investigations	Viral test positive	5	No
Investigations	Neurological, special senses and psychiatric investigations	Electroencephalogram abnormal	8	No
Investigations	Neurological, special senses and psychiatric investigations	Nerve stimulation test abnormal	4	No
Investigations	Neurological, special senses and psychiatric investigations	Otoacoustic emissions test abnormal	1	No
Investigations	Neurological, special senses and psychiatric investigations	Reflex test normal	1	No
Investigations	Physical examination topics	Body height below normal	2	No
Investigations	Physical examination topics	Body mass index decreased	1	No
Investigations	Physical examination topics	Body temperature	1	No

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Investigations	Physical examination topics	Body temperature decreased	5	No
Investigations	Physical examination topics	Body temperature fluctuation	1	No
Investigations	Physical examination topics	Breath sounds abnormal	3	No
Investigations	Physical examination topics	Head circumference abnormal	1	No
Investigations	Physical examination topics	Liver palpable subcostal	1	No
Investigations	Physical examination topics	Lymph node palpable	2	No
Investigations	Physical examination topics	Neurological examination abnormal	1	No
Investigations	Physical examination topics	Respiratory rate decreased	3	No
Investigations	Physical examination topics	Respiratory rate increased	4	No
Investigations	Physical examination topics	Skin turgor decreased	1	No
Investigations	Physical examination topics	Weight decreased	15	No
Investigations	Protein and chemistry analyses NEC	C-reactive protein increased	28	No
Investigations	Protein and chemistry analyses NEC	C-reactive protein increased	2	Yes
Investigations	Protein and chemistry analyses NEC	Inflammatory marker increased	2	No
Investigations	Protein and chemistry analyses NEC	Protein total abnormal	1	No
Investigations	Protein and chemistry analyses NEC	Protein total increased	1	No
Investigations	Renal and urinary tract investigations and urinalyses	Glucose urine present	1	No
Investigations	Renal and urinary tract investigations and urinalyses	Urine output decreased	2	No
Investigations	Renal and urinary tract investigations and urinalyses	White blood cells urine positive	1	No
Investigations	Toxicology and therapeutic drug monitoring	Anticonvulsant drug level above therapeutic	1	No
Investigations	Water, electrolyte and mineral investigations	Blood iron decreased	1	No
Investigations	Water, electrolyte and mineral investigations	Blood osmolarity increased	1	No
Investigations	Water, electrolyte and mineral investigations	Blood sodium decreased	1	No
Investigations	Water, electrolyte and mineral investigations	Serum ferritin increased	1	No
Metabolism and nutrition disorders	Acid-base disorders	Acidosis	4	No

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Metabolism and nutrition disorders	Acid-base disorders	Acidosis	3	Yes
Metabolism and nutrition disorders	Acid-base disorders	Alkalosis	1	No
Metabolism and nutrition disorders	Acid-base disorders	Ketoacidosis	1	Yes
Metabolism and nutrition disorders	Acid-base disorders	Ketosis	1	No
Metabolism and nutrition disorders	Acid-base disorders	Lactic acidosis	2	Yes
Metabolism and nutrition disorders	Acid-base disorders	Metabolic acidosis	4	Yes
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Appetite disorder	2	No
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Decreased appetite	5	No
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Decreased appetite	3	Yes
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Failure to thrive	2	Yes
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Feeding disorder neonatal	4	No
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Feeding disorder of infancy or early childhood	5	No
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Increased appetite	2	No
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Malnutrition	2	No
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Underweight	4	No
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Weight gain poor	3	No
Metabolism and nutrition disorders	Bone, calcium, magnesium and phosphorus metabolism disorders	Tetany	2	Yes
Metabolism and nutrition disorders	Diabetic complications	Diabetic ketoacidosis	3	Yes
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Dehydration	25	No
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Dehydration	2	Yes
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Electrolyte imbalance	1	No
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Fluid intake reduced	22	No
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Hypernatraemia	1	No
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Hypokalaemia	6	Yes
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Hyponatraemia	6	No
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Hypovolaemia	1	No
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Oligodipsia	30	No
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Polydipsia	5	No

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Metabolism and nutrition disorders	Food intolerance syndromes	Cow's milk intolerance	1	No
Metabolism and nutrition disorders	Food intolerance syndromes	Disaccharide metabolism disorder	1	No
Metabolism and nutrition disorders	Food intolerance syndromes	Lactose intolerance	2	No
Metabolism and nutrition disorders	Glucose metabolism disorders (incl diabetes mellitus)	Hyperglycaemia	4	No
Metabolism and nutrition disorders	Glucose metabolism disorders (incl diabetes mellitus)	Hyperinsulinaemia	1	No
Metabolism and nutrition disorders	Glucose metabolism disorders (incl diabetes mellitus)	Hypoglycaemia	4	Yes
Metabolism and nutrition disorders	Glucose metabolism disorders (incl diabetes mellitus)	Type 1 diabetes mellitus	7	Yes
Metabolism and nutrition disorders	Iron and trace metal metabolism disorders	Haemosiderosis	1	No
Metabolism and nutrition disorders	Iron and trace metal metabolism disorders	Iodine deficiency	1	No
Metabolism and nutrition disorders	Iron and trace metal metabolism disorders	Iron deficiency	2	No
Metabolism and nutrition disorders	Lipid metabolism disorders	Hypercholesterolaemia	1	No
Metabolism and nutrition disorders	Lipid metabolism disorders	Hyperlipidaemia	1	No
Metabolism and nutrition disorders	Lipid metabolism disorders	Hypertriglyceridaemia	1	No
Metabolism and nutrition disorders	Metabolism disorders NEC	Enzyme abnormality	1	No
Metabolism and nutrition disorders	Metabolism disorders NEC	Metabolic disorder	3	No
Metabolism and nutrition disorders	Metabolism disorders NEC	Mitochondrial cytopathy	1	Yes
Metabolism and nutrition disorders	Protein and amino acid metabolism disorders NEC	Hyperammonaemia	2	No
Metabolism and nutrition disorders	Protein and amino acid metabolism disorders NEC	Hypoalbuminaemia	4	No
Metabolism and nutrition disorders	Purine and pyrimidine metabolism disorders	Hyperuricaemia	1	No
Metabolism and nutrition disorders	Vitamin related disorders	Vitamin B12 deficiency	2	No
Metabolism and nutrition disorders	Vitamin related disorders	Vitamin K deficiency	2	No
Musculoskeletal and connective tissue disorders	Bone disorders (excl congenital and fractures)	Bone disorder	1	No
Musculoskeletal and connective tissue disorders	Bone disorders (excl congenital and fractures)	Bone pain	1	No
Musculoskeletal and connective tissue disorders	Bone disorders (excl congenital and fractures)	Osteitis	1	Yes
Musculoskeletal and connective tissue disorders	Connective tissue disorders (excl congenital)	Myofascitis	1	No
Musculoskeletal and connective tissue disorders	Connective tissue disorders (excl congenital)	Myofascitis	1	Yes

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Musculoskeletal and connective tissue disorders	Joint disorders	Arthralgia	3	No
Musculoskeletal and connective tissue disorders	Joint disorders	Arthritis	3	No
Musculoskeletal and connective tissue disorders	Joint disorders	Arthritis	1	Yes
Musculoskeletal and connective tissue disorders	Joint disorders	Arthropathy	1	No
Musculoskeletal and connective tissue disorders	Joint disorders	Joint contracture	1	No
Musculoskeletal and connective tissue disorders	Joint disorders	Joint hyperextension	5	No
Musculoskeletal and connective tissue disorders	Joint disorders	Joint range of motion decreased	1	No
Musculoskeletal and connective tissue disorders	Joint disorders	Joint swelling	5	No
Musculoskeletal and connective tissue disorders	Joint disorders	Juvenile arthritis	1	Yes
Musculoskeletal and connective tissue disorders	Joint disorders	Polyarthritis	1	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Floppy infant	1	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Hypotonia neonatal	4	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Muscle disorder	3	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Muscle hypertrophy	2	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Muscle rigidity	6	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Muscle rigidity	2	Yes
Musculoskeletal and connective tissue disorders	Muscle disorders	Muscle spasms	39	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Muscle spasms	1	Yes
Musculoskeletal and connective tissue disorders	Muscle disorders	Muscle tightness	1	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Muscle twitching	36	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Muscle twitching	1	Yes

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Musculoskeletal and connective tissue disorders	Muscle disorders	Muscular weakness	13	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Myalgia	4	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Myopathy	1	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Myosclerosis	2	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Myositis	4	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Myositis	1	Yes
Musculoskeletal and connective tissue disorders	Muscle disorders	Nuchal rigidity	4	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Rhabdomyolysis	1	Yes
Musculoskeletal and connective tissue disorders	Muscle disorders	Torticollis	3	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Trismus	2	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)	Delayed fontanelle closure	1	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)	Facial asymmetry	1	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)	Foot deformity	1	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)	Hip deformity	1	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)	Limb asymmetry	1	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)	Lordosis	1	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Groin pain	1	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Growth retardation	1	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Mastication disorder	1	No

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Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Mobility decreased	9	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Muscle contracture	2	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Musculoskeletal pain	1	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Musculoskeletal stiffness	39	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Pain in extremity	25	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Pain in extremity	1	Yes
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Posture abnormal	8	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Soft tissue disorder	2	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Soft tissue disorder	1	Yes
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Soft tissue haemorrhage	1	Yes
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Soft tissue necrosis	2	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Cutaneous neoplasms benign	Melanocytic naevus	1	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Haematopoietic neoplasms (excl leukaemias and lymphomas)	Histiocytosis haematophagic	1	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Leukaemias	B precursor type acute leukaemia	1	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Leukaemias	Myelodysplastic syndrome	1	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Lymphomas NEC	Lymphoma	1	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Miscellaneous and site unspecified neoplasms benign	Haemangioma	3	No
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Nervous system neoplasms benign	Cerebral hygroma	2	No

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Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Nervous system neoplasms malignant and unspecified NEC	Neuroblastoma	2	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Nervous system neoplasms malignant and unspecified NEC	Optic nerve glioma	1	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Skeletal neoplasms malignant and unspecified	Ewing's sarcoma	1	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Skin neoplasms malignant and unspecified	Neoplasm skin	1	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Soft tissue neoplasms benign	Lymphangioma	1	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Soft tissue neoplasms malignant and unspecified (excl sarcomas)	Soft tissue neoplasm	2	Yes
Nervous system disorders	Central nervous system infections and inflammations	Central nervous system inflammation	1	No
Nervous system disorders	Central nervous system infections and inflammations	Encephalitis	1	No
Nervous system disorders	Central nervous system infections and inflammations	Encephalitis	19	Yes
Nervous system disorders	Central nervous system infections and inflammations	Encephalitis haemorrhagic	1	Yes
Nervous system disorders	Central nervous system infections and inflammations	Encephalomyelitis	1	Yes
Nervous system disorders	Central nervous system infections and inflammations	Myelitis transverse	1	Yes
Nervous system disorders	Central nervous system vascular disorders	Blood brain barrier defect	1	Yes
Nervous system disorders	Central nervous system vascular disorders	Brain stem thrombosis	1	Yes
Nervous system disorders	Central nervous system vascular disorders	Cerebral haemorrhage	5	Yes
Nervous system disorders	Central nervous system vascular disorders	Cerebral infarction	1	Yes
Nervous system disorders	Central nervous system vascular disorders	Cerebral ischaemia	4	Yes
Nervous system disorders	Central nervous system vascular disorders	Cerebrovascular accident	1	Yes
Nervous system disorders	Central nervous system vascular disorders	Cerebrovascular disorder	1	Yes
Nervous system disorders	Central nervous system vascular disorders	Subarachnoid haemorrhage	3	Yes
Nervous system disorders	Central nervous system vascular disorders	Thalamus haemorrhage	1	Yes
Nervous system disorders	Central nervous system vascular disorders	Vasculitis cerebral	1	Yes
Nervous system disorders	Cranial nerve disorders (excl neoplasms)	Facial paresis	10	Yes
Nervous system disorders	Cranial nerve disorders (excl neoplasms)	Facial spasm	1	No

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Nervous system disorders	Cranial nerve disorders (excl neoplasms)	Paresis cranial nerve	1	No
Nervous system disorders	Cranial nerve disorders (excl neoplasms)	Tongue paralysis	2	Yes
Nervous system disorders	Cranial nerve disorders (excl neoplasms)	VIIth nerve paralysis	2	Yes
Nervous system disorders	Cranial nerve disorders (excl neoplasms)	VIth nerve paralysis	4	Yes
Nervous system disorders	Demyelinating disorders	Acute disseminated encephalomyelitis	3	Yes
Nervous system disorders	Demyelinating disorders	Demyelination	5	Yes
Nervous system disorders	Encephalopathies	Encephalopathy	14	Yes
Nervous system disorders	Encephalopathies	Hypoxic-ischaemic encephalopathy	7	Yes
Nervous system disorders	Encephalopathies	Leukoencephalopathy	2	Yes
Nervous system disorders	Encephalopathies	Periventricular leukomalacia	2	Yes
Nervous system disorders	Headaches	Headache	3	No
Nervous system disorders	Increased intracranial pressure and hydrocephalus	Brain oedema	11	Yes
Nervous system disorders	Increased intracranial pressure and hydrocephalus	Hydrocephalus	5	Yes
Nervous system disorders	Increased intracranial pressure and hydrocephalus	Intracranial pressure increased	4	Yes
Nervous system disorders	Mental impairment disorders	Autism	1	No
Nervous system disorders	Mental impairment disorders	Autism	5	Yes
Nervous system disorders	Mental impairment disorders	Cognitive disorder	2	No
Nervous system disorders	Mental impairment disorders	Disturbance in attention	2	No
Nervous system disorders	Mental impairment disorders	Memory impairment	1	No
Nervous system disorders	Mental impairment disorders	Mental impairment	7	No
Nervous system disorders	Mental impairment disorders	Mental retardation	5	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Athetosis	1	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Bradykinesia	1	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Choreoathetosis	2	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Dyskinesia	46	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Dyskinesia	1	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Dystonia	3	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Dystonia	1	Yes

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Nervous system disorders	Movement disorders (incl parkinsonism)	Extrapyramidal disorder	3	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Head titubation	6	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Hemiparesis	8	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Hemiplegia	4	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Hypokinesia	13	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Hypokinesia	2	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Monoparesis	5	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Monoplegia	5	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Motor developmental delay	6	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Movement disorder	15	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Opisthotonus	20	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Opisthotonus	1	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Paralysis	3	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Paralysis flaccid	1	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Paraplegia	1	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Paresis	4	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Postictal paralysis	1	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Psychomotor hyperactivity	9	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Quadriparesis	4	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Tardive dyskinesia	1	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Tremor	55	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Tremor	3	Yes
Nervous system disorders	Neurological disorders NEC	Altered state of consciousness	15	Yes
Nervous system disorders	Neurological disorders NEC	Aphasia	3	Yes
Nervous system disorders	Neurological disorders NEC	Areflexia	8	No
Nervous system disorders	Neurological disorders NEC	Ataxia	5	No
Nervous system disorders	Neurological disorders NEC	Ataxia	1	Yes
Nervous system disorders	Neurological disorders NEC	Balance disorder	10	No
Nervous system disorders	Neurological disorders NEC	Cerebellar ataxia	2	No

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Nervous system disorders	Neurological disorders NEC	Cerebral disorder	5	No
Nervous system disorders	Neurological disorders NEC	Cerebral disorder	1	Yes
Nervous system disorders	Neurological disorders NEC	Clonus	21	No
Nervous system disorders	Neurological disorders NEC	Coma	7	Yes
Nervous system disorders	Neurological disorders NEC	Coordination abnormal	7	No
Nervous system disorders	Neurological disorders NEC	Coordination abnormal	1	Yes
Nervous system disorders	Neurological disorders NEC	Crying	24	No
Nervous system disorders	Neurological disorders NEC	Depressed level of consciousness	122	Yes
Nervous system disorders	Neurological disorders NEC	Dizziness	4	No
Nervous system disorders	Neurological disorders NEC	Drooling	11	No
Nervous system disorders	Neurological disorders NEC	Dysaesthesia	1	No
Nervous system disorders	Neurological disorders NEC	Dysstasia	2	No
Nervous system disorders	Neurological disorders NEC	Fontanelle bulging	10	No
Nervous system disorders	Neurological disorders NEC	Fontanelle bulging	1	Yes
Nervous system disorders	Neurological disorders NEC	Fontanelle depressed	2	No
Nervous system disorders	Neurological disorders NEC	Grimacing	1	No
Nervous system disorders	Neurological disorders NEC	Hyperaesthesia	18	No
Nervous system disorders	Neurological disorders NEC	Hyperreflexia	2	No
Nervous system disorders	Neurological disorders NEC	Hypoaesthesia	1	No
Nervous system disorders	Neurological disorders NEC	Hyporeflexia	3	No
Nervous system disorders	Neurological disorders NEC	Lethargy	16	No
Nervous system disorders	Neurological disorders NEC	Lethargy	1	Yes
Nervous system disorders	Neurological disorders NEC	Loss of consciousness	169	Yes
Nervous system disorders	Neurological disorders NEC	Meningism	5	No
Nervous system disorders	Neurological disorders NEC	Motor dysfunction	10	No
Nervous system disorders	Neurological disorders NEC	Motor dysfunction	1	Yes
Nervous system disorders	Neurological disorders NEC	Myoclonus	32	No
Nervous system disorders	Neurological disorders NEC	Myoclonus	2	Yes
Nervous system disorders	Neurological disorders NEC	Nerve degeneration	1	No

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Nervous system disorders	Neurological disorders NEC	Nervous system disorder	10	No
Nervous system disorders	Neurological disorders NEC	Neurodegenerative disorder	1	No
Nervous system disorders	Neurological disorders NEC	Neurological symptom	2	No
Nervous system disorders	Neurological disorders NEC	Neurotoxicity	1	Yes
Nervous system disorders	Neurological disorders NEC	Nystagmus	12	No
Nervous system disorders	Neurological disorders NEC	Pleocytosis	1	No
Nervous system disorders	Neurological disorders NEC	Poor sucking reflex	1	No
Nervous system disorders	Neurological disorders NEC	Postictal state	3	No
Nervous system disorders	Neurological disorders NEC	Presyncope	2	No
Nervous system disorders	Neurological disorders NEC	Presyncope	21	Yes
Nervous system disorders	Neurological disorders NEC	Psychomotor skills impaired	11	No
Nervous system disorders	Neurological disorders NEC	Reflexes abnormal	1	No
Nervous system disorders	Neurological disorders NEC	Sensory loss	1	No
Nervous system disorders	Neurological disorders NEC	Slow response to stimuli	109	Yes
Nervous system disorders	Neurological disorders NEC	Somnolence	4	No
Nervous system disorders	Neurological disorders NEC	Somnolence	2	Yes
Nervous system disorders	Neurological disorders NEC	Speech disorder	2	No
Nervous system disorders	Neurological disorders NEC	Speech disorder developmental	5	No
Nervous system disorders	Neurological disorders NEC	Stupor	1	Yes
Nervous system disorders	Neurological disorders NEC	Subdural effusion	3	No
Nervous system disorders	Neurological disorders NEC	Syncope	38	Yes
Nervous system disorders	Neurological disorders NEC	Unresponsive to stimuli	11	No
Nervous system disorders	Neurological disorders NEC	Unresponsive to stimuli	32	Yes
Nervous system disorders	Neuromuscular disorders	Autonomic nervous system imbalance	2	No
Nervous system disorders	Neuromuscular disorders	Cholinergic syndrome	2	No
Nervous system disorders	Neuromuscular disorders	Hypertonia	54	No
Nervous system disorders	Neuromuscular disorders	Hypertonia	2	Yes
Nervous system disorders	Neuromuscular disorders	Hypotonia	427	No
Nervous system disorders	Neuromuscular disorders	Hypotonia	5	Yes

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Nervous system disorders	Neuromuscular disorders	Hypotonic-hyporesponsive episode	184	No
Nervous system disorders	Neuromuscular disorders	Hypotonic-hyporesponsive episode	5	Yes
Nervous system disorders	Neuromuscular disorders	Muscle contractions involuntary	6	No
Nervous system disorders	Neuromuscular disorders	Muscle spasticity	1	No
Nervous system disorders	Neuromuscular disorders	Neuromyopathy	1	No
Nervous system disorders	Neuromuscular disorders	Sensorimotor disorder	1	No
Nervous system disorders	Peripheral neuropathies	Demyelinating polyneuropathy	1	Yes
Nervous system disorders	Peripheral neuropathies	Guillain-Barre syndrome	5	Yes
Nervous system disorders	Peripheral neuropathies	Neuropathy peripheral	1	No
Nervous system disorders	Seizures (incl subtypes)	Atonic seizures	6	Yes
Nervous system disorders	Seizures (incl subtypes)	Clonic convulsion	8	Yes
Nervous system disorders	Seizures (incl subtypes)	Complex partial seizures	2	Yes
Nervous system disorders	Seizures (incl subtypes)	Convulsion	307	Yes
Nervous system disorders	Seizures (incl subtypes)	Convulsions local	1	Yes
Nervous system disorders	Seizures (incl subtypes)	Epilepsy	68	Yes
Nervous system disorders	Seizures (incl subtypes)	Febrile convulsion	244	Yes
Nervous system disorders	Seizures (incl subtypes)	Grand mal convulsion	74	Yes
Nervous system disorders	Seizures (incl subtypes)	Infantile spasms	46	No
Nervous system disorders	Seizures (incl subtypes)	Infantile spasms	15	Yes
Nervous system disorders	Seizures (incl subtypes)	Juvenile myoclonic epilepsy	3	Yes
Nervous system disorders	Seizures (incl subtypes)	Lennox-Gastaut syndrome	1	Yes
Nervous system disorders	Seizures (incl subtypes)	Myoclonic epilepsy	4	Yes
Nervous system disorders	Seizures (incl subtypes)	Partial seizures	1	No
Nervous system disorders	Seizures (incl subtypes)	Partial seizures	26	Yes
Nervous system disorders	Seizures (incl subtypes)	Petit mal epilepsy	14	Yes
Nervous system disorders	Seizures (incl subtypes)	Post-traumatic epilepsy	1	Yes
Nervous system disorders	Seizures (incl subtypes)	Seizure anoxic	1	Yes
Nervous system disorders	Seizures (incl subtypes)	Seizure like phenomena	5	Yes

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Nervous system disorders	Seizures (incl subtypes)	Status epilepticus	15	Yes
Nervous system disorders	Seizures (incl subtypes)	Tonic clonic movements	4	No
Nervous system disorders	Seizures (incl subtypes)	Tonic convulsion	11	Yes
Nervous system disorders	Sleep disturbances (incl subtypes)	Cataplexy	1	Yes
Nervous system disorders	Sleep disturbances (incl subtypes)	Circadian rhythm sleep disorder	3	No
Nervous system disorders	Sleep disturbances (incl subtypes)	Hypersomnia	13	No
Nervous system disorders	Sleep disturbances (incl subtypes)	Poor quality sleep	5	No
Nervous system disorders	Sleep disturbances (incl subtypes)	Sleep phase rhythm disturbance	1	No
Nervous system disorders	Spinal cord and nerve root disorders	Nerve root lesion	1	No
Nervous system disorders	Spinal cord and nerve root disorders	Radiculitis brachial	2	No
Nervous system disorders	Spinal cord and nerve root disorders	Spinal cord compression	1	No
Nervous system disorders	Spinal cord and nerve root disorders	Tethered cord syndrome	1	Yes
Nervous system disorders	Structural brain disorders	Brain injury	2	Yes
Nervous system disorders	Structural brain disorders	Cerebral atrophy	1	No
Nervous system disorders	Structural brain disorders	Cerebral atrophy	6	Yes
Nervous system disorders	Structural brain disorders	Cerebral ventricle dilatation	1	Yes
Nervous system disorders	Structural brain disorders	Subdural hygroma	2	No
Psychiatric disorders	Anxiety disorders and symptoms	Agitation	34	No
Psychiatric disorders	Anxiety disorders and symptoms	Agitation neonatal	1	No
Psychiatric disorders	Anxiety disorders and symptoms	Anxiety	13	No
Psychiatric disorders	Anxiety disorders and symptoms	Fear	3	No
Psychiatric disorders	Anxiety disorders and symptoms	Tension	2	No
Psychiatric disorders	Changes in physical activity	Decreased activity	8	No
Psychiatric disorders	Changes in physical activity	Restlessness	5	No
Psychiatric disorders	Changes in physical activity	Stereotypy	1	No
Psychiatric disorders	Changes in physical activity	Stereotypy	1	Yes
Psychiatric disorders	Changes in physical activity	Tic	1	No
Psychiatric disorders	Cognitive and attention disorders and disturbances	Attention deficit/hyperactivity disorder	1	No

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Psychiatric disorders	Cognitive and attention disorders and disturbances	Daydreaming	3	No
Psychiatric disorders	Communication disorders and disturbances	Communication disorder	1	No
Psychiatric disorders	Communication disorders and disturbances	Dysphemia	1	Yes
Psychiatric disorders	Communication disorders and disturbances	Mutism	1	No
Psychiatric disorders	Communication disorders and disturbances	Phonological disorder	1	No
Psychiatric disorders	Communication disorders and disturbances	Screaming	37	No
Psychiatric disorders	Deliria (incl confusion)	Confusional state	1	No
Psychiatric disorders	Deliria (incl confusion)	Delirium	1	Yes
Psychiatric disorders	Deliria (incl confusion)	Disorientation	6	No
Psychiatric disorders	Depressed mood disorders and disturbances	Morose	2	No
Psychiatric disorders	Depressed mood disorders and disturbances	Psychomotor retardation	7	No
Psychiatric disorders	Developmental disorders NEC	Autism spectrum disorder	1	No
Psychiatric disorders	Dissociative disorders	Dissociation	1	No
Psychiatric disorders	Disturbances in thinking and perception	Illusion	1	No
Psychiatric disorders	Disturbances in thinking and perception	Illusion	1	Yes
Psychiatric disorders	Eating disorders and disturbances	Eating disorder	5	No
Psychiatric disorders	Eating disorders and disturbances	Eating disorder	1	Yes
Psychiatric disorders	Eating disorders and disturbances	Food aversion	4	No
Psychiatric disorders	Eating disorders and disturbances	Food aversion	1	Yes
Psychiatric disorders	Eating disorders and disturbances	Merycism	1	No
Psychiatric disorders	Mood disorders and disturbances NEC	Apathy	67	No
Psychiatric disorders	Mood disorders and disturbances NEC	Apathy	3	Yes
Psychiatric disorders	Mood disorders and disturbances NEC	Emotional distress	1	No
Psychiatric disorders	Mood disorders and disturbances NEC	Inappropriate affect	1	No
Psychiatric disorders	Mood disorders and disturbances NEC	Listless	11	No
Psychiatric disorders	Mood disorders and disturbances NEC	Moaning	13	No
Psychiatric disorders	Mood disorders and disturbances NEC	Moaning	1	Yes
Psychiatric disorders	Mood disorders and disturbances NEC	Mood altered	3	No
Psychiatric disorders	Personality disorders and disturbances in behaviour	Aggression	1	No

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Psychiatric disorders	Personality disorders and disturbances in behaviour	Aggression	4	Yes
Psychiatric disorders	Personality disorders and disturbances in behaviour	Antisocial behaviour	2	No
Psychiatric disorders	Personality disorders and disturbances in behaviour	Impatience	1	No
Psychiatric disorders	Personality disorders and disturbances in behaviour	Indifference	3	No
Psychiatric disorders	Personality disorders and disturbances in behaviour	Personality change	5	No
Psychiatric disorders	Personality disorders and disturbances in behaviour	Personality disorder	1	No
Psychiatric disorders	Personality disorders and disturbances in behaviour	Social avoidant behaviour	7	No
Psychiatric disorders	Psychiatric and behavioural symptoms NEC	Abnormal behaviour	15	No
Psychiatric disorders	Psychiatric and behavioural symptoms NEC	Abnormal behaviour	1	Yes
Psychiatric disorders	Psychiatric and behavioural symptoms NEC	Breath holding	10	No
Psychiatric disorders	Psychiatric and behavioural symptoms NEC	Breath holding	3	Yes
Psychiatric disorders	Psychiatric and behavioural symptoms NEC	Decreased eye contact	5	No
Psychiatric disorders	Psychiatric and behavioural symptoms NEC	Regressive behaviour	1	No
Psychiatric disorders	Psychiatric and behavioural symptoms NEC	Staring	98	No
Psychiatric disorders	Psychiatric and behavioural symptoms NEC	Staring	1	Yes
Psychiatric disorders	Psychiatric disorders NEC	Mental disorder	1	No
Psychiatric disorders	Schizophrenia and other psychotic disorders	Psychotic disorder	1	Yes
Psychiatric disorders	Sexual dysfunctions, disturbances and gender identity disorders	Excessive masturbation	1	No
Psychiatric disorders	Sleep disorders and disturbances	Initial insomnia	1	No
Psychiatric disorders	Sleep disorders and disturbances	Insomnia	26	No
Psychiatric disorders	Sleep disorders and disturbances	Middle insomnia	1	No
Psychiatric disorders	Sleep disorders and disturbances	Sleep disorder	19	No
Psychiatric disorders	Suicidal and self-injurious behaviours NEC	Intentional self-injury	1	Yes
Renal and urinary disorders	Genitourinary tract disorders NEC	Urinary tract disorder	1	No
Renal and urinary disorders	Nephropathies	Nephritic syndrome	1	No
Renal and urinary disorders	Nephropathies	Nephrotic syndrome	2	No
Renal and urinary disorders	Nephropathies	Nephrotic syndrome	1	Yes
Renal and urinary disorders	Renal disorders (excl nephropathies)	Anuria	1	Yes
Renal and urinary disorders	Renal disorders (excl nephropathies)	Hydronephrosis	1	No

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Renal and urinary disorders	Renal disorders (excl nephropathies)	Oliguria	5	No
Renal and urinary disorders	Renal disorders (excl nephropathies)	Pyelocaliectasis	2	No
Renal and urinary disorders	Renal disorders (excl nephropathies)	Renal failure	1	No
Renal and urinary disorders	Renal disorders (excl nephropathies)	Renal failure	2	Yes
Renal and urinary disorders	Renal disorders (excl nephropathies)	Renal failure acute	3	Yes
Renal and urinary disorders	Renal disorders (excl nephropathies)	Renal hypertension	1	No
Renal and urinary disorders	Renal disorders (excl nephropathies)	Renal impairment	2	No
Renal and urinary disorders	Ureteric disorders	Ureteric stenosis	1	No
Renal and urinary disorders	Urinary tract signs and symptoms	Chromaturia	1	No
Renal and urinary disorders	Urinary tract signs and symptoms	Enuresis	2	No
Renal and urinary disorders	Urinary tract signs and symptoms	Haematuria	3	No
Renal and urinary disorders	Urinary tract signs and symptoms	Incontinence	1	Yes
Renal and urinary disorders	Urinary tract signs and symptoms	Leukocyturia	1	No
Renal and urinary disorders	Urinary tract signs and symptoms	Polyuria	3	No
Renal and urinary disorders	Urinary tract signs and symptoms	Proteinuria	1	No
Renal and urinary disorders	Urinary tract signs and symptoms	Urinary incontinence	1	No
Reproductive system and breast disorders	Breast disorders	Lactation disorder	1	No
Reproductive system and breast disorders	Male reproductive tract infections and inflammations	Balanitis	1	No
Reproductive system and breast disorders	Penile and scrotal disorders (excl infections and inflammations)	Acquired phimosis	1	Yes
Reproductive system and breast disorders	Reproductive tract disorders NEC	Oedema genital	2	No
Reproductive system and breast disorders	Testicular and epididymal disorders	Testicular retraction	1	No
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Asthma	1	No
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Asthma	8	Yes
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Bronchial hyperreactivity	1	No
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Bronchial hyperreactivity	1	Yes

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Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Bronchial obstruction	1	No
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Bronchitis chronic	1	No
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Bronchospasm	11	No
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Obstructive airways disorder	2	No
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Obstructive airways disorder	2	Yes
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Wheezing	4	No
Respiratory, thoracic and mediastinal disorders	Lower respiratory tract disorders (excl obstruction and infection)	Acute respiratory distress syndrome	1	Yes
Respiratory, thoracic and mediastinal disorders	Lower respiratory tract disorders (excl obstruction and infection)	Atelectasis	1	No
Respiratory, thoracic and mediastinal disorders	Lower respiratory tract disorders (excl obstruction and infection)	Atelectasis	1	Yes
Respiratory, thoracic and mediastinal disorders	Lower respiratory tract disorders (excl obstruction and infection)	Emphysema	3	No
Respiratory, thoracic and mediastinal disorders	Lower respiratory tract disorders (excl obstruction and infection)	Interstitial lung disease	3	Yes
Respiratory, thoracic and mediastinal disorders	Lower respiratory tract disorders (excl obstruction and infection)	Lung infiltration	1	No
Respiratory, thoracic and mediastinal disorders	Lower respiratory tract disorders (excl obstruction and infection)	Pneumonia aspiration	7	Yes
Respiratory, thoracic and mediastinal disorders	Lower respiratory tract disorders (excl obstruction and infection)	Pneumonitis	1	Yes
Respiratory, thoracic and mediastinal disorders	Lower respiratory tract disorders (excl obstruction and infection)	Pulmonary oedema	5	Yes
Respiratory, thoracic and mediastinal disorders	Neonatal respiratory disorders	Apparent life threatening event	2	No
Respiratory, thoracic and mediastinal disorders	Neonatal respiratory disorders	Apparent life threatening event	33	Yes
Respiratory, thoracic and mediastinal disorders	Neonatal respiratory disorders	Infantile apnoeic attack	1	Yes
Respiratory, thoracic and mediastinal disorders	Pleural disorders	Haemothorax	1	No
Respiratory, thoracic and mediastinal disorders	Pleural disorders	Pleural effusion	1	Yes

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Respiratory, thoracic and mediastinal disorders	Pulmonary vascular disorders	Pulmonary embolism	1	Yes
Respiratory, thoracic and mediastinal disorders	Pulmonary vascular disorders	Pulmonary hypertension	1	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Acute respiratory failure	2	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Apnoea	127	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Apnoeic attack	10	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Apnoeic attack	2	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Asphyxia	4	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Asphyxia	2	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Aspiration	10	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Aspiration	2	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Bradypnoea	2	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Choking	7	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Choking sensation	3	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Cough	72	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Cough	2	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Cyanosis central	2	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Cyanosis central	1	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Dry throat	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Dysphonia	5	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Dyspnoea	73	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Dyspnoea	2	Yes

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Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Hiccups	2	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Hyperventilation	1	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Hypopnoea	4	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Hypoventilation	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Hypoventilation	2	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Hypoxia	4	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Increased upper airway secretion	3	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Kussmaul respiration	1	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Lung disorder	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Nasal obstruction	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Oropharyngeal pain	2	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Productive cough	6	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Rales	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiration abnormal	30	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory acidosis	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory alkalosis	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory arrest	34	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory depression	1	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory disorder	28	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory disorder	1	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory distress	4	Yes

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Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory failure	8	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory tract congestion	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory tract inflammation	5	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Rhinorrhoea	5	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Sleep apnoea syndrome	3	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Sleep apnoea syndrome	1	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Sneezing	2	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Snoring	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Sputum increased	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Suffocation feeling	2	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Tachypnoea	11	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Tachypnoea	1	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Upper respiratory tract congestion	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Upper respiratory tract inflammation	3	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Use of accessory respiratory muscles	2	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Yawning	1	No
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract disorders (excl infections)	Epistaxis	4	No
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract disorders (excl infections)	Laryngeal oedema	1	Yes
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract disorders (excl infections)	Laryngospasm	3	No
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract disorders (excl infections)	Nasal congestion	1	No

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Respiratory, thoracic and mediastinal disorders	Upper respiratory tract disorders (excl infections)	Pharyngeal disorder	2	No
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract disorders (excl infections)	Pharyngeal erythema	32	No
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract disorders (excl infections)	Rhinitis allergic	1	No
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract disorders (excl infections)	Stridor	7	Yes
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract disorders (excl infections)	Tonsillar disorder	1	No
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract disorders (excl infections)	Tonsillar hypertrophy	3	No
Skin and subcutaneous tissue disorders	Angioedema and urticaria	Circumoral oedema	1	No
Skin and subcutaneous tissue disorders	Angioedema and urticaria	Urticaria papular	2	No
Skin and subcutaneous tissue disorders	Angioedema and urticaria	Urticaria pressure	1	No
Skin and subcutaneous tissue disorders	Angioedema and urticaria	Urticaria thermal	1	No
Skin and subcutaneous tissue disorders	Cornification and dystrophic skin disorders	Hyperkeratosis	1	No
Skin and subcutaneous tissue disorders	Cornification and dystrophic skin disorders	Skin hypertrophy	1	No
Skin and subcutaneous tissue disorders	Cutaneous neoplasms benign	Dermal cyst	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Blister	16	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Blister	1	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Decubitus ulcer	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Dermatitis	3	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Dermatitis atopic	8	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Dermatitis atopic	1	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Dermatitis bullous	6	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Dermatitis contact	1	Yes

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Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Dermatitis diaper	7	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Dermatitis exfoliative	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Drug eruption	2	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Dry skin	3	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Eczema	9	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Erythema	100	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Erythema	4	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Erythema multiforme	14	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Erythrosis	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Exfoliative rash	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Generalised erythema	4	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Granuloma skin	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Lichenification	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Lichen striatus	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Neurodermatitis	9	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Neurodermatitis	3	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Palmar erythema	2	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Papule	6	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Peau d'orange	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Pemphigoid	2	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Photosensitivity reaction	1	No

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Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Pruritus	14	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash	99	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash	2	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash erythematous	8	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash generalised	17	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash macular	19	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash maculo-papular	18	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash morbilliform	3	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash papular	7	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash pruritic	2	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash vesicular	2	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Scab	3	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Scab	1	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Scar	9	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Seborrhoeic dermatitis	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin chapped	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin discolouration	38	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin discolouration	1	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin disorder	6	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin exfoliation	7	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin induration	1	No

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Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin irritation	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin lesion	4	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin necrosis	2	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin odour abnormal	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin reaction	2	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin warm	17	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin warm	1	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Stevens-Johnson syndrome	1	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Swelling face	5	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Toxic skin eruption	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Yellow skin	5	Yes
Skin and subcutaneous tissue disorders	Pigmentation disorders	Melanodermia	1	No
Skin and subcutaneous tissue disorders	Pigmentation disorders	Schamberg's disease	1	No
Skin and subcutaneous tissue disorders	Pigmentation disorders	Skin depigmentation	1	No
Skin and subcutaneous tissue disorders	Skin and subcutaneous tissue disorders NEC	Erythema nodosum	3	No
Skin and subcutaneous tissue disorders	Skin and subcutaneous tissue disorders NEC	Lipoatrophy	1	Yes
Skin and subcutaneous tissue disorders	Skin and subcutaneous tissue disorders NEC	Palmar-plantar erythrodysaesthesia syndrome	1	No
Skin and subcutaneous tissue disorders	Skin and subcutaneous tissue disorders NEC	Skin ulcer	2	No
Skin and subcutaneous tissue disorders	Skin appendage conditions	Cold sweat	8	No
Skin and subcutaneous tissue disorders	Skin appendage conditions	Heat rash	1	No
Skin and subcutaneous tissue disorders	Skin appendage conditions	Hirsutism	1	No

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Skin and subcutaneous tissue disorders	Skin appendage conditions	Hyperhidrosis	37	No
Skin and subcutaneous tissue disorders	Skin appendage conditions	Hyperhidrosis	1	Yes
Skin and subcutaneous tissue disorders	Skin appendage conditions	Hypertrichosis	1	No
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Acute haemorrhagic oedema of infancy	1	Yes
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Cutaneous vasculitis	1	Yes
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Ecchymosis	15	No
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Ecchymosis	1	Yes
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Henoch-Schonlein purpura	7	Yes
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Increased tendency to bruise	1	No
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Leukocytoclastic vasculitis	2	Yes
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Livedo reticularis	9	No
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Lividity	16	No
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Petechiae	96	No
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Petechiae	4	Yes
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Purpura	21	No
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Purpura	1	Yes
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Skin haemorrhage	2	No
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Skin haemorrhage	1	Yes
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Skin oedema	1	No
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Vasculitic rash	1	Yes
Social circumstances	Lifestyle issues	Disability	1	Yes

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Social circumstances	Lifestyle issues	Immobile	3	No
Social circumstances	Lifestyle issues	Mentally late developer	1	No
Social circumstances	Lifestyle issues	Walking disability	1	No
Surgical and medical procedures	Gastrointestinal therapeutic procedures	Colectomy	1	No
Surgical and medical procedures	Gastrointestinal therapeutic procedures	Ileostomy	1	No
Surgical and medical procedures	Gastrointestinal therapeutic procedures	Small intestinal resection	1	No
Surgical and medical procedures	Haematological and lymphoid tissue therapeutic procedures	Haemostasis	2	No
Surgical and medical procedures	Male genital tract therapeutic procedures	Orchidectomy	1	Yes
Surgical and medical procedures	Nervous system, skull and spine therapeutic procedures	Neurosurgery	1	No
Surgical and medical procedures	Respiratory tract therapeutic procedures	Endotracheal intubation	1	No
Surgical and medical procedures	Respiratory tract therapeutic procedures	Mechanical ventilation	3	No
Surgical and medical procedures	Respiratory tract therapeutic procedures	Oxygen supplementation	2	No
Surgical and medical procedures	Skin and subcutaneous tissue therapeutic procedures	Skin lesion excision	1	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Abscess drainage	3	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Debridement	1	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Emergency care	1	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Enteral nutrition	1	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Hyperthermia therapy	1	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Light anaesthesia	1	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Macrophage activation	1	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Off label use	1	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Resuscitation	11	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Surgery	3	No
Vascular disorders	Aneurysms and artery dissections	Aneurysm	1	Yes
Vascular disorders	Arteriosclerosis, stenosis, vascular insufficiency and necrosis	Ischaemia	1	No
Vascular disorders	Arteriosclerosis, stenosis, vascular insufficiency and necrosis	Peripheral coldness	13	No
Vascular disorders	Arteriosclerosis, stenosis, vascular insufficiency and necrosis	Poor peripheral circulation	1	Yes

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Vascular disorders	Arteriosclerosis, stenosis, vascular insufficiency and necrosis	Vasospasm	1	No
Vascular disorders	Decreased and nonspecific blood pressure disorders and shock	Circulatory collapse	35	Yes
Vascular disorders	Decreased and nonspecific blood pressure disorders and shock	Hypotension	10	No
Vascular disorders	Decreased and nonspecific blood pressure disorders and shock	Hypotension	1	Yes
Vascular disorders	Decreased and nonspecific blood pressure disorders and shock	Hypovolaemic shock	1	Yes
Vascular disorders	Decreased and nonspecific blood pressure disorders and shock	Peripheral circulatory failure	1	Yes
Vascular disorders	Decreased and nonspecific blood pressure disorders and shock	Shock	9	Yes
Vascular disorders	Embolism and thrombosis	Embolism	1	Yes
Vascular disorders	Embolism and thrombosis	Jugular vein thrombosis	1	Yes
Vascular disorders	Embolism and thrombosis	Thrombosis	2	Yes
Vascular disorders	Lymphatic vessel disorders	Lymphoedema	2	No
Vascular disorders	Vascular disorders NEC	Angiopathy	2	Yes
Vascular disorders	Vascular disorders NEC	Capillary disorder	1	No
Vascular disorders	Vascular disorders NEC	Flushing	6	No
Vascular disorders	Vascular disorders NEC	Hyperaemia	18	No
Vascular disorders	Vascular disorders NEC	Hyperaemia	1	Yes
Vascular disorders	Vascular disorders NEC	Pallor	402	No
Vascular disorders	Vascular disorders NEC	Pallor	5	Yes
Vascular disorders	Vascular disorders NEC	Peripheral vascular disorder	1	No
Vascular disorders	Vascular disorders NEC	Vasodilatation	3	No
Vascular disorders	Vascular haemorrhagic disorders	Extravasation blood	1	No
Vascular disorders	Vascular haemorrhagic disorders	Haematoma	33	No
Vascular disorders	Vascular haemorrhagic disorders	Haematoma	1	Yes
Vascular disorders	Vascular haemorrhagic disorders	Haemorrhage	5	Yes
Vascular disorders	Vascular hypertensive disorders	Hypertension	6	No
Vascular disorders	Vascular inflammations	Kawasaki's disease	18	No
Vascular disorders	Vascular inflammations	Kawasaki's disease	2	Yes
Vascular disorders	Vascular inflammations	Vasculitis	23	Yes

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APPENDIX 5A : Fatal cases occurred in period

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Netherlands	19Jul2010		M	13Sep2010

7. & 13. DESCRIBE EVENT(S)

Meningitis viral, Convulsion, Yellow skin, Cyanosis, Dehydration, Diarrhoea, Somnolence, Crying, Vomiting,

This case was reported by a regulatory authority (NL-College ter Beoordeling van Geneesmiddelen # NL-LRB-111158) and described the occurrence of meningitis in a 2-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevenar) for prophylaxis.

The subject had no medical history and no concomitant medication.

On 13 September 2010 the subject received 1st dose of Infanrix hexa (unknown route, unknown injection site), 1st dose of Prevenar (unknown route, unknown injection site).

In September 2010, unspecified time after vaccination with Infanrix hexa and Prevenar, the subject experienced meningitis.

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [x] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA740A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 13Sep2010-13Sep2010

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar Injection E34002 (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 13Sep2010-13Sep2010

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0683335A NL2010/01987

24c. DATE RECEIVED: 09FEB2011

DATE OF REPORT: 17FEB2011

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

The subject was hospitalised.

On 25 September 2010, 12 days after vaccination with Infanrix hexa and Prevenar, the subject died from meningitis.

It was unknown whether an autopsy was performed. Hospital report was pending.

No further information could be obtained from regulatory authority.
Additional data will be sent to us in a proactive way. In the meanwhile, the case has been closed.

Follow up information received on 1 February 2011:

The case has received a second regulatory number : NL-LRB-116469

On 13 September 2010, 3 minutes after vaccination, the subject experienced crying and sleepiness on the same day.
On 18 September 2010, 5 days after vaccination, the subject was found in bed with eyes half-opened and a blue mouth. His skin was yellow/pale. He vomited pink, foaming milk. No fever was observed (37 degrees C).
The boy was hospitalized, diarrhea aggravated and dehydration was diagnosed.
Blood test and spinal tap were performed.
The boy had several afebrile convulsions and a MRI showed severe damage of the brain.

No further treatment was given.
On 25 September 2010, 12 days after vaccination, the subject died from viral meningitis.

The regulatory authority considered the events were unlikely to be related with vaccination with Infanrix hexa and Prevenar.

Additional information has been requested but could not be obtained from regulatory authority. The case has therefore been closed.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Blood test	Sep2010	unknown		
NMR	Sep2010	brain damage		
Spinal tap	Sep2010	unknown		

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	France		10 W	F	10Nov2010

7. & 13. DESCRIBE EVENT(S)

Sudden infant death syndrome, Respiratory tract congestion, Cough, Nasal congestion,

This case was reported by the French regulatory authority (AFSSaPS reference PS20101095) and described a sudden infant death in a 10-week-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) and pneumococcal vaccine (Prevenar, non-gsk) for prophylaxis.

The subject had mixted diet. At birth she weighed 2.99 kg and her heigh was 49.5 cm. She had no neonatal disorder. Medical condition included jaundice with abnormal skin reflection on 01 October 2010.

On 09 November 2010, the subject received primary course of Infanrix hexa (batch A21CA777A as data entry and 121CA777A as reported, intramuscular, injection site unknown) and a primary course of

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [X] PATIENT DIED AS OUTCOME OF EVENT
- [X] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA777A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 09Nov2010-09Nov2010

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [X] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [X] N/A

14. IDENTIFIED DRUG(S) Prevenar Injection E74711 (Pneumococcal vac NonGSK) Other

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 09Nov2010-09Nov2010

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [X] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [X] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

2.99 kg and 49.5 cm at birth, no neonatal disorder

The subject had mixted diet.

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0688734A

24c. DATE RECEIVED: 13DEC2010

DATE OF REPORT: 20DEC2010

24d. REPORT SOURCE: [ ] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [X] INITIAL [ ] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

Prevenar (batch E74711, intramuscular, injection site unknown).
On 10 November 2010, the subject presented with bronchial and nasal congestions, cough, and serous fluid in tympanum (with crying at night) which was diagnosed before the administration of vaccines (medical condition). At 19:00, the subject received her last bottle (250 ml). She went to bed at 19:15 and she was layed in her parent's bed, on a pillow. At 21:45, the father went to bed and found the subject unconscious. Mobile emergency medical unit was contacted which arrived at 22:00. At 22:23 pm, a pediatric mobile emergency medical unit arrived. Resuscitation procedure was started. The subject was intubated and received adrenaline. She was hospitalized and died at 00:00. Tracheal aspiration was positive for klebsiella pneumoniae.

It was unknown whether an autopsy was performed.

Causal relationship of vaccination with Infanrix hexa and Prevenar and sudden infant death was assessed as dubious, according to the French method of imputability.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Tracheal aspiration	10Nov2010	positive for kle		

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
JAUNDICE	01Oct2010	Unknown	Unknown
SEROUS FLUID IN TYMPANUM	Unknown	Unknown	Yes
CRYING AT NIGHT	Unknown	Unknown	Yes
KLEBSIELLA PNEUMONIAE INFECTION	Unknown	Unknown	Yes

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
PRIVACY	Sweden	14Feb2010		F	26Nov2010

7. & 13. DESCRIBE EVENT(S)

Meningitis, Sepsis, Shock, Pneumococcal infection, Renal impairment, Hepatic function abnormal, Pyrexia, Diarrhoea, Vomiting,

This case was reported by a consumer and described the occurrence of meningitis in a 9-month-old female subject who was vaccinated with synflorix (GlaxoSmithKline) and combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) for prophylaxis. A physician or other health care professional has not verified this report.

Previous and/or concurrent vaccination included bacillus calmette-guerin vaccine (non-gsk) ;non-GSK manufacturer;unknown;unknown given on 28 October 2010; diphtheria and tetanus toxoids and acellular pertussis vaccine ;GlaxoSmithKline;unknown;unknown given on 20 May 2010; hepatitis B vaccine recombinant ;manufacturer unspecified;unknown;unknown given on 20 May 2010; synflorix ;GlaxoSmithKline;unknown;unknown given on 20 May 2010.

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Synflorix Injection ASPNA017CK (Pneumoc.polysac S.Type 1 + Pneumoc.polysac S.Type 4 + Pneumoc.polysac S.Type 5 + Pneumoc.polysac S.Type 6B + Pneumoc.polysac S.Type 7F + Pneumoc.polysac S.Type 9V + Pneumoc.polysac S.Type 14 +

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 17Aug2010-17Aug2010

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA674A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 17Aug2010-17Aug2010

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

Synflorix (GlaxoSmithKline) 20May2010 - 20May2010
(Pneumoc.polysac S.Type 1 + Pneumoc.polysac S.Type 4 + Pneumoc.polysac S.Type 5 + Pneumoc.polysac S.Type 6B + Pneumoc.polysac S.Type 7F + Pneumoc.polysac S

Infanrix hexa (GlaxoSmithKline) 20May2010 - 20May2010
(Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax)

Hepatitis B vaccine (Unk Manufacturer) 20May2010 - 20May2010
(Hepatitis B vaccine)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0700040A SE2011/00097

24c. DATE RECEIVED: 21FEB2011

DATE OF REPORT: 21FEB2011

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

Concurrent medications included Paracetamol for her growing teeth.

On 17 August 2010, the subject received 2nd dose of Synflorix (administration site and route unknown, batch number not provided).

On 26 November 2010, 101 days after vaccination with Synflorix, the subject experienced fever, vomiting and diarrhea. This continued the whole day between 11 am to 6 pm. She suddenly got better and she was not vomiting and her fever went down.

She got fluid replacement and was able to urinate.

On 27 November 2010, at 7 am, the subject was not breathing any longer.

At the hospital, they tried to save her during 40 minutes.

The subject died on 27 November 2010 from meningitis and sepsis. An autopsy was performed and showed abnormal renal function, hepatic function abnormal and possible pneumococcal infection. The body was in shock.

Follow-up information received on 18 February 2011:

This case was also reported by a nurse.

The subject was healthy and didn’t have any other medicines.

Previous and/or concurrent vaccination included bacillus calmette-guerin vaccine (non-gsk) ;non-GSK manufacturer;unknown;unknown given on 28 May 2010; combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. ;GlaxoSmithKline;unknown;unknown given on 20 May 2010; hepatitis B vaccine recombinant ;manufacturer unspecified;unknown;unknown given on 20 May 2010; synflorix ;GlaxoSmithKline;unknown;unknown given on 20 May 2010.

On 17 August 2010, the subject received also a 2nd dose of Infanrix hexa.

On 26 November 2010, at 6 am, the subject got fever (40 deg.C).

The subject was treated with paracetamol (Alvedon).

Until 3.30 am, she received fluid replacement and then her parents let her rest.

On 27 November 2010, at 6.49 am, she sighed in a strange way and stopped breathing.

Follow-up information received on 21 February 2011:

The batch numbers and route were provided.

Bacillus calmette-guerin vaccine (non-gsk) was as initially reported, administered on 28 October 2010.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Body temperature	26Nov2010	40deg.C		

CONCOMITANT DRUGS AND DATES OF ADMINISTRATION

BCG vaccine (Other) (Bacillus Calmette-Guerin)	28Oct2010 - 28Oct2010
Paracetamol	Unknown

CONFIDENTIAL

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
PRIVACY	France	10Apr2010		M	07Mar2011

7. & 13. DESCRIBE EVENT(S)

Sudden death, Pyrexia, Lymphadenopathy, Emphysema, Product quality issue, Cardio-respiratory arrest, Asphyxia, Febrile convulsion,

This case was reported by a physician and described the occurrence of death (cause unknown) in a 10-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix Hexa, GlaxoSmithKline) for prophylaxis.

The subject had no known pathology and took no concurrent medication. Vaccinal history included one dose of DTPa-IPV-Hib vaccine (Infanrixquinta, GlaxoSmithKline) administered on 31 August 2010 and one dose of tuberculosis vaccine (BCG) on 01 June 2010. The vaccination schedule of the subject did not comply with French medical authority recommendations. The subject''s medical history included bronchiolitis during last winter.

On 07 March 2011, the subject received a second dose of Infanrix Hexa (batch A21CA598F, route and injection site unknown). During the

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA598F (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 07Mar2011-07Mar2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADMINISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [ ] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [ ] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

Vaccinal history included one dose of DTPa-IPV-Hib vaccine (Infanrixquinta, glaxoSmithKline) administered on 31 August 2010 and one dose of tuberculosis vaccine (BCG) on 01 June 2010. The vaccination schedule of the subject did not comply with French medical authority redcommendations.
The subject had no known pathology.

The subject was born at 41 weeks of amenorrhea by normal vaginal way. He weighed 4.09 kg

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0705290A

24c. DATE RECEIVED: 21APR2011

DATE OF REPORT: 29APR2011

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

CONFIDENTIAL

7. & 13. DESCRIBE EVENT(S)

following night, the subject experienced fever. Mobile emergency medical unit was contacted by the parents. On their arrival, the subject was dead.
No diagnostic was made, sudden infant death was suspected.
An autopsy was agreed by the parents (not a complete forensic). Results were not available at the time of reporting.

According to the reporter, a causal relationship between the death and Infanrix Hexa was not established.

Upon follow-up received from the AFFSaPS (reference TO20110471A) on 22 March 2011:
On 31 August 2010, tuberculosis vaccine (BCG) was made instead of 01 June 2010 (inconsistent information given).
Clinical examination was normal before vaccination.

Infanrix Hexa was administered intramuscularly at 11:00 on 07 March 2011. At 15:00, he presented with fever which resolved after paracetamol administration. The evening meal was taken without reportable incident.
During the following night, fever recurred and the parents called the mobile emergency unit.
On 08 March 2011, the subject was dead on mobile emergency medical unit arrival. He was found, by his father, lay on his stomach with face on his pillow. There were no signs of inhalation or vomiting. There was no sign of righting reflex, normaly present at this age.
Post mortem analyses were negative for C-reactive protein, blood culture and cerebrospinal fluid. Post-mortem virus tests were negative excepted positive for Respiratory Syncytial Virus in nose sample.
Anatomical pathology evidenced major mesenteric adenopathy.
Further informations conerning autopsy report were pending.

According to the French method of assessment, the AFSSaPS considered the causal relationship between vaccination with Infanrix Hexa and sudden death as dubious.

Upon follow-up received from quality department on 31 March 2011:

A product complaint has been recorded (Ref 2011-13789).
QA analysis revealed the complaint to be unsubstantiated. A complete review of the batch records had been performed and no deviation that could have an impact on the product was highlighted. A search was also performed in the GSK safety database for the final bulk A21CA598 and it did not reveal a safety signal.

Upon follow-up received from a physician on 05 April 2011:

The subject was born at 41 weeks of amenorrhea by normal vaginal way. He weighed 4.09 kg and measured 50 cm with a head circumference of 37 cm. APGAR scores at 1 and 5 min were at 10. No congenital abnormality or fetal distress were observed. The pregnancy occurred without problem. It was not known if the mother took any treatment during this pregnancy or during breast feeding or if she had smoked. He was breast fed until October 2010. He had a normal growth (in or upper the 97th percentile) with a normal head circumference. At the time of event, he weighed 11.34 kg.
The subject had no known allergy, no know congenital metabolic or enzymatic abnormality. Medical history did not included cyanosis, respiratory arrest or apnea episodes, gastroesophagal reflux, convulsion, sleep disorder, surgery, maltreatment.
Within the 2 weeks before death, the subject had no pathology including no infection, no fever, no excessive sweat during sleep, no snore during sleep, no vomiting, no modification of appetite, no diarrhea or modification of stools, no dyspnea, no abnormal crying, no lethargy. He was not admitted to emergency unit. It was unknown if he was exposed to contagious disease.
The father was 25-year-old. The mother was 24-year-old and had two other children (from another father). Both had no relevant medical history. It was not known if they were smokers. The family had a city life. During the last winter, the family moved house.

Infanrix hexa was administered intramuscularly in unknown thigh.

The assessment of this reporter was not provided.

Upon follow-up received from AFSSaPS on 14 April 2011:

Autopsy results were provided and evidenced major lymphoid hyperplasia of mesenteric lymph nodes, of intestinal lymphoid tissu and of appendix with cellular dystrophy suggestive of viral etiology possibly subclinical.
No Cytomegalovirus, Epstein-Barr virus or Herpes virus infection was found.
At lung level, bilateral pseudo-emphysemateous pulmonary lesions were noticed, suggestive of suffocation phenomenon as no resuscitation was attempted.
No sign suggestive of massive inhalation, no sign suggestive of infectious pneumopathy

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and no visceral congenital anomaly were reported.
According to the AFSSAPS, based on the French method of assessment, the events were unlikely related to vaccination with Infanrix hexa.

Follow-up was received on 21 April 2011 from the AFSSAPS :
Psychomotor development was normal.
The subject had one half-brother and one half-sister aged 6 and 5 years with medical history of convulsions. The half-brother was treated with Micropakine.
On 07 March 2011, at 03:00PM, body temperature was at 39.6 Celsius degrees.
On 08 March 2011, around midnight, the father still had not heard from him while he usually woke up at this time for his feed. When the father went to the bedroom, the subject was in ventral decubitus with the face on his pillow, he had cyanosis and was cold. The mobile emergency unit arrived and cardiorespiratory arrest was confirmed (the subject could not be resuscitated). His body temperature was at 35 Celsius degrees.
Skull and skeleton ultrasounds were normal.
The AFSSAPS reported that the respiratory syncytial virus responsibility in digestive inflammatory lesions was unlikely. Concerning the responsibility of Infanrix hexa vaccination, the administration was too recent to provide a probable explanation for the inflammation.
In conclusion, no clear explanation was found to the subject death. Hypothesis of respiratory asphyxia as cause of death was made, due to circumstances in which the subject was found as well as the aspect of his lungs at autopsy. Another hypothesis was febrile convulsion.

Post mortem tests: C reactive protein negative, CSF negative, blood culture negative and virus tests negative excepted positive for Respiratory Syncytial Virus in nose sample.

Autopsy:
-major lymphoid hyperplasia of mesenteric lymph nodes, of intestinal lymphoid tissu and of appendix with cellular dystrophy suggestive of viral etiology possibly subclinical.
-no Cytomegalovirus, Epstein-Barr virus or Herpes virus infection.
-bilateral pseudo-emphysemateous pulmonary lesions suggestive of suffocation phenomenon as no resuscitation was attempted.
-no sign suggestive of massive inhalation.
-no sign suggestive of infectious pneumopathy.
-no visceral congenital anomaly.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Autopsy	Mar2011	see text		
Blood culture	08Mar2011	negative		
Body temperature	07Mar2011	39.6Celsius degr		
Body temperature	08Mar2011	35Celsius degr		
C-reactive protein	08Mar2011	negative		
CSF test	08Mar2011	negative		
Full blood count	08Mar2011	normal		
Physical examination	07Mar2011	normal		
Scan NOS whole body	08Mar2011	normal		
Ultrasound skull	08Mar2011	normal		

OTHER RELEVANT HISTORY

and measured 50 cm with a head circumference of 37 cm. APGAR scores at 1 and 5 min were at 10. No congenital abnormality of fetal distress were observed. The pregnancy occurred without problem. It was not known if the mother took any treatment during this pregnancy or during breast feeding or if she smoke. He was breast fed until October 2010. He had a normal growth (in or upper the 97th percentile) with a normal head circumference.
The subject had no known allergy, no know congenital metabolic or enzymatic abnormality.
Medical history did not included cyanosis, respiratory arrest or apnea episodes, gastroesophagal reflux, convulsion, sleep disorder, surgery, maltreatment.
Within the 2 weeks before death, the subject had no pathology including no infection, no fever, no excessive sweat during sleep, no snore during sleep, no vomiting, no modification of appetite, no diarrhea or modification of stools, no dyspnea, no abnormal crying, no lethargy. He was not admitted to emergency unit. It was unknown if he was exposed to contagious disease.
The father was 25-year-old. The mother was 24-year-old and had two other children (other father). Both had no relevant medical history. It was not known if they were smokers. The family had a city life. During the last winter, the family moved house.
The subject had one half-brother and one half-sister aged 6 and 5 years with medical history of convulsions. The half-brother was treated with Micropakine.

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
BRONCHIOLITIS	Unknown	Unknown	No
POSSIBLE VIRAL INFECTION	Unknown	Unknown	Yes

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Thailand		2 M	F	10Mar2011

7. & 13. DESCRIBE EVENT(S)

Shock, Respiratory arrest, Cardiac arrest, Pyrexia, Somnolence, Hypotonia, Vomiting, Crying, Apnoea,

This case was reported by a physician and described the occurrence of fatal shock in a 2-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis.

The subject was born by C-section. Apgar score was 10 at 0 and 5 min. Birth weight was 3.2 kg and experienced a normal growth and development.
Medical condition included a possible genetic abnormality due to a family history of death after vaccination (subject's brother died 2 years ago after vaccination with DTwP).

On 9 March 2011, the subject received unspecified dose of Infanrix hexa (.5 ml, unknown route of adminstration).

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA959B (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 09Mar2011-09Mar2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADMINISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [ ] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [ ] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0706503A TH2011/00009

24c. DATE RECEIVED: 21MAR2011

DATE OF REPORT: 29MAR2011

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

The subject was normal before vaccination.

On 10 March 2011, 24 hours after vaccination with Infanrix hexa, the subject experienced shock. She experienced low-grade fever, drowsiness and stopped breathing. The subject was floppy and had no heart rate.

Cardiopulmonary resuscitation was performed during 3 hours but the subject did not respond to it.

The physician considered the events were probably related to vaccination with Infanrix hexa.

The subject died on 10 March 2011 from cardiorespiratory arrest. An autopsy was not performed.

Follow-up received on 21 March 2011:
The subject’s brother was 2 month-old when he died (11 years ago), after received DTwP which was EPI vaccine (no record available).

After vaccination (no specific time available), the subject experienced vomiting (single episode) and had colicky crying at home.

On 10 March 2011, the subject was taken to the clinic due to fever and crying. After massive crying, the subject experienced apnea and no heart beat was detected after stimulation.

Cardiopulmonary resuscitation was performed for 10 minutes and subject responded by crying. One hour later, the subject experienced apnea again and resuscitation was continued for 3 hours without any response.

No lab results nor autopsy results were available. Shock was the final diagnosis.

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
GENETIC ABNORMALITY	Unknown	Unknown	Yes

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
PRIVACY	Italy	07Apr2010		M	26Mar2011

7. & 13. DESCRIBE EVENT(S)

Hypotonia, Hyperhidrosis, Pyrexia,

This case was reported by a regulatory authority (IT-Agenzia Italiana del Farmaco # 137473) and described the occurrence of hypotonia nos in a 11-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) and pneumococcal vaccines (non-gsk) (Prevenar 13) for prophylaxis.

The subject was born after 41 weeks + 3 days, normal pregnancy and spontaneous delivery.

Concurrent medical conditions included severe respiratory distress at birth. He was reanimated and resigned from the prenatal intensive care on 20 May 2010. He was not able to feed spontaneously (dysphagia) so a nasogastric tube was inserted with pump infusion.

According to the doctor, the subject had contraindication to the

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CB001A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 25Mar2011-25Mar2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar 13 Injection E87109 (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 25Mar2011-25Mar2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

Paracetamol	Unknown
Vitamin	Unknown
Vigabatrin	Unknown
Topiramate	Unknown
Antibiotics	Unknown
Bronchodilator	Unknown

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0712016A IT2011/00988

24c. DATE RECEIVED: 04APR2011

DATE OF REPORT: 12APR2011

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [x] INITIAL [ ] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

vaccine.

He was hospitalised from 22 May 2010 to 25 May 2010 due to respiratory distress. From 14 to 21 July 2010 due to seizures.
On 18 August 2010, diagnostic results showed cerebral palsy, gastroesophageal reflux, hypoxic-ischemic encephalopathy of grade 3, microcephaly, psychomotor retardation and spastic quadriplegia (mainly the upper limbs).

Concurrent medications included Paracetamol (Tachipirina), Vitamin, Vigabatrin, Topiramate, Antibiotics (Antibiotic), Bronchodilator and Steroid.

On 25 March 2011, the subject received 3rd dose of Infanrix hexa (intramuscular, right thigh) and 3rd dose of Prevenar 13 (intramuscular, left thigh).

On 26 March 2011, 1 day after vaccination with Infanrix hexa and Prevenar 13, the subject experienced fever (38 to 38.5 deg.C).

On 27 March 2011, 2 days after vaccination with Infanrix hexa and Prevenar 13, the subject experienced hypotonia nos and crisis of sweating.

The regulatory authority reported that the events were possibly related to vaccination with Infanrix hexa and Prevenar 13.

The subject died on 28 March 2011, cause of death was not reported. It was unknown whether an autopsy was performed.

Follow-up information received on 15 July 2011:

As no additional information could be obtained, the case has been closed.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Body temperature	26Mar2011	38-38.5deg.C		

CONCOMITANT DRUGS AND DATES OF ADMINISTRATION

Steroid	Unknown

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
HYPOXIC-ISCHEMIC ENCEPHALOPATHY	Unknown	Unknown	Yes
CEREBRAL PALSY	Unknown	Unknown	Unknown
SEIZURE	Unknown	Unknown	No
DYSPHAGIA	Unknown	Unknown	Unknown
RESPIRATORY DISTRESS	Unknown	Unknown	No
NASOGASTRIC TUBE INSERTION	Unknown	Unknown	Yes
MICROCEPHALY	Unknown	Unknown	Yes
GASTROESOPHAGEAL REFLUX	Unknown	Unknown	Unknown
SPASTIC QUADRIPLEGIA	Unknown	Unknown	Yes
PSYCHOMOTOR RETARDATION	Unknown	Unknown	Yes

CONFIDENTIAL

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
PRIVACY	Italy	21Nov2010		F	23Apr2011

7. & 13. DESCRIBE EVENT(S)

Cardiac arrest, Multi-organ failure, Pneumonia aspiration, Cerebral ischaemia, Sudden infant death syndrome, Unresponsive to stimuli, Peripheral coldness, Staring, Musculoskeletal stiffness, Pyrexia, Somnolence,

This case was reported by a regulatory authority (IT-Agenzia Italiana del Farmaco # 139520) and described the occurrence of cardiac arrest in a 5-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevenar 13) for prophylaxis.

On an unspecified date, the subject received 1st dose of Infanrix hexa (unknown route of administration, unknown site of injection, batch number not provided).

At an unspecified time after vaccination with 1st dose of Infanrix Hexa, the subject experienced fever. This is the reason why the

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) 1) Infanrix hexa Injection (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 10Feb2011-10Feb2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [x] YES [ ] NO [ ] N/A

14. IDENTIFIED DRUG(S) 2) Infanrix hexa Injection A21FA980A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 14Apr2011-14Apr2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0716780A IT2011/01280

24c. DATE RECEIVED: 14SEP2011

DATE OF REPORT: 15SEP2011

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 2 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
PRIVACY	Italy	21Nov2010		F	23Apr2011

7. & 13. DESCRIBE EVENT(S)

second dose was not administered in the last 4 weeks.

On 14 April 2011, the subject received 2nd dose of Infanrix hexa (.5 ml, intramuscular, unknown route of administration), and 2nd dose of Prevenar 13 (.5 ml, intramuscular, unknown route of administration, batch number not provided).

On 14 April 2011, less than one day after vaccination with 2nd doses of Infanrix hexa and Prevenar 13, the subject experienced fever (more than 39 Deg.C).

On 15 April 2011, the fever was resolved.

In the afternoon of 15 April 2011, the subject did not respond to stimuli. She was admitted at the first aid with cold extremities, fixed gaze, overtone, stiff neck and normotensive fontanel. Afterwards, the subject recovered completely.

At the neurological visit, the subject was alert, reactive and the

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT DIED AS OUTCOME OF EVENT
- ☐ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) 3) Prevenar 13 Injection (Pneumococcal vac NonGSK) Other

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 10Feb2011-10Feb2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☒ YES ☐ NO ☐ N/A

14. IDENTIFIED DRUG(S) 4) Prevenar 13 Injection E57714 (Pneumococcal vac NonGSK) Other

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 14Apr2011-14Apr2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

B0716780A IT2011/01280

24c. DATE RECEIVED: 14SEP2011

DATE OF REPORT: 15SEP2011

24d. REPORT SOURCE: ☐ HEALTH PROFESSIONAL ☐ STUDY ☐ LITERATURE

25a. REPORT TYPE: ☐ INITIAL ☐ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

state of drowsiness has been related to vaccination. Electroencephalogram was without clear anomalies irritative.

On 23 April 2011 (night), the subject had a cardiac arrest. After 20 minutes of reanimation the cardiac activity resumed but with irreversible neurological sequelae.

The regulatory authority reported that fever, stiff neck, fixed gaze, cold extremities, unresponsive to stimuli and cardiac arrest were possibly related to vaccination with Infanrix hexa and Prevenar 13, but almost certainly for drowsiness.

On 25 April 2011, the subject died, cause of death is not specified. It was unknown whether an autopsy was performed.

Follow-up information received on 19 May 2011:

The parents of the subject were young, both were born in 1992. No information regarding important diseases or neonatal problems were reported. Artificial sucking from the early days due to maternal hypogalactia, was reported. The subject’s growth had always been regular, between 50 Deg and 75 Deg percentile.

The first dose of the vaccines Infanrix Hexa and Prevenar 13 were administered on 10 February 2011. Within weeks of vaccination with 1st dose of Infanrix Hexa and Prevenar 13, the subject experienced fever.

An autopsy was performed and there had been no element attributed to encephalitis. The histological evaluation was in course.

Follow-up information received on 6 September 2011:

An autopsy was performed and the results were reported on the basis of available information and histological investigations.

The death occurred at 15:10 on 25 April 2011.

The death was caused by multiple organ failure, ab-ingestis pneumonia, cerebral anoxia, following sudden cardiac arrest.

Other significant causes were not found, therefore cardiac arrest might correspond to Sudden Infant Death Syndrome (SIDS).

There was no available scientific evidence to show a causal relationship between vaccine administrations and cardiac arrest.

Follow-up information received on 14 September 2011:

No concomitant medication was reported. The subject was in good health before vaccination.

Full report on resuscitation measures and full autopsy report were not available.

The rationale for the diagnosis of sudden infant death syndrome was as following as: since other significant causes were not found, therefore cardiac arrest was placed within a sudden infant death syndrome (SIDS).

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Body temperature	14Apr2011	more than 39Deg.		
Electroencephalogram	Apr2011	see textunits		

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
PRIVACY	France	15Apr2009		F	27Oct2010

7. & 13. DESCRIBE EVENT(S)

Death,

This case was reported by the French regulatory authority (FR-Agence Francais de Securite Sanitaire des Produits de Sante # NT20110388) and described the occurrence of unexplained death in a 18-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis.

The subject had no known and relevant medical history.

On 26 October 2010, the subject received an unspecified dose of Infanrix hexa (batch A21CA724A, intramuscular, injection site unknown).

On 27 October 2010, 1 day after vaccination with Infanrix hexa, the subject was found dead after her nap.
Autopsy did not identify any cause of death. Respiratory aspiration

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA724A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 26Oct2010-26Oct2010

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADMINISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [ ] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [ ] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

No known and relevant medical history

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0727175A

24c. DATE RECEIVED: 20JUN2011

DATE OF REPORT: 28JUN2011

24d. REPORT SOURCE: [ ] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [x] INITIAL [ ] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

was assessed as not very probable.
No other information was available.

According to the French method of assessment, the AFSSaPS considered the causal relationship between vaccination with Infanrix hexa and unexplained death as dubious.

2010
-Autopsy: no identified cause of death

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Autopsy	2010	see text		

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Australia	08Jun2011		M	21Jul2011

7. & 13. DESCRIBE EVENT(S)

Death,

This case was reported by a consumer and described the occurrence of death unspecified in a 6-week-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline), live attenuated human rotavirus vaccine (Rotarix) and pneumococcal vaccines (non-gsk) (Prevenar 13) for prophylaxis. A physician or other health care professional has not verified this report.

On 20 July 2011, the subject received unspecified dose of Infanrix hexa (administration site and route unknown), an unspecified dose of Rotarix (route unknown) and an unspecified dose of Prevenar 13 (unknown).

On 21 July 2011, 14 hours after vaccination with Infanrix hexa, Prevenar 13 and Rotarix, the subject died for unknown reasons.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) 1) Infanrix hexa Injection A21CA972B (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 20Jul2011-20Jul2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) 2) Rotarix Liquid AROLA366CA (Rotavirus vaccine) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 20Jul2011-20Jul2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0735723A AU2011/00410

24c. DATE RECEIVED: 27JUL2011

DATE OF REPORT: 01AUG2011

24d. REPORT SOURCE: [ ] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [x] INITIAL [ ] FOLLOW-UP

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INTERNATIONAL EVENT REPORT

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I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Australia	08Jun2011		M	21Jul2011

7. & 13. DESCRIBE EVENT(S)

The subject died on 21 July 2011, cause of death was not reported.
An autopsy was performed. Autopsy results are not yet available.

Further information has been expected.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT DIED AS OUTCOME OF EVENT
- ☐ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) 3) Prevenar 13 Injection (Pneumococcal vac NonGSK) Other

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 20Jul2011-20Jul2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. IDENTIFIED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADMINISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

B0735723A AU2011/00410

24c. DATE RECEIVED: 27JUL2011

DATE OF REPORT: 01AUG2011

24d. REPORT SOURCE: ☐ HEALTH PROFESSIONAL ☐ STUDY ☐ LITERATURE

25a. REPORT TYPE: ☐ INITIAL ☐ FOLLOW-UP

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Germany	08Oct2010		M	23Jan2011

7. & 13. DESCRIBE EVENT(S)

Sudden infant death syndrome, Death, Vomiting, Cardiomyopathy,

This case was reported by a physician via another manufacturer and described the occurrence of possible sudden infant death syndrome (SIDS) in a 3-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis.

Co-suspect vaccinations included 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer Pharma).

Concurrent or previous medical conditions included hyperbilirubinemia.
At the time of vaccination the subject was otherwise healthy.

On 18 January 2011 the subject received the first dose of Infanrix hexa (0.5 ml, intramuscular, unknown) and the first dose of Prevenar 13 (0.5 ml, intramuscular, unknown), contralaterally.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA922C (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 18Jan2011-18Jan2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar 13 Injection E90728 (Pneumococcal vac NonGSK) PFIZER

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 18Jan2011-18Jan2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

D-fluoretten (Colecalciferol + Sodium Fluoride) — Unknown

Simethicone — Unknown

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

D0070324A

24c. DATE RECEIVED: 11AUG2011

DATE OF REPORT: 16AUG2011

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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D0070324A	DESK COPY	(Page 2 of 3)

7. & 13. DESCRIBE EVENT(S)

Less than one week post vaccination with Infanrix hexa and Prevenar 13, In January 2011, the subject experienced possible sudden infant death syndrome (SIDS).

The subject died on an unknown date between 18 January 2011 (date of vaccination) and 24 January 2011 (date when police has informed the physician) from possible sudden infant death syndrome (SIDS). It was unknown whether an autopsy was performed.

The reporting physician considered that the event was unlikely related to vaccination with Infanrix hexa and/or Prevenar 13.

The case was received from Pfizer Pharma GmbH, Berlin, Germany. The other manufacturer has already reported this case under international number DE-PFIZER-INC-2011025551.

The same case was reported on 18 February 2011 by the same physician via a sales representative and described the occurrence of death - at present cause unknown - in a 4-month-old subject of unspecified gender who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis.

Co-suspect vaccinations included 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer Pharma).

On the same unspecified date the subject received an unspecified dose of Infanrix hexa (0.5 ml, unknown) and an unspecified dose of Prevenar 13 (0.5 ml, unknown).

Approximately three days post vaccination with Infanrix hexa and Prevenar 13, on an unspecified date, the subject was found dead in prone position lying in vomit.

At present the cause of death was unknown. It was unknown whether an autopsy was performed.

Follow-up information was received on 21 February 2011 from the reporting physician.

Case D0070369A was identified as a duplicate of this case (D0070324A). Duplicate case D0070369A was voided prior to submission of any reports to regulatory authorities. All future correspondence will be submitted to this case, the case of record D0070324A.

The subject has no underlying or concurrent medical conditions or other risk factors.

On 18 January 2011 the subject received the first doses of Infanrix hexa (lot number: A21CA922C) and Prevenar 13.

For the next three days following vaccination with Infanrix hexa and Prevenar 13 the subject was well.

Then the subject died from at present unknown cause. The subject was found dead in prone position lying in vomit.

An autopsy was performed. At the moment the result of autopsy was unknown.

Follow-up information was received on 28 February 2011 from the reporting physician.
The reported lot number for Prevenar 13 was E90728, not E40728.
According to this follow-up information the subject died five days post vaccination with Infanrix hexa and Prevenar 13, on 23 January 2011, and not three days post vaccination with Infanrix hexa and Prevenar 13 as reported initially.

The subject has no underlying or concurrent medical conditions or other risk factors.
Concurrent medications included colecalciferol + sodium fluoride (D-Fluoretten) for prophylaxis and simethicone (Espumisan) as needed for infantile colic.

On 18 January 2011 the subject received the first dose of Infanrix hexa (0.5 ml, intramuscular, left thigh) and the first dose of Prevenar 13 (0.5 ml, intramuscular, right thigh), contralaterally.

Approximately five days post vaccination with Infanrix hexa and Prevenar 13, on 23 January 2011, the subject died from at present unknown cause. The subject received no treatment. An autopsy was performed on an unknown date, but the autopsy report was not available at the moment.

The reporting physician considered that death from at present unknown cause was unlikely related to vaccination with Infanrix hexa and/or Prevenar 13.

The reporting physician also provided the answers to a GSK questionnaire asking for

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additional information in cases of sudden infant death:

The parents were married..
No further social anamnesis of the parents was provided.
The subject had no brothers and two sisters.

None of the following diseases were known in family history: metabolic disorders or inborn errors of metabolism, cardiac problems, non-accidental injury in child or non-accidental injury in siblings.
It was unknown, whether or not family history included SIDS or SUD, near miss, infant death due to other reason or epilepsy or convulsions.

It was unknown whether or not the mother or the father was smoking.
No information was provided whether or not the mother or the father was abusing alcohol and/or drugs.
The subject’s family was living in a city.

The mother had been pregnant for unknown times, with three deliveries, unknown stillbirth and unknown abortion.

During present pregnancy there was no maternal illness or complication during pregnancy.
It was unknown whether or not conditions during present pregnancy included maternal smoking or maternal medication.
It was unknown whether or not the mother took any medication during breast feeding.
It was unknown whether or not there was any fetal distress.

The subject was born by normal delivery at 38 weeks of pregnancy with a birth weight of 3130 g, a length of 49 cm and an Apgar score of 10/10.
No information was provided concerning birth defects.
No information was provided concerning breast-feeding.
No information was provided concerning development (growth and weight gain) since birth.

The subject had none of the following pre-existing diseases: allergies, inborn errors of metabolism or enzymatic abnormalities, episodes of cyanosis, stop breathing or apnea, gastroesophageal reflux, convulsions, sleep disorder, past surgery or mistreatment prior to contact with social worker.
The subject had none of the following conditions in the past two weeks: emergency room visit, exposure to contagious disease, infection, fever, excessive sweating during sleep, loud breathing or snoring during sleep, vomiting, appetite changes, diarrhea or stool changes, dyspnea, abnormal crying or lethargy.
There were no recent changes of the way of life..

The date, time and kind of the subject’s last meal were unknown.

On 23 January 2011 the subject was found dead under unknown circumstances in the bed.
The subject was found for an unknown reason by chance.
No information was provided concerning resuscitation used to revive the subject.
It was unknown whether or not the subject was sleeping alone and where the subject was sleeping.
When placed, the position of body was unknown.
When found, the position of body was unknown.
All other conditions when sleeping and when found dead, including sleeping or supporting surface (type of mattress), items in contact with subject or in immediate environment (e.g. cuddly toys), number of blankets covering the subject, body and room temperature at the time when the subject was found, the type of room heating and the responsible person looking after the subject, were unknown.

No information was provided concerning adverse events following the last vaccination.

Follow-up information was received on 11 August 2011 by phone from the reporting physician.

According to the reporting physician, in the meantime, there had been signs of possible cardiomyopathy.

No further information will be available.

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
HYPERBILIRUBINEMIA	Unknown	Unknown	Unknown

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Germany	14Feb2011		F	17May2011

7. & 13. DESCRIBE EVENT(S)

Death,

This case was reported by a health professional via a regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2011016343) and described death of a 3-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) and pneumococcal vaccines (non-gsk, Prevenar 13) for prophylaxis.

Previous vaccinations with Infanrix hexa and Prevenar 13 (on 14 April 2011) have been well tolerated. On 16 May 2011 the subject received the second dose of Infanrix hexa (intramuscular, unknown thigh) together with the second dose of Prevenar 13 (intramuscular, unknown thigh). In the morning of the following day, on 17 May 2011, the subject was found dead.

An autopsy was performed and a preliminary autopsy report was provided. According to the autopsy protocol very early in the

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CB004A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 16May2011-16May2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar 13 Injection F08783 (Pneumococcal vac NonGSK) Other

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 16May2011-16May2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

D0071496A

24c. DATE RECEIVED: 08AUG2011

DATE OF REPORT: 10AUG2011

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

morning of 17 May 2011 the subject had been found "cold and lifeless" by her parents. On 05:02 an emergency physician had been called. Cardiopulmonary resuscitation by the parents and later by the emergency personal failed and death was testified.
Policemen were involved at 06:20. Interrogation of the subject’s parents revealed that the subject and her four siblings had always been healthy. On 16 May 2011 the subject had received vaccinations with Infanrix hexa and Prevenar 13. At this time the subject had suffered from a mild intestinal infection. On 17 May 2011 around 0:00 the subject’s mother had seen her daughter in a good condition and sleeping.
Autopsy revealed signs of otitis media. Otherwise autopsy resulted normally and the cause of death could not be identified. Toxicological, microbiological, virological and histological examinations were planned.

Follow-up information was received on 08 August 2011 via the regulatory authority by means of structured information and the final autopsy report.

The following narrative was provided by the regulatory authority:
"Follow-up information was received from the institut of legal medicine Halle (Saale) on 04 August 2011:
The final autopsy report was provided.
Significant findings:
- affluant cerumen in the right ear, evidence of yellowish mucus in both middle ears, histological evidence of inflammatory cells
- hyperaemia and cyanosis of the brain
- slightly enlarged liver
- bleedings at the back side of the pericardium and of the heart
- bleedings at the back sides of both lungs
- peritoneum in the pelvis minor with bleedings
- organs without pathological findings
- focal emphysematous expansion of the lung tissue (as a consequence of resuscitation)
- exclusion of trauma with fatal outcome
- evidence of injections at both thighs
The causes and mode of of death could not be clarified. The infant had been suffering from an acute unilateral otitis media at the time of death (smear from the left middle ear: proof of Haemophilus influenzae; smear from the right middle ear: no proof of microorganisms). Within the scope of additional examinations no alcohol (alcohol concentration 0.00 %) or other pharmacologic agents (chemical-toxicologic examination without pathological findings) could be detected. There was neither evidence of an allergic reaction (total IgE 5.65 kU/l, reference <20kU/l) nor of a gastrointestinal infection. Nor was there any evidence of a postvaccinal disorder."

According to the autopsy report, the onset date of the subject’s otitis media was "very recent", but it could not be clarified whether it had been prior to or following the vaccination. Although no evidence of a relation of the event to the vaccination was found during the autopsy, the close temporal relation might be seen as an indication that the subject’s death was possibly related to the vaccination with Infanrix hexa and Prevenar 13.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Blood alcohol	May2011	0.00%		
Hemophilus influenzae test positive	May2011	positive		
IgE	May2011	5.65kU/l		20

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
INTESTINAL INFECTION	Unknown	Unknown	Yes
OTITIS MEDIA	Unknown	Unknown	Yes

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Germany	03Jul2011		M	07Sep2011

7. & 13. DESCRIBE EVENT(S)

Death,

This case was reported by a German regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2011029271) and described the occurrence of unexplained death in a 9-week-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis.

Co-suspect vaccinations included 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Pfizer Pharma).

Pregnancy and birth had been normal. The subject's medical history included neonatal jaundice.
The subject was developing normal. Family history included no allergies.
Concurrent medical conditions included suspicion of congenital hip dysplasia. Hip ultrasonography, performed on 09 August 2011, showed type IIa left and type I right. Follow-up hip ultrasonography,

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [x] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CB094A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 05Sep2011-05Sep2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar 13 Injection F22933 (Pneumococcal vac NonGSK) PFIZER

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 05Sep2011-05Sep2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

RotaTeq (Sanofi Pasteur MSD) (Rotavirus vaccine Non-GSK)	09Aug2011 - 09Aug2011
D-fluoretten (Colecalciferol + Sodium Fluoride)	Unknown
Paracetamol	Unknown

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

D0072663A

24c. DATE RECEIVED: 11OCT2011

DATE OF REPORT: 18OCT2011

24d. REPORT SOURCE: [ ] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

CONFIDENTIAL

7. & 13. DESCRIBE EVENT(S)

performed on 05 September 2011, showed type I both sides.
At the time of vaccination, on 05 September 2011, the subject was well. The subject showed small white plaques in oral mucus (oropharyngeal plaques) left but most likely no oral candidiasis.
Previous vaccination with Rotavirus vaccine (non-GSK) (RotaTeq; Sanofi Pasteur MSD), given orally at 2 ml on 09 August 2011, was well tolerated.
Concurrent medications included colecalciferol + sodium fluoride (D-Fluoretten) and paracetamol (Ben-u-ron).

On 05 September 2011 the subject received the first dose of Infanrix hexa (0.5 ml, intramuscular, unknown thigh lateral) and the first dose of Prevenar 13 (.5 ml, intramuscular, unknown thigh lateral).

Approximately two days post vaccination with Infanrix hexa and Prevenar 13, on 07 September 2011, the subject died. The cause of death was unknown (death unexplained).

The event had also been reported as life threatening.

An autopsy was performed on 07 September 2011 at an institute for forensic pathology. At the time of reporting, on 08 September 2011, examinations had not been finished and no autopsy results have been reported.

The German regulatory authority (DE-Paul-Ehrlich-Institut) has requested further information.

Quality test result was received on 11 October 2011. A complete review of the batch records has been performed by Quality Assurance and Production. No deviation that could impact the quality of the product has been highlighted during the GlaxoSmithKline Biologicals investigation.

At the moment no further information was available.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Body height	09Aug2011	57cm		
Body mass index	09Aug2011	16.7		
Childhood audiometry normal	08Jul2011	normal		
Head circumference	09Aug2011	39cm		
Investigation	09Aug2011	normal		
Ultrasound scan	09Aug2011	possible hip dys		
Weight	08Jul2011	4kg		
Weight	09Aug2011	5.430kg		
Weight	05Sep2011	6.285kg		

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
NEONATAL JAUNDICE	08Jul2011	Unknown	No
CONGENITAL HIP DYSPLASIA	09Aug2011	Unknown	Yes
OROPHARYNGEAL PLAQUE	05Sep2011	Unknown	Unknown

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Germany	03May2011		M	20Sep2011

7. & 13. DESCRIBE EVENT(S)

Circulatory collapse, Sepsis, Shock, Crying, Pallor,

This case was reported by a regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2011030856) and described the occurrence of circulatory failure in a 5-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis.

Co-suspect vaccination included 13-valent pneumococcal vaccine (non-GSK) (Prevenar 13, Pfizer). First vaccination with both vaccines on 23 August 2011 was well tolerated.
Information on medical history and concomitant medication was not provided.

On 20 September 2011 the subject received 2nd dose of Infanrix hexa (unknown route and application site), 2nd dose of Prevenar (unknown route and application site).

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [x] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [x] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CB094A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 20Sep2011-20Sep2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar 13 Injection F08782 (Pneumococcal vac NonGSK) PFIZER

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 20Sep2011-20Sep2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

D0072852A

24c. DATE RECEIVED: 03NOV2011

DATE OF REPORT: 04NOV2011

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

On 21 September 2011, 1 day after vaccination with Infanrix hexa and Prevenar, the subject experienced circulatory depression, differential diagnosis was symptoms of acute sepsis.

The regulatory authority reported that the events were life threatening.

The subject died from circulatory depression or possible sepsis. An autopsy was performed.

Follow-up information was received on 28 September 2011 via the German regulatory authority (PEI).

Infanrix hexa was given intramuscular in the left thigh and Prevenar 13 was given intramuscular in the right thigh. Different lot numbers were reported on follow-up.

Approximately 20 hours after vaccination with Infanrix hexa and Prevenar 13, the subject experienced shock with circulatory failure.

An emergency physician was called and the subject was hospitalized on emergency to an intensive care unit.
Approximately 10 hours after onset of symptoms the subject died despite intensive care.

According to follow-up information received on 07 October 2011 via the German regulatory authority (PEI), the lot number A21CB094A was documented in vaccination certificate, while there was no documentation for the mentioned lot numbers A21CB105A and A21CB115A.

Quality test result was received on 11 October 2011. A complete review of the batch records has been performed by Quality Assurance and Production. No deviation that could impact the quality of the product has been highlighted during the GlaxoSmithKline Biologicals investigation.

Case D0072949A was identified as a duplicate of case D0072852A and will be voided. All future correspondence will be submitted to the case of Record D0072852A.

The duplicate case was reported by a physician, via a sales representative and stated the following:

On 20 September 2011 in the evening, less than one day after vaccination with Infanrix hexa and Prevenar, the subject had been crying and turned grey while lying in bed. The vaccinating physician was consulted and admitted the infant to hospital, where the subject died on 21 September 2011.

Follow-up information was received on 27 October 2011 via the German regulatory authority (PEI).
Information about anamnesis was provided by a hospital report from intensive care treatment after birth.

The mother had been pregnant for the first time. The mother had former surgery because of false lung vein opening and received permanent treatment with bisoprolol.
The subject was delivered prematurely in 31+4 weeks of gestation, by section from breech presentation after pathologic CTG. There was no premature rupture of the amnion and amniotic fluid was clear. The subject had an APGAR of 6/10/10, a weight of 1490 g, length of 39 cm, head circumference of 32.6 cm, navel artery pH was 7.16.

After birth the subject had neonatal respiratory distress syndrome grade I with continuous positive airway pressure for 24 hours.
The subject developed possible meconium ileus due to microcolon, transient intestinal transportation disorder, cholestatic hepatosis after parenteral nutrition, with increased transaminases (alanine aminotransferase 131 U/l, aspartate aminotransferase 100 U/l, creatine kinase 342 U/l, total bilirubin 3 mg/dl, direct bilirubin 2.75 mg/dl).
Additional diagnoses after birth included neonatal anemia and iron deficiency, asymmetry from lying, small hemangioma right gluteal and dystrophic growth and weight increase.
On the sixth day of life, the subject’s condition worsened and he was transferred to an intensive care unit for neonates. Intravenous antibiotics were given for seven days.
The subject had abdominal distension since birth and not yet passed meconium. Acute abdomen was suspected on the seventh day of life. The subject was transferred to a pediatric chirurgic unit for further intervention, but after conservative treatment the symptoms resolved.

Test results were normal for ions, blood gases, immune reactive trypsin (tested on 06 May and 06 June 2011), sonogram of head, abdomen and hip (Graf classification Ib) and hearing screening. Cytomegalovirus (CMV) and toxoplasmosis IgM and IgG antibodies were negative.
Initially increased Thyroid stimulating hormone normalised on control. Bile acid was

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increased (74.6 mcmol/l), pancreatic kinase was decreased (68 mcg/g). Eye examination showed vascularisation limit zone III at both sides.
The subject was discharged after 39 days in good condition and received rachitis prophylaxis and iron substitution.

No further details about the reported event were provided.

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
PREMATURE BABY 26 TO 32 WEEKS	Unknown	Unknown	No
NEONATAL RESPIRATORY DISTRESS SYNDR	Unknown	Unknown	No
CONTINUOUS POSITIVE AIRWAY PRESSURE	Unknown	Unknown	No
MECONIUM ILEUS	Unknown	Unknown	No
INTESTINAL DISORDER	Unknown	Unknown	No
HEPATOSIS	Unknown	Unknown	No
NEONATAL ANEMIA	Unknown	Unknown	No
IRON DEFICIENCY	Unknown	Unknown	No
HEMANGIOMA	Unknown	Unknown	No
DYSTROPHY	Unknown	Unknown	No
ACUTE ABDOMEN	Unknown	Unknown	No

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APPENDIX 5B : Fatal follow-up cases

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Netherlands	18Apr2009		F	Jun2009

7. & 13. DESCRIBE EVENT(S)

Sudden infant death syndrome, Depressed level of consciousness, Hypotonia, Pallor,

This case was reported by a healthcare professional and described the occurrence of cot death in a 2-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-GSK) (Prevenar) for prophylaxis.

On an unspecified date, the subject received 1st dose of Infanrix hexa (unknown route), 1st dose of Prevenar (unknown route). No lot number available.

1 day after vaccination with Infanrix hexa and Prevenar, the subject experienced death nos.

The subject died, cause of death is not specified. It was unknown whether an autopsy was performed.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [x] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA487A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 16Jun2009-16Jun2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar Injection (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 16Jun2009-16Jun2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0580597A NL2009/01225

24c. DATE RECEIVED: 17NOV2010

DATE OF REPORT: 24NOV2010

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

This was all the available information. The reporter will send additional details in a proactive way.

Follow up information received on 2 July 2009 from regulatory authority:
The subject had no medical history and no concomitant medication.
On 16 June 2009 the subject received 1st dose of Infanrix hexa (unknown route), 1st dose of Prevenar (unknown route).

1 day after vaccination with Infanrix hexa and Prevenar, the subject was found in bed nonresponsive, floppy and pale.

The subject died on 17 June 2009, cause of death was not reported.

Follow up information received on 4 November 2010:

The subject’s medical history included fetal distress (emergency cesarean section at 36 weeks). Birth weight 2250 g. Apgar after 1 minute 7, after 5 minutes 8 while being respirated. Oxygen saturation after 1 minute: 77 - 88 %.
Low blood pressure: 44/20 and 66/40. Hemoglobin after birth 2,0 after which she received two transfusions with erythrocytes and then Hemoglobin 5,2 mmol/l.

The baby was checked in hospital at 2.5 week-old: growth and development good.

At age 4 and 8 weeks (8 weeks = 16 June 2009), the subject was checked at child health clinic and showed a normal development and growth.

On 16 June 2009 at 16:00, the subject received 1st dose of Infanrix hexa and 1st dose of Prevenar.

The baby was fed during the night at 4:00 and she was normal.
The subject was found dead in bed lying at side with free airway at 8:45.
An autopsy was performed and showed no indications for cause of death, therefore conclusion was cot death, relation with vaccination was not possible to assess.

The healthcare professional considered the events were clinically significant (or requiring intervention).

Follow up information received on 17 November 2010:

The subject’s medical history included anemia; hemoglobin was 2.2 mmol/L. After erythrocyte transfusion, hemoglobin was 5.2 mmol/L.

Cardiopulmonary resuscitation (CPR) was started by the parents. Ambulance was called and after 1 hour the CPR was stopped at the hospital.
Letter from pediatrician revealed no abnormalities in post mortal examinations.
Possible hypothesis was choking due to aspiration.
Conclusion was sudden infant death syndrome.

The regulatory authority considered the events were unlikely to be related to vaccination with Infanrix hexa and Prevenar.

No further information was available.

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
EMERGENCY CESAREAN SECTION AT 36 WE	Unknown	Unknown	Unknown
ANEMIA REQUIRING TRANSFUSION	Unknown	Unknown	Unknown

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
PRIVACY	Italy	23May2009		F	10Aug2009

7. & 13. DESCRIBE EVENT(S)

Sudden death, Cardiac arrest, Convulsion, Hypokinesia,

This case was reported by a regulatory authority (IT-Agenzia Italiana del Farmaco # 106091) and described the occurrence of sudden death in a 2-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) for prophylaxis.

On 10 August 2009, the subject received unspecified dose of Infanrix hexa (unknown route and injection site).

On 10 August 2009, less than one day after vaccination with Infanrix hexa, the subject experienced convulsions.

The subject was hospitalised from 14 August until 19 August 2009.

At discharge, therapy with luminale was given.

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [x] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA579A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 10Aug2009-10Aug2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADMINISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [ ] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [ ] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0605003A IT2009/02495

24c. DATE RECEIVED: 20JUL2011

DATE OF REPORT: 25JUL2011

24d. REPORT SOURCE [ ] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE [ ] INITIAL [x] FOLLOW-UP

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B0605003A	DESK COPY	(Page 2 of 2)

7. & 13. DESCRIBE EVENT(S)

At the time of reporting, the event was resolved with sequelae.

The regulatory authority reported that the event was possibly related to vaccination with Infanrix hexa.

Follow up information received on 14 December 2009 :
Last convulsion episode was on 18 October 2009.
The baby showed a regular growth but a light motor retardation in respect of the age.
Her weight was 7.10 Kg.
Diagnostic tests as Karyotype, Ultrasonography, Computerized axial tomography and Nuclear magnetic resonance were negative.
She was treated with Luminalette 15 mg 3 times per day.

Follow up information received on 01 June 2010 :
The subject died due to a cardiac arrest.

Target Folllow Up Questionaire has been sent together with questions from medical review.

As no further details could be obtained from AIFA, the case has been closed.

Follow-up information received on 29 November 2010:

The subject died on 5 March 2010.

Follow-up information received on 14 December 2010:

After autoptic exam, the physician reported that the convulsions and cardiac arrest were unrelated to vaccination with Infanrix hexa.

Follow-up information received on 20 July 2011:

The autoptic exam report confirmed that the event was a suddenly death with no specified cause.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Computerized axial tomography		Negative		
Karyotype analysis		Negative		
Nuclear magnetic resonance imaging		Negative		
Ultrasound scan		Negative		

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Netherlands	07Aug2009		M	16Nov2009

7. & 13. DESCRIBE EVENT(S)

Sudden infant death syndrome, Depressed level of consciousness, Mouth haemorrhage, Nasopharyngitis,

This case was reported by a healthcare professional and described the occurrence of cot death in a 14-week-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevenar) for prophylaxis.

On 12 November 2009 the subject received unspecified dose of Infanrix hexa (unknown route, unknown injection site), unspecified dose of Prevenar (unknown route, unknown injection site).

On 16 November 2009, 4 days after vaccination with Infanrix hexa and Prevenar, the subject experienced death (unspecified).

The subject died on 16 November 2009, cause of death was not reported. It was unknown whether an autopsy was performed.

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) 1) Infanrix hexa Injection A21CA524A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 06Oct2009-06Oct2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) 2) Prevenar Injection D37370 (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 06Oct2009-06Oct2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0608494A NL2009/02314

24c. DATE RECEIVED: 05NOV2010

DATE OF REPORT: 10NOV2010

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 2 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Netherlands	07Aug2009		M	16Nov2009

7. & 13. DESCRIBE EVENT(S)

Follow up information received on 5 November 2010:
Child was born at term and weighed 4120 g.
On 2 October 2009, The subject visited healthcare centre for viral infection.

On 6 October 2009, the subject received 1st dose of Infanrix hexa (unknown route, unknown injection site), 1st dose of Prevenar (unknown route, unknown injection site).

In the beginning of November, 2 weeks before death, the subject had a common cold.

On 12 November 2009 the subject received 2nd dose of Infanrix hexa (unknown route, unknown injection site) and 2nd dose of Prevenar (unknown route, unknown injection site)

The subject had no adverse events after vaccinations.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT DIED AS OUTCOME OF EVENT
- ☐ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) 3) Infanrix hexa Injection A21CA530A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 12Nov2009-12Nov2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. IDENTIFIED DRUG(S) 4) Prevenar Injection D91963 (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 12Nov2009-12Nov2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

B0608494A NL2009/02314

24c. DATE RECEIVED: 05NOV2010

DATE OF REPORT: 10NOV2010

24d. REPORT SOURCE: ☐ HEALTH PROFESSIONAL ☐ STUDY ☐ LITERATURE

25a. REPORT TYPE: ☐ INITIAL ☐ FOLLOW-UP

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B0608494A	DESK COPY	(Page 3 of 3)

7. & 13. DESCRIBE EVENT(S)

On 16 November 2009, 4 days after vaccination with Infanrix hexa and Prevenar, the subject was brought to day care centre. He had no fever. He burped well after being fed and put into bed at 9:25 lying on abdomen (with permission mother).
Every 20 minutes, the baby was checked.
At 12:00, the subject was nonresponsive and had blood in mouth.

Reanimation was started immediately, 3 times adrenaline (Epinephrine) and sodium chloride (NaCl), and oxygen.
The child arrived at hospital, reanimation was proceeded by intubation, no output.
Echocardiography showed no activity, resuscitation was stopped.

The subject died on 16 November 2009 from sudden infant death syndrome.

An autopsy was performed and showed the following: In lungs, fluid retention (consolidations). Boy was normally developed with head circumference and weight far above average. Weight of lungs 184g, normal is 65g. Neuropathologic examinations revealed no abnormalities.
Brain edema which terminally occurred and signs of blood damming were present.

General conclusion: no cause of death found in autopsy or toxicological Investigations.
Tryptase: 4.2 mcg/l blood from heart (normal: lower than 11.5 mcg/l for adults).
No indication for anaphylactic reaction. In addition, time period of 4 days is too long to suspect an anaphylactic reaction.

No indications for a relation with vaccinations.

No further information was available.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Echocardiography	16Nov2009	no activity		

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
VIRAL INFECTION	02Oct2009	Unknown	Unknown

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APPENDIX 5C : Fatal cases - late breaking info

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
PRIVACY	Belgium	25Jul2011		F	21Oct2011

7. & 13. DESCRIBE EVENT(S)

Sepsis, Purpura fulminans, Pyrexia, Diarrhoea, Purpura,

This case was reported by a pharmacist and by another health professional and described the occurrence of septicemia in a 3-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), live attenuated human rotavirus vaccine (Rotarix) and pneumococcal vaccines (non-gsk) (Prevenar) for prophylaxis.

The subject was a premature baby. Concurrent medical conditions included cold.

On 13 October 2011, the subject received 1st dose of Infanrix hexa (route and injection site unknown, batch number not provided), 1st dose of Rotarix (route unknown, batch number not provided) and 1st dose of Prevenar (route and injection site unknown, batch number not provided).

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [x] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) 1) Infanrix hexa Injection (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 13Oct2011-13Oct2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) 2) Rotarix Unknown (Rotavirus vaccine) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 13Oct2011-13Oct2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0762668A BE2011/00449

24c. DATE RECEIVED: 30NOV2011

DATE OF REPORT: 08DEC2011

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [x] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 2 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
PRIVACY	Belgium	25Jul2011		F	21Oct2011

7. & 13. DESCRIBE EVENT(S)

On 21 October 2011, 8 days after vaccination with Infanrix hexa, Prevenar and Rotarix, the subject experienced fever and diarrhea.

The subject was hospitalised.

The subject died in the night 21 and 22 October 2011 from septicemia. It was unknown whether an autopsy was performed.

The subject's twin sister had received the same vaccination without problem.

Information inadvertently not recorded in the initial report:

The event septicemia was added.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT DIED AS OUTCOME OF EVENT
- ☐ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) 3) Prevenar Injection (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 13Oct2011-13Oct2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. IDENTIFIED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADMINISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

B0762668A BE2011/00449

24c. DATE RECEIVED: 30NOV2011

DATE OF REPORT: 08DEC2011

24d. REPORT SOURCE: ☐ HEALTH PROFESSIONAL ☐ STUDY ☐ LITERATURE

25a. REPORT TYPE: ☐ INITIAL ☐ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

Follow-up information received on 30 November 2011 and 2 December 2011 from 2 newspapers and from a consumer via a web forum:

The mother’s medical history included allergy and the family history included baby sudden death. The organisation who administered the vaccines was not aware that the subject had a cold.

When the subject developed fever (39.9 deg.C) on 21 October 2011, the subject was treated by her parents with an antipyretic drug (suppository) and was taken to the hospital.

At the hospital, gastroenteritis was firstly diagnosed, and after this diagnosis was changed to a pulmonary infection. The subject was treated with an antibiotic. But at 11 pm, her body was covered with purpura. The subject died at about 3 o’clock in the morning on 22 October 2011, 9 hours after she arrived at the hospital. Her body was covered with blue plaques.

The diagnosis of purpura fulminans reported. The consumer also reported that rapid meningococcal meningitidis was mentioned, but no lumbar puncture and no hemoculture were performed therefore they could not conclude to this diagnosis.

The subject’s parents lodged a complaint against "X" because of the lack of information provided before the vaccination about the risks and the lack of precaution taken regarding the family history.

The subject’s twin sister of this case also experienced an adverse event after vaccination with same vaccines. At an unspecified time following vaccination with Infanrix hexa, Prevenar and Rotarix, the subject’s twin sister experienced apnea. At the time of reporting, the event was improved.Please see case B0767303A for details about the subject’s twin sister.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Body temperature	21Oct2011	39.9deg.C		

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
COLD	Unknown	Unknown	Unknown
PREMATURE BIRTH	Unknown	Unknown	Unknown

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 4)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Germany	03May2011		M	20Sep2011

7. & 13. DESCRIBE EVENT(S)

Respiratory failure, Shock, Cardiovascular insufficiency, Screaming, Pallor, Restlessness, Renal failure, Hyperkalaemia, Pneumonia viral, Rash macular, Sinus tachycardia, Anuria, Vomiting, Hypotonia, Irritability, Faeces discoloured, Lactic acidosis,

This case was reported by a regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2011030856) and described the occurrence of respiratory failure in a 5-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis.

Co-suspect vaccination included 13-valent pneumococcal vaccine (non-GSK) (Prevenar 13, Pfizer). First vaccination with both vaccines on 23 August 2011 was well tolerated.
Information on medical history and concomitant medication was not provided.

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [x] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [x] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CB094A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 20Sep2011-20Sep2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar 13 Injection F08782 (Pneumococcal vac NonGSK) PFIZER

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 20Sep2011-20Sep2011

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

D0072852A

24c. DATE RECEIVED: 09DEC2011

DATE OF REPORT: 13DEC2011

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

On 20 September 2011 the subject received 2nd dose of Infanrix hexa (unknown route and application site), 2nd dose of Prevenar (unknown route and application site).

On 21 September 2011, 1 day after vaccination with Infanrix hexa and Prevenar, the subject experienced circulatory depression, differential diagnosis was symptoms of acute sepsis.

The regulatory authority reported that the events were life threatening.

The subject died from circulatory depression or possible sepsis. An autopsy was performed.

Follow-up information was received on 28 September 2011 via the German regulatory authority (PEI).

Infanrix hexa was given intramuscular in the left thigh and Prevenar 13 was given intramuscular in the right thigh. Different lot numbers were reported on follow-up.

Approximately 20 hours after vaccination with Infanrix hexa and Prevenar 13, the subject experienced shock with circulatory failure.

An emergency physician was called and the subject was hospitalized on emergency to an intensive care unit.
Approximately 10 hours after onset of symptoms the subject died despite intensive care.

According to follow-up information received on 07 October 2011 via the German regulatory authority (PEI), the lot number A21CB094A was documented in vaccination certificate, while there was no documentation for the mentioned lot numbers A21CB105A and A21CB115A.

Quality test result was received on 11 October 2011. A complete review of the batch records has been performed by Quality Assurance and Production. No deviation that could impact the quality of the product has been highlighted during the GlaxoSmithKline Biologicals investigation.

Case D0072949A was identified as a duplicate of case D0072852A and will be voided. All future correspondence will be submitted to the case of Record D0072852A.

The duplicate case was reported by a physician, via a sales representative and stated the following:

On 20 September 2011 in the evening, less than one day after vaccination with Infanrix hexa and Prevenar, the subject had been crying and turned grey while lying in bed. The vaccinating physician was consulted and admitted the infant to hospital, where the subject died on 21 September 2011.

Follow-up information was received on 27 October 2011 via the German regulatory authority (PEI).
Information about anamnesis was provided by a hospital report from intensive care treatment after birth.

The mother had been pregnant for the first time. The mother had former surgery because of false lung vein opening and received permanent treatment with bisoprolol.
The subject was delivered prematurely in 31+4 weeks of gestation, by section from breech presentation after pathologic CTG. There was no premature rupture of the amnion and amniotic fluid was clear. The subject had an APGAR of 6/10/10, a weight of 1490 g, length of 39 cm, head circumference of 32.6 cm, navel artery pH was 7.16.

After birth the subject had neonatal respiratory distress syndrome grade I with continuous positive airway pressure for 24 hours.
The subject developed possible meconium ileus due to microcolon, transient intestinal transportation disorder, cholestatic hepatosis after parenteral nutrition, with increased transaminases (alanine aminotransferase 131 U/l, aspartate aminotransferase 100 U/l, creatine kinase 342 U/l, total bilirubin 3 mg/dl, direct bilirubin 2.75 mg/dl).
Additional diagnoses after birth included neonatal anemia and iron deficiency, asymmetry from lying, small hemangioma right gluteal and dystrophic growth and weight increase.
On the sixth day of life, the subject’s condition worsened and he was transferred to an intensive care unit for neonates. Intravenous antibiotics were given for seven days.
The subject had abdominal distension since birth and not yet passed meconium. Acute abdomen was suspected on the seventh day of life. The subject was transferred to a pediatric chirurgic unit for further intervention, but after conservative treatment the symptoms resolved.

Test results were normal for ions, blood gases, immune reactive trypsin (tested on 06 May and 06 June 2011), sonogram of head, abdomen and hip (Graf classification Ib) and hearing

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screening. Cytomegalovirus (CMV) and toxoplasmosis IgM and IgG antibodies were negative. Initially increased Thyroid stimulating hormone normalised on control. Bile acid was increased (74.6 mcmol/l), pancreatic kinase was decreased (68 mcg/g). Eye examination showed vascularisation limit zone III at both sides.
The subject was discharged after 39 days in good condition and received rachitis prophylaxis and iron substitution.

No further details about the reported event were provided.

An autopsy report was received via the German regulatory authority (PEI) on 09 December 2011.

Autopsy was performed on 23 September 2011.

According to the report, events after vaccination also included nocturnal restlessness, increasing pallor, renal failure and hyperkaliemia.

Pre-existing underlying medical condition included subacute florid lymphocytic interstitial pneumonia, probably of viral origin, significant activation of the bronchio-alveolar lymphatic system, accumulation of alveolar macrophages, focal beginning alveolar reaction, capillary ectasia and occlusion of the big bronchia by mucus.

The cause of death was identified as respiratory failure with protracted shock due to interstitial pneumonia, probably of viral origin. Pathogenic microorganisms were not detected.
Evidences of shock included Paltauf dots at the pleura visceralis, fresh necrosis of the kidneys, disseminated hemorrhage of the small intestine, hemorrhage of the mucous membrane of the stomach, multiple stasis hemorrhage of the spleen.

Additional findings showed macular exanthema situated at the right lower leg and cervical and para-oesophageal soft tissue hemorrhage.
There was no reaction at the injection site.

Hemorrhages were also considered to be caused by intensive care measures.

Follow-up received on 12 December 2011 included a complete hospital report.

The subject was hospitalized on 21 September 2011 at 09:30.
In hospital the subject was diagnosed with death after ventricular tachycardia with hyperkaliemia and acute circulatory shock of unclear genesis with anuria and hyperkaliemia.

According to the hospital report, the subject had developed normally within the last months. Childhood examination U4 (performed in 3rd to 4th month of life) showed anemia (hemoglobin 8.5 g/dl).
The subject’s mother had arterial hypertension and received bisoprolol. She formerly underwent surgery because of wrong lung vein ostium.

After the subject had received the vaccinations, there was nothing abnormal during the day. In the night, around 01:00 o’clock the subject had been drinking about 200 ml.
At 03:00 the subject started crying, which increased despite treatment with simethicone (Sab). He was vomiting twice. There was a transient improvement after receiving caraway suppository at 05:00.
In the morning the subject became pale with strange breathing.

When hospitalized, the subject was in bad condition, with circulatory depression, tachycardia with heart rate over 210 per min, pallor, muscle hypotonia, high irritability, moaning breathing. Green stool was excreted once.
Supraventricular tachycardia could be excluded by electrocardiogram (ECG), which showed sinus tachycardia.
Blood gas analysis showed acidosis with increased lactate and potassium. The subject received volume bolus via infusion on the head.
After sudden worsening of condition with fall in oxygen saturation the subject received ketamine and diazepam.
There was a short phase of bradycardia with the need for cardiac massage.
The subject received further volume via intra-osseous access, as well as dobutamine, adrenaline (Adrenalin), claforan for suspected sepsis and hydrocortisone for circulatory support.

Echocardiogram excluded dilated cardiomyopathy, but showed reduced pump function of heart.
Sonogram of head excluded acute bleeding. Abdominal sonogram was normal.

The subject’s body temperature had decreased to 33.1 degC rectal and exogenous warmth treatment was started.
Blood test results challenged the diagnosis of sepsis, without fever and with no relevant

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inflammatory signs. Ammonia was increased, which was considered a possible sign for metabolic disorder.

The subject received central vein catheter in V. jugularis interna and arterial catheter in V. femoralis at the right, but no stabilization could be achieved. Katecholamines were increased.
The subject still had no diuresis and was treated with frusemide (Lasix).

In further course the subject developed increasing potassium values, T-wave elevation, ventricular tachycardia, anuria and no improvement of the situation. Further treatment was without success.

At 16:20 further cardiac problems developed, but because of the bad situation no defibrillation was started. The subject died at 16:21 in the parent’s presence.

The hospital physician stated that after exclusion of cardiac, cerebral and abdominal causes, the event was most likely an atypical sepsis without fever and inflammatory signs. However, postmortal cultures of blood and cerebrospinal fluid also showed no germs.

Despite of the autopsy results, the cause of death still kept unclear for the hospital physician. He stated that there were no radiologic signs for pneumonia and artificial respiration had been successful, with normalization of blood gas values.

A metabolic disorder was considered possible, but it was more likely that lactic acidosis and hyperammonia were a secondary effect of shock.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Ammonia	21Sep2011	1031mccg/dl		
C-reactive protein	21Sep2011	0.9mg/dl	0	0.6
Heart rate	21Sep2011	over 210per min		
Lactate	21Sep2011	8.7mmol/l		
Respiratory rate	21Sep2011	40per min		
White blood cell count	21Sep2011	31270per mcl	6000	17500

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
PREMATURE BABY 26 TO 32 WEEKS	Unknown	Unknown	No
NEONATAL RESPIRATORY DISTRESS SYNDR	Unknown	Unknown	No
CONTINUOUS POSITIVE AIRWAY PRESSURE	Unknown	Unknown	No
MECONIUM ILEUS	Unknown	Unknown	No
INTESTINAL DISORDER	Unknown	Unknown	No
HEPATOSIS	Unknown	Unknown	No
NEONATAL ANEMIA	Unknown	Unknown	No
IRON DEFICIENCY	Unknown	Unknown	No
HEMANGIOMA	Unknown	Unknown	No
DYSTROPHY	Unknown	Unknown	No
ACUTE ABDOMEN	Unknown	Unknown	No
LYMPHOCYTIC INTERSTITIAL PNEUMONIA	Unknown	Unknown	Yes
VIRAL PNEUMONIA	Unknown	Unknown	Yes
BRONCHIAL CONGESTION	Unknown	Unknown	Yes
ANEMIA	Unknown	Unknown	Yes

APPENDIX 4 : PSUR - 23 OCTOBER 2009 to 22 OCTOBER 2010

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CONFIDENTIAL TO REGULATORY AUTHORITIES

Biologicals Clinical Safety and Pharmacovigilance

Site de Wavre Nord, Avenue Fleming 20, B-1300 Wavre, Belgium

Combined Diphtheria, Tetanus and Acellular Pertussis, Hepatitis B enhanced Inactivated Poliomyelitis and *Haemophilus influenzae* type B vaccine

Infanrix hexa™

Safety Update

International Birthdate: 23 October 2000 (European Union)

Data Lock Points: 23 October 2009 to 22 October 2010

Author Dominique Parmentier Safety Scientist

Report No 15 - 16 December 2010

Reviewer Thomas Breuer, MD Senior Vice President Head of Global Vaccines Development, GSK Biologicals Date 16/12/10

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EXECUTIVE SUMMARY

- Infanrix hexa is currently registered in 88 countries. Worldwide Marketing Authorisation status for Infanrix hexa is provided in Appendix 1A.

- During the period under review, no regulatory actions have been taken for safety reasons.

- Post-marketing exposure to Infanrix hexa during the PSUR reporting period is estimated to be between 2,995,430 and 11,981,722 subjects. Number of subjects exposed since launch until the Data Lock Point (DLP) of this report is estimated as being between 15,156,658 and 60,626,633.

- The data received during the reporting period referred to a total of 2080 reports of which 1216 cases fulfilled the ICH E2C criteria for inclusion in the main line listings and summary tabulations of this report.

- Amendments to the Reference Safety Information (RSI) made during the reporting period include addition of a warning statement about "syncope": "Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints".

- No further amendments to the RSI are considered necessary at the present time.

- The benefit/risk profile of Infanrix hexa™ continues to be favourable.

- The Company will continue to monitor all cases of thrombocytopenia, injection site nodule and nodule, anaphylaxis, abscess and injection site abscess, important neurological events including encephalitis and encephalopathy, erythema multiforme, Henoch-Schonlein purpura, petechiae and purpura.

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1. INTRODUCTION

This is the 15th Periodic Safety Update Report (PSUR) for Infanrix hexa™ which covers the reporting period 23 October 2009 to 22 October 2010.

This PSUR covers all formulations and indications for the product(s) and is prepared according to all applicable regulations [ICH, 1996; ICH, 2003; Volume 9A, 2008; CHMP/PhVWP, 2007; EMEA/CHMP, 2006].

1.1. Pharmacology and Indications

Infanrix hexa™ contains the following antigens adsorbed onto aluminium salts: diphtheria toxoid, tetanus toxoid, three purified pertussis antigens [pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin (PRN; 69 kiloDalton outer membrane protein)], the purified major surface antigen (HBsAg) of the hepatitis B virus (HBV) and purified polyribosyl-ribitol-phosphate capsular polysaccharide (PRP) of Haemophilus influenzae type b (Hib), covalently bound to tetanus toxoid. It also contains three types of inactivated polio viruses (type 1: Mahoney strain; type 2: MEF-1 strain; type 3: Saukett strain).

The tetanus and diphtheria toxoids are obtained by formaldehyde treatment of purified Corynebacterium diphtheriae and Clostridium tetani toxins. The acellular pertussis vaccine components are obtained by extraction and purification from phase I Bordetella pertussis cultures, followed by irreversible detoxification of the pertussis toxin by glutaraldehyde and formaldehyde treatment, and formaldehyde treatment of FHA and PRN. The diphtheria toxoid, tetanus toxoid and acellular pertussis components are adsorbed onto aluminium salts.
The surface antigen of the HBV is produced by culture of genetically-engineered yeast cells (Saccharomyces cerevisiae) which carry the gene coding for the major surface antigen of the HBV. This HBsAg expressed in yeast cells is purified by several physico-chemical steps. The HBsAg assembles spontaneously, in the absence of chemical treatment, into spherical particles of 20 nm in average diameter containing non-glycosylated HBsAg polypeptide and a lipid matrix consisting mainly of phospholipids. Extensive tests have demonstrated that these particles display the characteristic properties of the natural HBsAg.

The three polioviruses are cultivated on a continuous VERO cell line, purified and inactivated with formaldehyde.
The Hib polysaccharide is prepared from Hib, strain 20,752 and after activation with cyanogen bromide and derivatisation with an adipic hydrazide spacer is coupled to tetanus toxoid via carbodiimide condensation. After purification the conjugate is adsorbed on aluminium salt, and then lyophilised in the presence of lactose as stabiliser.
Infanrix hexa™ meets the World Health Organisation requirements for manufacture of biological substances, of diphtheria, tetanus, pertussis and combined vaccines, of hepatitis B vaccines made by recombinant DNA techniques, of inactivated poliomyelitis vaccines and of Hib conjugate vaccines.

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Infanrix hexa™ is indicated for primary and booster immunisation against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and *Haemophilus influenzae* type b in infants from the age of 6 weeks and may be given to infants who received a first dose of hepatitis B vaccine at birth.

The primary vaccination schedule (such as 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months; 3, 5 and 11 or 12 months; 6, 10, 14 weeks) consists of three doses of 0.5 ml. An interval of at least one month should be respected between doses.
If it is intended to administer Infanrix hexa™ according to the EPI schedule (Expanded Program on Immunisation; 6, 10, 14 weeks of age), then the vaccinee must receive a dose of hepatitis B vaccine at birth.

1.2. Presentations

A 0.5 ml dose of the vaccine contains not less than 30 IU of adsorbed diphtheria toxoid, not less than 40 IU of adsorbed tetanus toxoid, 25 mcg of adsorbed PT, 25 mcg of adsorbed FHA, 8 mcg of adsorbed pertactin, 10 mcg of adsorbed recombinant HBsAg protein, 40 D-antigen units of type 1 (Mahoney), 8 D-antigen units of type 2 (MEF-1) and 32 D-antigen units of type 3 (Saukett) of the polio virus. It also contains 10 mcg of adsorbed purified capsular polysaccharide of Hib (PRP) covalently bound to 20-40 mcg tetanus toxoid (T).

2. WORLDWIDE MARKET AUTHORISATION STATUS

Infanrix hexa™ was first approved in the Europe Union on 23 October 2000 (centralised procedure) and is currently licensed in 88 countries. Details of all countries where Infanrix hexa™ is currently approved are presented in Appendix 1A. Details of countries where the marketing authorisations have been withdrawn are presented in Appendix 1B.

3. UPDATE OF REGULATORY AUTHORITY OR MARKETING AUTHORISATION HOLDER ACTIONS TAKEN FOR SAFETY REASONS

During the period under review, no actions have been taken for safety reasons concerning withdrawal, revocation, rejection, suspension or failure to obtain a renewal of a Marketing Authorisation; neither have there been any dosage modifications, changes in target population, formulation changes, restriction on distribution, or clinical trial suspension.

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4. CHANGES TO REFERENCE SAFETY INFORMATION

Changes to the Reference Safety Information (RSI), including rationale, are communicated to Regulatory Agencies on an ongoing basis.

The RSI in effect at the beginning of the reporting period is presented in Appendix 2A.

The RSI is the Global Prescriber Information (GPI) of the Global Datasheet (GDS) version number 10 dated 21 October 2010; the Core Safety Information (CSI) is highlighted in this document by shaded text.

Changes to the CSI during the reporting period include the following:

Addition of a warning statement about "syncope" in all injectable vaccines: *Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.*

The RSI in effect at the end of the reporting period is presented in Appendix 2B.

5. PATIENT EXPOSURE

5.1. Market Experience

An estimation of the total patient exposure can be calculated from the number of doses distributed, which is the only data available with regard to patient exposure in a post-marketing setting. The assumption is made that one dose distributed will equal one subject exposed to vaccination.

It is important to note that the sales database from which data are issued is an in-house „living" database and is subject to updates and corrections depending on information provided by GSK local country subsidiaries (e.g. some vaccine batches may be returned to GSK central office). In the sales database, corrections and updates are posted on related period/month and therefore, could be slightly different from original PSUR data. Donations are not included.

During the period covered by this report 11,981,722 doses of Infanrix hexa™ have been distributed. Since launch until the data lock point (DLP) of this PSUR, 60,626,633 doses have been distributed. As vaccination with Infanrix hexa™ could vary between 1 and 4 doses per subject in accordance with local recommendations, post-marketing exposure to Infanrix hexa™ during the PSUR reporting period is estimated to be between 2,995,430 and 11,981,722 subjects The number of subjects exposed since launch until the data lock point of this report is estimated as being between 15,156,658 and 60,626,633.
The market experience during the reporting period of this PSUR is comparable to that of the previous reporting period.

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6. INDIVIDUAL CASE HISTORIES

6.1. Definitions

LISTEDNESS

Listedness is automatically assigned by GSK at the MedDRA Preferred Term (PT) level.

An event is only considered listed if it is included in the CCSI under all circumstances. Events that are only listed in specific situations (e.g. in overdose, for a specific indication, as part of a hypersensitivity reaction or post-treatment) are assessed as „unlisted". Lack of efficacy is assessed as listed. This is supported by CIOMS V which acknowledges that no vaccine can be expected to be effective in all patients.

Listed Case:

A case is considered listed if all Adverse Events (AEs) are covered by the Company Core Safety Information (CCSI) when it is entered onto the safety database. This may be different from the RSI used for this PSUR. Note: For clinical trials and PMS cases, only serious, attributable events must be in the CSI for the case to appear as listed.

Unlisted Case:

A case where at least one AE was not covered by the CSI at the time of case entry.

SERIOUSNESS

Serious Case:

A case involving an untoward medical occurrence that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in disability/incapacity or is a congenital anomaly/birth defect.

Medical or scientific judgement is exercised in deciding whether other reports should also be considered serious, such as those involving important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the subject or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These events are also considered serious. Examples of such events are invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias, convulsions that do not result in hospitalisation, or development of drug dependency or drug abuse. In GSK, such medically important events are termed GSK „medically serious AEs" (see below).

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GSK Medically Serious AE:

As proposed by CIOMS V, GSK maintains a list of all events considered to be „medically serious" that is regularly reviewed and updated by the company Safety Physicians. This list of MedDRA Lower Level Terms (LLTs) is automatically applied to all spontaneous, post-marketing and literature cases as they are entered onto the safety database. Inclusion of „medically serious" events makes the case serious at case level.

Other Definitions

Attributability:

A clinical trial case is classified as „attributable" if the investigator or the company consider there is a reasonable possibility that a serious AE was caused by the study medication. These cases may also contain individual non-serious AEs. A clinical trial case is also considered „attributable" if the investigator does not specify causality for any serious AE.

Primary Adverse Event:

The main AE described by the reporter. If a diagnosis and associated signs/symptoms have been provided, GSK will consider the diagnosis the primary AE. Where the main AE is not clear, GSK assigns the most serious medical condition the reporter thought was associated with the drug as the primary AE.

6.2. Cases Presented as Line Listings

The following type of cases received by GSK from worldwide sources during the reporting period and referenced below are considered to fulfil ICH E2C criteria for inclusion in the main line listings and/or summary tabulations of this report:

- all serious adverse reactions and non-serious unlisted adverse reactions from spontaneous notifications (including published reports);
- all non-serious listed adverse reactions from spontaneous reporting;
- all serious adverse reactions (attributable to the vaccine by either investigator or sponsor) available from studies or named-patient/compassionate use;
- all serious adverse reactions from regulatory authorities.

In addition, the type of cases mentioned below is included as a line listing as well:

- all serious and non-serious (listed and unlisted) adverse reactions reported by patients/consumers and other non-healthcare professionals (non-medically verified cases).

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The type of cases making up the PSUR line listings within Appendices 3 is summarised below and in Table 1.

Appendix 3A contains:

- all serious cases from spontaneous notifications (including published reports and regulatory reports but excluding non-medically verified reports);
- all unblinded serious cases arising from clinical trials considered related by sponsor or investigator;
- all non-serious unlisted cases from spontaneous notifications (including published reports but excluding non-medically verified reports and reports received solely from regulatory authorities).

Appendix 3B contains all serious attributable clinical trial cases unblinded during the reporting period which were not included in a previous report because they were still blinded.

It is company policy that only those clinical trial reports which are expedited to regulatory authorities are unblinded on the safety database during study conduct. Clinical trial reports that are not expedited will be unblinded on study completion. Any clinical trial reports meeting ICH E2C criteria but not included in a previous PSUR, are included as follow-up information in Appendix 3B.

In order to ensure no cases are missed, GSK uses a broad search strategy to retrieve clinical trial cases unblinded during the reporting period. Therefore, Appendix 3B may include some cases which have already been included in a previous PSUR (e.g. non-blinded clinical trial cases).

Appendix 3C contains all non-serious listed cases from spontaneous notifications including published reports but excluding all non-medically verified reports and all reports received solely from regulatory authorities.

Appendix 3D contains all non-medically verified cases, whether serious or non-serious, listed or unlisted.

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Table 1 Appended Line Listings

Format	Appendix	Case Type
Line Listing	3A	All serious spontaneous cases (excluding consumer reports), all serious attributable clinical trial cases and all non-serious unlisted cases (excluding consumer and regulatory reports)
	3B	All serious attributable clinical trial cases which were received prior to the period of this PSUR but unblinded during the reporting period. *No cases have been received so Appendix 3B is empty.*
	3C	All non-serious listed cases (excluding consumer and regulatory authority reports)
	3D	All non-medically verified cases

Explanation of line listings content

Within the line listings a case is considered serious if it fulfils the ICH definition of serious (see section 6.1). Serious cases are identified by a "#" beside the case ID.

An unlisted case contains at least one AE that is not covered by the CSI which was in place at the time of data entry.

The AEs within a case are presented at MedDRA PT level. System Organ Class (SOC) is assigned automatically according to the Primary AE.

Literature citations for all published cases are noted in the „Comments" column of the line listing.

6.3. Cases Presented as Summary Tabulations

An aggregate summary for each of the line-listings is presented in Appendices 4 as summarised below and in Table 2. All AEs are presented at MedDRA PT level within summary tabulations.

Appendix 4A contains all reported adverse events for cases included in Appendix 3A, meaning adverse events from all serious spontaneous cases (excluding consumer reports), all serious attributable clinical trial cases and all non-serious unlisted cases (excluding consumer and regulatory reports).

Appendix 4B contains all reported adverse events for cases included in Appendix 3C, meaning adverse events from all non-serious listed cases (excluding consumer and regulatory authority reports).

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Appendix 4C contains all reported adverse events from non-medically verified serious cases + non-medically verified non-serious unlisted cases.

Appendix 4D contains all reported adverse events from non-medically verified non-serious listed cases.

Appendix 4E is a cumulative tabulation of all unlisted events from serious unlisted spontaneous reports (including non-medically verified reports) and all serious unlisted reactions from clinical trial cases reported since launch.

Of note, differences may appear between numbers in the previous PSUR cumulative counts of unlisted events for the following reasons:

- changes in the listedness of some adverse events due to an update in the Reference Safety Information;
- increased consistency in the listedness assessment has been achieved following implementation of an automated listedness attribution applied to the case reports received;
- in "old" cases diagnostics could have been coded with signs and symptoms. These signs and symptoms are not included in the cumulative count anymore.
- in the previous tables all adverse events, listed and unlisted were taken into account while in the new outputs, only the unlisted adverse events are provided.

Table 2 Appended Summary Tabulations

Summary Tabulation	4A	All reported AEs for cases included in Appendix 3A
	4B	All reported AEs for cases included in Appendix 3C
	4C	All reported AEs from non-medically verified serious cases and non-serious unlisted cases
	4D	All reported AEs from non-medically verified non-serious listed cases
	4E	Cumulative tabulation of all unlisted events from serious unlisted spontaneous reports and all serious unlisted reactions from clinical trial cases reported since launch

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Explanation of summary tabulations content

The following information is important when evaluating the summary tabulations.

Seriousness

Adverse events from spontaneous, post-marketing or literature cases are only classified as serious within the tabulations if they are on the list of GSK medically serious terms (see Section 6.1). Therefore, although an AE may reside in a case that fulfils the ICH criteria of serious, if the event is not on the list of GSK medically serious terms it will appear within the non-serious column in the summary tabulations.

GSK believes that applying the GSK medically seriousness criteria to AEs will provide a consistent and more meaningful presentation of data within the tabulations, and help with aggregation of terms for signal review activities. Counts of events are presented in the tabulations for the reporting period of the PSUR and cumulatively (Appendix 4E).

Note: In rare situations an event may appear in both the ***serious and non serious*** *columns within the summary tabulations, this may occur for the following reasons:*

- *GSK only applies its list of medically serious terms to events reported in spontaneous reports, literature cases and post-marketing surveillance studies. Serious criteria for events originating from clinical trial cases are determined by the reporter. Therefore, as events can originate from different report sources seriousness assessments may differ.*

- *The GSK medically serious list is compiled at the MedDRA LLT level. Summary tabulations present counts of events at the MedDRA PT level. A PT may therefore have both serious and non serious LLTs associated with it.*

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Overview

An overview of the 2080 reports received in the time period is presented below.

Table 3 Reports received in Time Period of PSUR

REPORTS FULFILLING ICH E2C CRITERIA	NUMBER OF CASES
Serious Unlisted	465
Serious Listed	48
Non-serious Unlisted	649
Non-Serious Listed	54
TOTAL (ICH E2C criteria)	**1216**
OTHER REPORTS	
Non-Medically Verified	289
Regulatory, non-serious	575
TOTAL (Other reports)	**864**

GRAND TOTAL (All reports)	**2080**

The 2080 reports were received from 41 countries, mainly France (645 reports, 31%), Italy (602 reports, 28.9%) and Germany (339 reports, 16.3%).

Based on the initial reporting source, 783 cases were received from healthcare professionals and 1297 cases by non-healthcare professionals (consumers, regulatory authorities, representatives, literature, other).

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Table 4 shows the numbers of AEs by System Organ Class (SOC) for the whole dataset of cases received in the time period.

Table 4 Table of all AEs by SOC for all cases received in the time period of the PSUR

System Organ Class	Number of Cases
General disorders and administration site conditions	666 (32%)
Injury, poisoning and procedural complications	639 (30.7%)
Nervous system disorders	280 (13.5%)
Skin and subcutaneous tissue disorders	189 (9.1%)
Infections and infestations	75 (3.6%)
Respiratory, thoracic and mediastinal disorders	34 (1.6%)
Psychiatric disorders	27 (1.3%)
Vascular disorders	26 (1.3%)
Gastrointestinal disorders	24 (1.2%)
Blood and lymphatic system disorders	20 (1%)
Cardiac disorders	20 (1%)
Eye disorders	17 (0.8%)
Metabolism and nutrition disorders	15 (0.7%)
Musculoskeletal and connective tissue disorders	14 (0.7%)
Immune system disorders	11 (0.5%)
Investigations	9 (0.4%)
Surgical and medical procedures	9 (0.4%)
Congenital, familial and genetic disorders	2 (0.1%)
Hepatobiliary disorders	1 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps	1 (0%)
Social circumstances	1 (0%)
Total Cases	**2080**

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Compared to the previous PSUR period the SOC General disorders and administration site conditions raised from 20.5% to 32% in this PSUR and Injury, poisoning and procedural complications from 24.2% to 30.7% (two-fold increase of cases of inappropriate schedule of drug administration and wrong drug administered due to solicited interviews – see section on medication errors).

6.4. Manufacturer's Analysis of Individual Case Histories

As a company policy, all incoming adverse events are reviewed on an ongoing basis to detect any new safety signal. Once identified, all available data relating to the adverse events under review are routinely evaluated in a cumulative manner for a possible causal association with the suspect product.

The selection of the adverse events of interest as described in this section is based on the following criteria: reporting frequency, medical significance, severity of the events, mechanisms of action, issues that are being monitored, or requests by regulatory authorities.

The events of interest are described for all cases (irrespective of source, seriousness and listedness) within the PSUR review period. The events from the non-serious reports received solely from regulatory authorities are not included in the Line Listings and Summary Tabulations as per guideline E2C(R1). Separate Line Listings and Summary Tabulations are provided for consumer reports as per guideline E2C(R1). Therefore some reports may be reviewed and described in this section but will not appear in the line listing and summary tabulations of the PSUR.

The events are presented by MedDRA System Organ Classes (SOCs). Reports with a fatal outcome are discussed separately, regardless of the SOC of the primary AE is classified by MedDRA.

Where relevant, a company comment is provided.

6.4.1. Cases with a Fatal Outcome

A total of 14 cases with a fatal outcome were received during the reporting period. Narratives are presented in Appendix 5A. Note that non-medically verified reports are included. The narratives are produced directly from the safety database using a standard search strategy. The search strategy retrieves all cases in which the patient died or which are coded with MedDRA PTs indicating that death occurred. Thus the case narratives may include reports where the adverse event outcome is not specified as fatal in the line listings as well as reports of intra-uterine death or stillbirth.

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The following fatal cases are considered as possible Sudden Death:

Case **B0601431A** - MedDRA Preferred Term: Sudden infant death syndrome

This case was reported by a healthcare professional and described the occurrence of cot death in a 3-month-old female who was vaccinated with the 2nd doses of Infanrix hexa™ and Prevenar on 21 October 2009. Two days after vaccinations, the subject died in bed. The parents found the baby lying on the belly. Autopsy did not reveal any cause of death.

Company comment: Suspected case of SIDS, autopsy did not reveal clear cause of death. No details on medical history available. The subject received concomitant vaccination with Prevenar.

Case **B0605003A** - MedDRA Preferred Terms: Cardiac arrest, Convulsion, Hypokinesia

This case was reported by the Italian regulatory authority and described the occurrence of cardiac arrest in a 2-month-old female who was vaccinated with an unspecified dose of Infanrix hexa™ on 10 August 2009. Less than one day after vaccination, the subject experienced convulsions. The subject was hospitalised from 14 August until 19 August 2009. At the time of reporting, the event was resolved with sequelae. Last convulsion episode was on 18 October 2009. The baby showed a regular growth but a light motor retardation in respect of the age. Her weight was 7.10 kg. Diagnostic tests as karyotype, ultrasonography, computerized axial tomography and nuclear magnetic resonance were negative. She was treated with Luminalette. According to the follow up information received on 01 June 2010, the subject died due to a cardiac arrest at an unspecified time after vaccination.

Company comment: Case of Sudden Unexpected Death in Infancy (SUDI). The subject had a history of convulsions since 2-months of age, which started less than one day after vaccination with Infanrix hexa™. The final diagnosis was not reported, however, the child received anticonvulsive treatment. Cause of death was reported as cardiac arrest, but circumstances of death were not available. It was unknown whether an autopsy was performed.

Case **B0608494A** - MedDRA Preferred Terms: Sudden infant death syndrome, Depressed level of consciousness, Mouth haemorrhage, Nasopharyngitis

This case was reported by a healthcare professional and described the occurrence of cot death in a 14-week-old male who was vaccinated with the 2nd dose of Infanrix hexa™ and Prevenar on 12 November 2009. The child was born at term and weighed 4120 g. The child had a history of viral infection before vaccination with the 1st dose of Infanrix hexa™ and Prevenar. In the beginning of November, 2 weeks before death, the subject had a common cold. The subject did not experience any adverse events after vaccination. Four days after vaccination with Infanrix hexa™ and Prevenar, the subject was brought to day care centre. He had no fever.

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He burped well after being fed and was put into bed at 9:25 lying on the abdomen (with permission of the mother) and he was being checked every 20 minutes. At 12:00, the subject was nonresponsive and had blood in his mouth. Reanimation was started immediately and the the child was admitted to hospital. The child died on 16 November 2009 from sudden infant death syndrome. An autopsy was performed and did not reveal any cause of death found in autopsy or on toxicological investigation.

Company comment: Possible case of SIDS. The subject had viral infections as medical history. No adverse events were reported after vaccinations. The subject was placed in prone position into bed. No clear cause of death was found on the autopsy.

Case **B0639243A** - MedDRA Preferred Terms: Sudden infant death syndrome, Asphyxia

This case was reported by a physician and described the occurrence of sudden infant death in a 7-week-old female four days after vaccination with unspecified doses of Rotarix and Infanrix hexa™. The reporter informed that the subject experienced suffocation during sleep.

Company comment: Case of SUDI or suspected SIDS. No medical history and circumstances of death were reported. The subject, according to the reporter, experienced asphyxia during sleep. It was unknown whether an autopsy was performed.

Case **B0657890A** - MedDRA Preferred Terms: Sudden infant death syndrome, Apnoeic attack, Pallor, Oxygen saturation decreased, Heart rate decreased

This case was reported by a healthcare professional and described the occurrence of sudden infant death syndrome in a 2-month-old male who was vaccinated with unspecified doses of Infanrix hexa™, RotaTeq and Prevenar on 27 April 2010. Concurrent medical condition included premature birth at 26 weeks of gestation. Twelve hours after vaccination, the subject went dusky and experienced apnoea attack, reduced oxygen saturation and decreased heart rate. The subject was hospitalised. Relevant test results included: heart rate more than 100 bpm, pO2 over 94 %, normal cranial ultrasound and ophthalmological examination. The subject was treated with mechanical ventilation, stayed under observation for 48 hours and was discharged. Three days after discharge, the subject had another episode of apnoea and could not be resuscitated. The subject died from sudden infant death syndrome 5 days after vaccination.

Company comment: Case of SUDI. The subject died due to apnoea attack, likely related to his severe prematurity. It was unknown whether an autopsy was performed.

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Case **D0064259A** - MedDRA Preferred Terms: Cardiac arrest, Sudden infant death syndrome, Sepsis, Viral infection, Resuscitation, Pyrexia, Loss of consciousness, Cyanosis

This case was reported by the German regulatory authority and described the occurrence of cardiovascular arrest in a 3-month-old male who was vaccinated with the 2nd dose of Infanrix hexa™ and Prevenar on 29 September 2009. The subject's parents have separated about two weeks prior to the events. The subject was cared for by the father with the help of his sister-in-law and mother-in-law. The subject did not experience any adverse event between date of vaccination and date of death. Approximately three days post-vaccination, in the morning around 07:30 the subject appeared normal. About half an hour later, at around 08:00, the subject was supposed to be fed with a bottle. The subject was found unconscious and the subject's body was blue (cyanosis). Upon arrival of an emergency physician the pupils were medium wide, no pulse could be determined and oxygen saturation could not be measured. The subject was intubated and cardiopulmonary resuscitation was started. Under ongoing resuscitation the subject was transferred to a hospital. In hospital the subject was treated with adrenaline and atropine. Echocardiography and ECG both showed no detectable heart reaction. Body temperature, taken in the ear, was 39.4 degC. Resuscitation was without success and was stopped. An autopsy was performed, but results were not conclusive. According to autopsy both SIDS and viral infection were possible causes of death. External force and shaken baby syndrome were excluded by autopsy.

Company comment: Case of SUDI. The subject died due to cardiac arrest 3 days after multiple vaccinations. The autopsy results were inconclusive and considered SIDS and viral infection as possible causes of death.

Case **D0064689A** - MedDRA Preferred Term: Sudden infant death syndrome

This case was reported by the German regulatory authority and described the occurrence of SIDS in 3-month-old male subject who was vaccinated with unspecified doses of Synflorix and Infanrix hexa™ on 04 November 2009. The subject has no underlying or concurrent medical conditions or other risk factors. The subject has received previous vaccination with Synflorix™ and Infanrix hexa™. It was unknown how previous vaccinations were tolerated. Approximately nine days post-vaccinations, the subject was found lifeless in bed in supine position covered by a cushion/pillow. An emergency physician was only able to certify death. Police reported that the children's room was severely overheated and in the whole apartment people had been smoking. Autopsy was performed and showed age-corresponding state of development and very good state of care. Multiple punctual haemorrhages up to the size of a pinhead were found under the thymus capsule, subepicardial and on the surface of the lungs. Distinct disorder of blood distribution was seen in the lungs as well as increased fluid and blood content in the lungs and foam in the respiratory tract (pulmonary edema). Neither signs of external force by a third party nor signs of shaken baby syndrome have been detected.

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No signs of organic malformation have been detected. The cause of death could not be unambiguously determined. Punctual haemorrhages under the thymus capsule, subepicardial and on the surface of the lungs were normally seen within the scope of SIDS and therefore the autopsy performing physicians considered SIDS. Possible risk factors associated with SIDS included coverage with a pillow, severely overheating, not feeding with breast milk and passive smoking. Furthermore autopsy showed increased water retention of the lungs as well as distinct disorder of blood distribution within the lungs, which could be signs of a beginning pulmonary infection. Microbiological examinations, performed on 20 November 2009, showed solitary *St. aureus* in both pulmonary swabs and a single *St. aureus* colony in the spleen swab as potential infectious agent, but this bacterium was also known as normal bacterial flora of the upper respiratory tract. All other bacteria found belong either to physiological intestinal flora or were normal parts of the throat and skin flora. Therefore infectious events could be excluded with some probability.

Company comment: Case of SUDI. The subject died 9 days after multiple vaccinations. The autopsy results were inconclusive and considered SIDS (in presence of numerous risk factors) and pulmonary infection as possible causes of death.

Case **D0065445A** - MedDRA Preferred Term: Sudden infant death syndrome

This case was reported by a physician and described the occurrence of SIDS in a 3-month-old female one day after vaccination with the 1st dose of Infanrix hexa™ and Prevenar on 09 December 2009. The subject's development and weight gain were normal, her medical history was unsuspicious. She was breast-fed for three months. Post-vaccinations the subject did not experience fever. Next morning after vaccinations, the subject was normally drinking and was put in bed. Approximately two to three hours later, the subject was found lifeless in bed in supine position. The subject died on 10 December 2009 from SIDS. An autopsy was performed, but no results were available.

Company comment: Suspected case of SIDS. The subject died 1 day after multiple vaccinations. Subject's medical history was unsuspicious, no adverse event were reported after vaccinations. Autopsy was performed, but the results were not available.

Case **D0066068A** - MedDRA Preferred Term: Sudden infant death syndrome

This case was reported by a physician and described the occurrence of possible SIDS in a 3-month-old male who was vaccinated with unspecified doses of Infanrix hexa™ and Prevenar on 29 December 2009. The subject had three healthy siblings. He was a healthy term baby and was breast-fed. The subject's mother did not smoke. The subject had received the last meal, consisting of mother's milk on 29 December 2009 in the evening. Later on in the evening, the subject was found dead under unknown circumstances in bed. An autopsy was performed. The results of autopsy were inconclusive and showed no obvious cause of death. Therefore cause of death was considered to be SIDS.

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Company comment: Possible case of SIDS. The subject died less than 1 day after multiple vaccinations. Subject's medical history included healthy term baby, without underlying condition. Autopsy did not reveal clear cause of death.

Case **D0067790A** - MedDRA Preferred Terms: Sudden infant death syndrome, Death, Apnoea, Cardiac arrest, Loss of consciousness, Resuscitation

This case was reported by the German regulatory authority and described the occurrence of SIDS in a 9-week-old male who was vaccinated with Infanrix hexa™ and Prevenar on 31 March 2010. Complication during pregnancy included cranial haemorrhage of the mother due to cerebral artery aneurysm in the 19th week of gestation. The subject was born in the 33rd week of pregnancy by Caesarean section. At that time the subject was immature with a birth weight of 1805g with mild respiratory distress syndrome. Postnatal the subject showed good adaptation, but chest X-ray, performed on 28 January 2010, showed mixed picture of mild neonatal respiratory distress syndrome and wet lung. Repeated sonography and neonatal screening were normal. Concurrent medications included colecalciferol and iron salt. For the third child health check, performed on 04 March 2010, the subject showed normal development concerning weight, length and head circumference. The subject showed no pathologic findings except mild hydrocele. However, according to percentile curve of the WHO the subject was in reduced nutritional condition with a weight of 3700g and a height of 55cm. Approximately 3 days after vaccinations in the morning the subject experienced apnoea. When the emergency care team arrived the subject was unconscious. Cardiac arrest with apnoea and asystole was diagnosed. Resuscitation was unsuccessful. Concurrent medical conditions included old contusion and hematoma on right side of chest. An autopsy was performed and macroscopically, did not reveal unambiguous cause of death. All autopsy findings were suggestive for SIDS. The findings not consistent with SIDS (skin fissures in the corner of mouth, ecchymoses in area of central chest wall, hemorrhage in capsule of adrenal gland and kidney) can be explained with plausibility by long and continuous resuscitation. Further toxicological examination could not identify the cause of death. According to the report on the histological examination, results largely confirmed the findings of the autopsy.

Besides unspecific signs of death, punctuate haemorrhage of the organs' connective tissue coatings and pulmonary emphysema were considered the essential findings. Acute emphysema could be interpreted as evidence of suffocation. It was concluded that definite cause of death could be identified, neither in histological examinations nor in toxicological tests. It was discussed that the toxicological tests covered a certain spectrum of substances only and would miss some rare and exceptional substances. Because of the combination of pulmonary emphysema and the fissures at the left corner of the mouth, which had been observed during the autopsy, death due to suffocation following violent obstruction of respiratory orifices could not be excluded. Likewise it could not be excluded that these findings were caused during the reanimation procedures.

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Company comment: Case of SUDI. Preterm subject, with respiratory distress in medical history, died approximately 3 days after multiple vaccinations. Autopsy did not reveal clear cause of death. Majority of findings were within SIDS, however violent obstruction of respiratory tract could not be excluded.

The following fatal cases were significantly confounded by concomitant disease and/or medication and/or vaccination and are not suggestive of sudden death:

Case **B0661542A** - MedDRA Preferred Terms: Metabolic disorder, Ataxia, Balance disorder, Diplopia, Strabismus, Nervous system disorder

This case was reported by a physician and described the occurrence of ataxia in a 6-month-old male who was vaccinated with the 3rd doses of Infanrix hexa™ and Prevenar in March 2010. The subject's medical history included episodes of shaking head, arms and legs several times a day, which occurred at the age of 5 months. Five days after vaccinations, the subject experienced ataxia, instability and diplopia (described as strabismus). The physician suspected a possible neurological alteration. The subject was hospitalized and some relevant tests (NMR, ECG, CSF, other unspecified laboratory tests, nasopharyngeal exudates) were performed and showed normal results. Catecholamine and muscular biopsy results were pending. The ataxia remained until the age of 9 months. The shaking moves have repeated in some occasions. The subject was hospitalized in an intensive care due to a possible aspiration from 16 to 24 June 2010. He underwent EEG in July 2010 and it showed 3 lesions compatible with metabolic disorder. The final diagnosis was a possible metabolic disease with very limited clinical picture. According to the follow-up information received in August 2010, the subject died in July 2010 due to a possible metabolic disorder of a mitochondrial origin.

Company comment: The subject died due to a possible metabolic disorder of a mitochondrial origin several months after 3d vaccination with Infanrix hexa™ and Prevenar. It was unknown whether an autopsy was performed.

The following cases were considered too poorly documented to allow for an appropriate medical assessment:

Case **B0599802A**- MedDRA Preferred Term: Death, Adverse drug reaction

This case was reported by a healthcare professional and described the occurrence of death NOS (not otherwise specified) in a 4-month-old female who was vaccinated with the 3rd dose of Infanrix hexa™ and Prevenar on 15 October 2009. Eleven days after vaccination the subject experienced death NOS. The subject experienced adverse drug reaction and was found dead in her bed after her afternoon nap. The subject had no concomitant medication and no relevant medical history. The subject was transferred to hospital. Hospital report was pending. No autopsy was performed. Follow-up information has been requested.

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Case **D0063296A** - MedDRA Preferred Term: Death

This case was reported by the German regulatory authority and described the occurrence of death in a 12-week-old male who was vaccinated with unspecified doses of Infanrix hexa™ and Prevenar on 9 January 2006. The subject"s mother suffered from epilepsy. The subject was exposed in utero to levetiracetam during about the first three months of pregnancy. The rest of pregnancy and birth was inconspicuous, except for fracture of a clavicle. Concurrent medical conditions included agitation and crying abnormal (whiny baby). Approximately 11 days post-vaccination, the subject died. The cause of death was not further specified. It was unknown whether an autopsy was performed.

Case **D0069211A** - MedDRA Preferred Term: Death

This case was reported by a physician and described the occurrence of unspecified death in a child of unspecified gender who was vaccinated on an unspecified date with an unspecified 6-valent vaccine and unspecified pneumococcal vaccine (manufacturers unspecified). One day after vaccinations, the subject was hospitalised to a paediatric intensive care unit and reanimated, but died from unknown cause. An autopsy was performed. Follow-up information has been requested.

6.4.2. Other adverse event of interest

6.4.2.1. Blood and lymphatic system disorders

6.4.2.1.1. Idiopathic thrombocytopenic purpura, Thrombocytopenia, Thrombocytopenic purpura

Eleven serious cases including the event idiopathic thrombocytopenic purpura (n=6), thrombocytopenia (n=6) or thrombocytopenic purpura (n=1) were received during the period of this PSUR and are described below.

Case **B0615557A**- MedDRA Preferred Term: Thrombocytopenia

This case was reported by the Italian regulatory authority and described the occurrence of thrombocytopenia in a 5-month-old male who was vaccinated with Infanrix hexa™. No information was provided regarding medical history. On 14 October 2009 the subject received the 2nd dose of Infanrix hexa™. On 5 November 2009, 22 days after vaccination, the subject experienced thrombocytopenia. The subject was hospitalised. At the time of reporting the outcome of the event was unspecified.

Company comment: The symptoms and signs leading to this diagnosis in a 5 month-old-baby were not reported. No results of any diagnostic tests to exclude other causes of thrombocytopenia were reported.

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Case **B0619820A-** MedDRA Preferred Terms: Idiopathic thrombocytopenic purpura, Haematoma, Rectal haemorrhage, Purpura

This case was reported by a physician and described the occurrence of purpuric spots in a 3-month-old male who was vaccinated with Infanrix hexa™ and Prevenar. Past vaccinal history included a first injection of Infanrix quinta at an unspecified date, without problem. The subject had no past medical history of purpuric spots. On 04 December 2009, the subject received a 2nd dose of Infanrix hexa™ and an unspecified primary dose of Prevenar. In the evening the subject presented with several purpuric spots on the body (not specifically on lower limbs). At an unspecified date, the subject developed small hematomas. On 21 December 2009, new purpuric spots had appeared on trunk, anal area, neck and nape of the neck. Events included also rectal haemorrhage. The subject was hospitalised and a diagnosis of idiopathic thrombocytopenic purpura was made. Platelet count showed thrombocytopenia. He was treated with immunoglobulin which was inefficient. He was then given a transfusion on unspecified date and events resolved. On 03 March 2010, the subject received a third dose of Infanrix quinta, without recurrence of the events.

Company comment: No data confirming immunological cause of the event was provided. Detailed diagnostic tests are lacking. On the basis of the information provided, the time to onset appears to be rather short. Immunoglobulin therapy was inefficient and subject recovered only after blood transfusion. Negative re-challenge after 3d dose of Infanrix quinta.

Case **B0630988A-** MedDRA Preferred Terms: Thrombocytopenic purpura, Viral infection, Pyrexia, Rash, Petechiae, Ecchymosis

This case was reported by the Italian regulatory authority and described the occurrence of thrombocytopenic purpura in a 12-month-old female after vaccination with a 3rd dose of Infanrix hexa™ and unspecified dose of MMR II (non-GSK). Previous vaccinations were well tolerated. Fifteen days after vaccination with Infanrix hexa™ and MMR II and a few days after a viral infection (with fever and exanthema), the subject was hospitalized on 30 June 2007 with petechia and ecchymosis. Platelet count gradually rose on 30 June 2007: 4000; on 2 July 2007: 8800; on 5 July 2007: 13500; on 13 July 2007: 17500 and on 20 August 2007: 161000. The subject was diagnosed with thrombocytopenic purpura and was treated with prednisone.

Company comment: The event was observed 15 days after multiple vaccinations and a few days after onset of an acute viral illness.

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Case **B0652855A** - MedDRA Preferred Terms: Purpura, Petechiae, Thrombocytopenia

This case was reported by the French regulatory authority and described the occurrence of purpura in a two-month-old female who was vaccinated with Rotarix, Infanrix hexa™ and Prevenar. During the ninth month of pregnancy, her mother received an unspecified dose of swine flu H1N1 vaccine (unknown manufacturer). On 03 February 2010, the subject received an unspecified dose of BCG vaccine (non-gsk). On 01 March 2010, the subject was vaccinated with an unspecified dose of Rotarix, Infanrix hexa™ and Prevenar. Six days after vaccination, the subject developed purpura and petechia around mouth and then, on hands and feet. On 08 March 2010, petechia had extended to the abdomen. The subject had no fever. On 10 March 2010, the subject was hospitalised. Blood work-up showed WBC at 5.5 G/L with neutrophils at 2.5 G/L, Hb 9.2 g/dL, platelets count at 4 G/L (thrombocytopenia), C-reactive protein at 1 mg/L, normal value of liver enzymes. Viral serologies were negative for EBV, CMV and Toxoplasma and positive for Parvovirus (Parvovirus B19 serology). Coombs test was negative. The subject was treated with normal immunoglobulin. On 11 March 2010, platelet count was at 47 G/L.
The purpura and petechia resolved within an unspecified period of time. Outcome of thrombocytopenia was unspecified.

Company comment: This two-month-old female experienced thrombocytopenia 6 days after multiple vaccinations. Positive serology test to Parvovirus infection provides a plausible alternative explanation for the reported events.

Case **B0656703A**- MedDRA Preferred Terms: Idiopathic thrombocytopenic purpura, Petechiae, Abnormal behaviour, Purpura

This case was reported by the French regulatory authority and described the occurrence of idiopathic thrombopenic purpura in a 2-month-old male who was vaccinated on 19 March 2010 with unspecified doses of Infanrix hexa™ and Prevenar. Medical conditions were unspecified. On 27 March 2010, eight days after vaccinations, the subject presented with disturbed behavior and purpuric rash which generalized on 28 March 2010, without fever. On 28 March 2010, the subject was hospitalized. Full blood count showed platelet at 14000/mm3, Hb at 12.6 g/dl and WBC 12270/mm3. Treatment with cefotaxime and vancomycine was started. The subject was transferred in another hospital. Physical examination showed petechiae on soft palate and tongue and purpuric spots all over the body. Lab tests showed platelet lower than 10000/mm3 and reticulocytes at 57200/mm3. Coombs test was negative. Cerebral CT scan and thorax X-ray were normal. On 28 and 30 March 2010, normal immunoglobulin was administered at 0.8 g/kg. Clinical course was favourable with platelet at 136000/mm3 on 31 March 2010. The reporter concluded to an idiopathic thrombopenic purpura. At the time of reporting, the events were resolved without sequelae.

Company comment: Medical conditions were not reported. The narrative did not exclude recent infection, based on increase value of WBC, which may be a trigger of the event. Coombs test was negative.

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Case **B0665357A**- MedDRA Preferred Term: Thrombocytopenia

This case was reported by the Italian regulatory authority and described the occurrence of thrombocytopenia in a male subject of unspecified age who was vaccinated at an unspecified date with an unspecified dose of Infanrix hexa™. The subject was hospitalised. At the time of reporting, the outcome of the event was unspecified.

Company comment: This report lacks important information for medical assessment.

Case **D0066805A**- MedDRA Preferred Terms: Idiopathic thrombocytopenic purpura, Haematoma, Petechiae, Mouth haemorrhage

This case was reported by a physician and described the occurrence of idiopathic thrombocytopenic purpura in a 12-month-old female who was vaccinated with Priorix™ Tetra and Infanrix hexa™. The subject"s medical history included influenza-like infection one week prior to vaccination. The subject had no relevant underlying or concurrent medical conditions and received no concomitant medication. Former vaccinations with Infanrix hexa™ in February 2009, March 2009 and April 2009 were well tolerated. On 27 November 2009 the subject received the 1st dose of Priorix™ Tetra and the 4th dose of Infanrix hexa™. On 16 December 2009, 19 days after vaccination with Infanrix hexa™ and Priorix™ Tetra, the subject experienced ITP. Diagnosis was based on laboratory test (haemogram). The subject was hospitalised from 20 December 2009 to 28 December 2009 due to suspected chronic idiopathic thrombocytopenia. At admission the subject was in good general conditions, nutritional status normal, petechiae on neck to left shoulder and on the top of the head fronto-temporal (left side), multiple hematoma different in size and age on legs and sporadic on arms, one hematoma on bottom (right side), small petechiae on roof of mouth - soft palate. Other physical and neurological examinations were without findings. Blood tests showed slight signs of anaemia and infection. In the course of hospital stay remission of petechiae with gradual increase of thrombocytes was achieved. During check-up after hospital discharge there was only a minimal increase of thrombocytes up to 30000. A sonography performed on 20 January 2010 was normal. The duration of ITP was two weeks. Required treatment did not include blood transfusion, platelet transfusion, gamma globulin, and corticosteroid.

Company comment: This 12-month-old female experienced ITP 19 days after administration of the 4th dose of Infanrix hexa™ and the 1st dose of Priorix tetra. The subject's influenza-like infection one week before may be considered as a plausible alternative explanation for the reported events. The purpura resolved, but thrombocytopenia persisted after hospital discharge. No tests confirming immunological cause of ITP were provided.

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Case **D0067175A-** MedDRA Preferred Terms: Idiopathic thrombocytopenic purpura, Thrombocytopenia, Petechiae

This case was reported by the German regulatory authority and described the occurrence of idiopathic thrombocytopenic purpura in a 4-month-old female who was vaccinated with Infanrix hexa™ and Prevenar. There was no concurrent medical condition. On 28 July 2009 the subject received 1st dose of Infanrix hexa™ and Prevenar. On 28 August 2009, 31 days after vaccinations, the subject experienced ITP and thrombocytopenia (platelet count was 4000/mcl). The subject was hospitalised for further diagnostics because of increasing petechiae. After discharge from hospital beginning of September 2009, the subject visited the hospital for regular follow ups. Platelet count was normalizing quickly. After 8 weeks, in October 2009, the events were resolved spontaneously. After the 2nd vaccination with Infanrix hexa™ and Prevenar on 4 November 2009, the events did not recur.

Company comment: This 4-month-old female subject experienced ITP 31 days after administration of multiple vaccines. The case lacks data to confirm immunological cause of the event. No treatment provided in a hospital and results of laboratory tests were reported. Negative re-challenge after the 2d doses.

Case **D0067177A -** MedDRA Preferred Terms: Thrombocytopenia, Idiopathic thrombocytopenic purpura, Gastroenteritis, Petechiae, Haematoma, Vomiting, Diarrhoea, Injection site inflammation, Injection site induration, Incorrect route of drug administration

This case was reported by the German regulatory authority and described the occurrence of thrombocytopenia in a 15-month-old female who was vaccinated with Priorix Tetra, Infanrix hexa™ and Prevenar. Previous 3 vaccinations with Infanrix hexa™ and Prevenar on 7 April, 14 May and 5 July 2009 were well tolerated. On 29 January 2010 the subject received 1st dose of Priorix. The subject"s medical history included premature baby. Concurrent medications included Iron salt. Previous medications included Paracetamol a few days before start of the events.
On 25 February 2010 the subject received the 4th doses of Infanrix hexa™ (right thigh) and Prevenar (left thigh). On 25 February 2010, less than one day after vaccinations, the subject experienced livid injection site inflammation and injection site induration (3 x 5 cm) on the left thigh. On 25 February 2010, a blood sample was taken because of a ferrum therapy. This blood sample showed thrombocytopenia of 25 G/l. The parents did not see any petechiae or hematoma. The subject was hospitalised. On admission examination, the subject was in good general condition. There were solitary petechiae and 2 small hematomas on right knee. ITP was diagnosed. The subject did not receive therapy for thrombocytopenia.
During hospital stay, since 04 March 2010 the subject experienced gastroenteritis with recurrent vomiting and watery stools. The subject was treated with parenteral hydration. After gastroenteritis was improved, thrombocyte count increased (34 G/l), the subject left the hospital in good general condition. At the time of reporting the outcome of ITP, injection site inflammation, injection site induration, petechiae and hematoma was unspecified. It was reported that the last blood test in March 2010 showed normal platelet count.

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Company comment: Events occurred on the same day as of vaccination with Infanrix hexa™ and Prevenar. There were no symptoms of bleeding, and the thrombocytopenia was diagnosed on blood test. Reported time to onset of less than 1 day is rather short. Underlying iron therapy suggests anaemia of unspecified genesis. It was reported that no specific therapy was prescribed and thrombocytopenia resolved spontaneously. .

Case **D0068471A** - MedDRA Preferred Terms: Idiopathic thrombocytopenic purpura, Petechiae, Haematoma, Hypochromic anaemia, Upper respiratory tract infection, Rhinitis, Pyrexia, Constipation

This case was reported by the German regulatory authority and described the occurrence of ITP in an 8-month-old male who was vaccinated with Infanrix-IPV/Hib, Infanrix hexa™ and Prevenar. Concurrent medical conditions included constipation and rhinitis. On 03 July 2008 and 28 August 2008 the subject received the 2 dose of Infanrix hexa™ and Prevenar. Vaccinations have been well tolerated. On 10 November 2008 the subject received a dose of Infanrix-IPV/Hib and developed 25 days later, on 05 December 2008, ITP. Thrombotic thrombocytopenic purpura, leukaemia, von Willebrand syndrome and infection were excluded. Diagnosis of ITP was supported by results of blood counts and bone marrow puncture. The subject was hospitalized because of hematoma and petechiae. The subject was treated with a single dose of intravenous immunoglobulin. Thrombocytes count increased to 49 000 cells/mcl. Then thrombocytes went down to 14000 cells/mcl again, and the subject was hospitalized again. A few days prior to this hospitalization the subject had developed rhinitis. At the time of hospitalization, mild hematoma was observed on the subject‟s forehead. The subject was treated with intravenous immunoglobulin and thrombocyte count increased to 72000cells/mcl. Hypochromic microcytic anemia was evident in lab results on 12 December 2008. Subsequently the subject was treated with steroids. The subject was hospitalized again between 08 and 09 February 2009 because of fever and upper respiratory tract infection which started on 06 February 2009. Diagnosis also included ITP and chronic constipation. At the time of hospitalization the subject had hematoma and petechiae. The subject‟s thrombocytes were 25 000 cells/mcl on 08 February 2009 and 54000 cells/mcl on 09February 2009. The subject was treated with Metamizol. Beginning of April 2010, thrombocytes count showed 60000 cells/mcl. Fourteen days later, on 27 April 2010, the subject developed again haematomas, which was diagnosed as relapsing ITP. During further course, thrombocyte count decreased to 10000 cells/mcl, but the subject had minor haematoma and petechiae. Concurrent immune defect was excluded. Lymphocyte sub-typing on 13 May 2010 showed normal result except of mildly decreased B-lymphocytes cell count, weakened antibody-dependent cell-mediated cytotoxicity and decreased cell count of natural killer cells.
Since 03 June 2010, the subject was treated with mycophenolate mofetil (CellCept) for immune suppression, which was well tolerated. Thrombocyte count increased slowly (up to 87000/mcl on 01 July 2010). Due to again decreased thrombocyte counts (22000/mcl), subject‟s mother decided to discontinue treatment with CellCept on 17 July 2010. On 21 July 2010, the subject went to see the doctor. He had no haematomas and no petechiae. His state in general was uneventful.

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Company comment: The subject experienced a first episode of chronic ITP 25 days after dose of Infanrix-IPV/Hib vaccine. No immune cause of this event was confirmed. No clear triggers of further episodes were reported.

Case **D0069059A** - MedDRA Preferred Terms: Warm type haemolytic anaemia**,** Thrombocytopenia, Jugular vein thrombosis, Jaundice acholuric, Incorrect route of drug administration

This case was reported by a consumer via the German regulatory authority and described the occurrence of warm type hemolytic anemia in a 4-month-old male 5 days after vaccination on 5 August 2010 with the 1st dose of Infanrix hexa™ and Prevenar. The subject was hospitalised from 10 to 21 August 2010 and from 29 August to 29 September 2010. Another dose of both vaccines was administered at an unspecified date. According to the hospital report from second hospitalisation, the subject"s medical history included neonatal jaundice in the first six days of life. No haemolytic or congenital diseases were known in the family. The grandmother lost two infants within the first year of life, but the cause of death was unknown. The subject had an upper airway infection approximately four weeks prior to hospitalisation. When admitted, the subject showed scleral jaundice, skin jaundice, firm liver was palpable 4 cm below rip bow, spleen palpable adjacent. Blood tests showed low values of haemoglobin and RBC, high bilirubin and reticulocyte counts and a normal platelet count. The subject was diagnosed with autoimmune haemolytic anaemia, haemolytic jaundice, thrombocytopenia with suspect immune thrombocytopenia and jugular vein thrombosis at the right. The subject was first hospitalised to an intensive care unit. Because of distinct anaemia and haemolysis, the subject was treated with red blood cells. Autoimmune antibodies of warm type could be detected as a cause of haemolysis. Treatment with prednisolone was without success, with high haemolysis parameters and transfusion in further course. Because additional development of immune thrombocytopenia was suspected, treatment with immunoglobulin was started, but the effect was lasting only a short time. Finally treatment with rituximab was started, which was well tolerated. Haemolysis parameters normalised and haemoglobin value stabilised at 8.1 g/dl.

Company comment: Subject developed haemolytic anaemia 5 days after vaccination with the 1st dose of Infanrix hexa™ and Prevenar. The subject had neonatal jaundice at birth and a respiratory infection approximately 3 weeks before vaccinations. Warm type haemolytic anaemia was diagnosed, but no laboratory tests were provided. Immune thrombocytopenia was suspected, however platelets count was normal.

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6.4.2.1.2. Warm type haemolytic anaemia

One serious case was reported with the PT „warm type haemolytic anaemia".

This case (**D0069059A**) is described in section 6.4.2.1.1 on thrombocytopenia.

6.4.2.2. Cardiac disorders

6.4.2.2.1. Cyanosis

Fifty cases including the event cyanosis were identified during the period of this report.

Most cases (45/50) were reported in association with a concurrent disease likely to have caused cyanosis, as shown in Table 5. Only 1 concurrent disease is shown per case, however more than 1 relevant concurrent disease may have been reported for a given case.

Table 5 Concurrent diseases reported in 44 cyanosis cases identified during the period of this PSUR

Concurrent disease	Case IDs
Seizures (n=13)	B0604826A; B0629094A; B0641899A; B0669299A; B0670625A; B0676877A; B0677130A; D0066414A; D0067732A; D0068664A; D0068927A; D0069021A; D0069116A
HHE (n=4)	B0632568A; B0661768A; B0668109A; B0677571A
Hypotonia (n=14)	B0604992A; B0614414A; B0614538A; B0629247A; B0636914A; B0641793A; B0643302A; B0645116A; B0647347A; B0649654A; B0651462A; B0657507A; B0657949A; D0068505A
Hypertonia (n=1)	B0675492A
Apnoea (n=7)	B0632575A; B0633537A; B0653466A; B0660128A; B0661622A; B0673252A; D0065856A
Dyspnoea (n=1); Respiration abnormal (n=1)	B0651949A; B0658025A
ALTE (n=1)	D0064655B
(Pre)Syncope (n=2)	B0656982A; B0679695A
SIDS (n=1)	D0064259A (described in section 6.4.1)

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Of the 5 remaining cases:

Case **B0639439A** reported restlessness, crying uncontrollably, leukocytosis, cyanosis and injection site reaction occurring less than 1 day after vaccination in a 1-month-old male. Blood smear showed increased leukocytosis with deviation to the right. At the time of reporting, the events were resolved.

Case **B0642862A** reported perioral cyanosis and cyanosis on both-legs and on vulva in a 2-month-old female on the same day as vaccination with Infanrix hexa™ and Prevenar. Subject was treated with Paracetamol. Events resolved.

Case **B0651924A** reported cyanosis and fever (38 degC) in a 3-month-old male who was vaccinated with Infanrix hexa™ and Prevenar. EEG was negative. The subject was treated with paracetamol. At the time of reporting, the events were resolved.

Case **B0675235A** reported cyanosis with discomfort, emotional distress, erythema and screaming in a 2-month-old female on the same day as vaccination with unspecified doses of Infanrix hexa™ and Prevenar. The subject was treated with paracetamol (Calpol). The events resolved on the same day.

Case **B0677866A** reported persistent inconsolable crying associated with mottled skin, cyanosis and tachycardia in a 4-month-old male a few hours with Infanrix hexa™ and Prevenar. The subject was hospitalised and treated with Saccharose, paracetamol (Doliprane) and codeine phosphate (Codenfan). Events subsequently slowly improved.

6.4.2.3. Eye disorders

6.4.2.3.1. Gaze palsy

During the reporting period 24 cases of gaze palsy, all serious, have been received.

It concerned 15 males and 9 females, aged between 1 month and 2 years (median: 5.5 months). Time to onset ranged between less than 1 day to 7 days (median: less than 1 day). Outcome was reported as resolved in 19 cases, unresolved in 1 case and unknown at time of reporting in 4 cases.

Table 6 summarises cases of gaze palsy. Cases with bolded event terms are also analysed/summarised in the relevant sub-sections of section 6.4 of this PSUR.

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Table 6 Overview of cases of gaze palsy

Case ID	Age	Gender	Events PT Comma Sep	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Case Outcome
B0599801A	2 Months	Male	Depressed level of consciousness, Crying, Hyperhidrosis, Vasodilatation, Gaze palsy, Pyrexia, Inflammation	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		3 Seconds	Resolved
B0613669A	2 Months	Male	**Infantile spasms**, Gaze palsy, Muscle spasms, Sleep disorder, Condition aggravated, Motor dysfunction, Hypertonia	Infanrix-polio-HIB, Infanrix hexa		1 Weeks	Resolved
B0614538A	2 Months	Male	Respiration abnormal, Gaze palsy, Loss of consciousness, Pallor, **Cyanosis**, Hypotonia	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		5 Hours	Resolved
B0642185A	15 Months	Female	Altered state of consciousness, Gaze palsy, **Tonic convulsion**, **Convulsion**, **Epilepsy**, Gastroenteritis, **Febrile convulsion**, Hypertonia, Ear infection, Gastritis, Nasopharyngitis, Hypotonia, Body temperature increased, Vomiting, Diarrhoea, Pyrexia	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		5 Days	Unknown
B0646907A	11 Months	Male	**Convulsion**, Pallor, Gaze palsy, Loss of consciousness, Hypotonia, Pyrexia, Pain, Fatigue	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		2 Hours	Resolved
B0647634A	2 Months	Female	Gaze palsy, Pyrexia, Mental impairment, Crying	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Resolved
B0651462A	2 Months	Female	Loss of consciousness, Gaze palsy, Pallor, **Cyanosis**, Hypotonia, Vomiting	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		6 Hours	Resolved

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Case ID	Age	Gender	Events PT Comma Sep	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Case Outcome
B0652090A	12 Months	Male	**Convulsion**, Gaze palsy, Loss of consciousness, Pyrexia, Otitis media, Pallor	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Resolved
B0656946A	1 Months	Male	**Febrile convulsion**, Loss of consciousness, Gaze palsy, Pain, Skin warm, Respiration abnormal, Pyrexia, Crying	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		8 Hours	Resolved
B0660020A	11 Months	Female	Pneumonia, Loss of consciousness, Gaze palsy, **Convulsion**, Nasopharyngitis, Drooling, Pallor, Pyrexia	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		2 Hours	Resolved
B0662920A	2 Years	Female	Hypotonic-hyporesponsive episode, Depressed level of consciousness, Gaze palsy, Respiration abnormal, Injection site inflammation, Vomiting, Cold sweat, Injection site pain, Pallor, Pyrexia	Infanrix hexa		5 Hours	Resolved
B0668856A	2 Months	Male	Gaze palsy, Crying, Pyrexia, **Myoclonus**	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		4 Hours	Resolved
B0669299A	6 Months	Male	**Grand mal convulsion**, Loss of consciousness, Gaze palsy, **Cyanosis**, Pyrexia, Salivary hypersecretion, Somnolence, Hyperaemia, Escherichia urinary tract infection, Electroencephalogram abnormal	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Unknown
B0669438A	16 Months	Male	**Febrile convulsion**, Gaze palsy, Unresponsive to stimuli, Pyrexia	Infanrix hexa		1 Days	Resolved

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Case ID	Age	Gender	Events PT Comma Sep	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Case Outcome
B0675842A	12 Months	Male	**Convulsion**, Leukocytosis, Shock, Gaze palsy, Loss of consciousness, Pyrexia	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Cetirizine hydrochloride, Infanrix hexa, Pneumococcal vaccines (Non-GSK)	4 Hours	Unknown
D0064655B	3 Months	Male	Apparent life threatening event, **Cyanosis**, Hypotonia, Gaze palsy, Fatigue, Somnolence, Sleep apnoea syndrome, Gastroenteritis rotavirus, Apnoea, Apathy	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Rotavirus vaccine	0 Days	Unknown
D0066414A	5 Months	Female	**Convulsion**, **Febrile convulsion**, **Atonic seizures**, **Grand mal convulsion**, Pyrexia, Diarrhoea, Gaze palsy, **Cyanosis**, Disturbance in attention, Staring, Pharyngeal erythema, Rhinitis, Leukocytosis, Gastroenteritis, Gastroenteritis norovirus	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK), Ergocalciferol	0 Days	Unresolved
D0066491A	2 Months	Female	**Convulsion**, Gaze palsy, Muscle spasms, Tremor	Synflorix, Infanrix hexa	Ferrous glycine sulphate, Vitamin D	6 Hours	Resolved
D0067186A	14 Months	Female	**Febrile convulsion**, Loss of consciousness, Cataplexy, Gaze palsy, Pyrexia, Vaccination complication	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Resolved
D0067732A	3 Months	Male	**Convulsion**, Gaze palsy, Musculoskeletal stiffness, **Cyanosis**	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Resolved
D0067882A	5 Months	Male	Hypotonic-hyporesponsive episode, Gaze palsy, Hypotonia, Mental impairment, Feeling abnormal, Neutropenia	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Resolved

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Case ID	Age	Gender	Events PT Comma Sep	Suspect Drugs PT Comma Sep	Concurrent Drugs PT Comma Sep	Time To Onset Since Last Dose	Case Outcome
D0068260A	23 Months	Male	**Febrile convulsion**, Pyrexia, Diarrhoea, Gaze palsy, **Grand mal convulsion**, Pallor, Vomiting, Gastroenteritis	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		0 Days	Resolved
D0068398A	8 Months	Male	**Febrile convulsion**, Gaze palsy, Respiratory arrest, Respiratory tract infection, Pharyngeal erythema, Feeling of relaxation, Skin discolouration, Vaccination complication	Infanrix hexa, Pneumococcal vaccines (Non-GSK)		1 Days	Resolved
D0068914A	14 Months	Female	**Febrile convulsion**, Pyrexia, Fatigue, Gaze palsy, Loss of consciousness, **Grand mal convulsion**, Oxygen saturation decreased, Disorientation, Somnolence, Tachycardia, Pharyngeal erythema	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	0 Days	Resolved

6.4.2.3.2. Retinal haemorrhage

During the period of this report, two cases of retinal haemorrhage were received.

In case **B0677766A** the event was reported in the context of status epilepticus. This case is described in section 6.4.2.8.3 on seizures.

Case **B0636708A** - MedDRA Preferred Terms: Anaemia, Apnoea, Metabolic acidosis, Retinal haemorrhage, Child maltreatment syndrome

This case was reported by the Italian regulatory authority and described the occurrence of anaemia in a 3-month-old female who was vaccinated with unspecified dose of Infanrix hexa™ and Prevenar. On 3 July 2009, less than one day after vaccination, the subject experienced anaemia, apnoea, metabolic acidosis, retinal bleeding. The reporter suspected a shaken baby syndrome. The subject was hospitalised. At the time of reporting the events were resolved.

Company comment: The symptoms and tests results confirming the diagnosis of retinal haemorrhage were not reported. Child maltreatment syndrome was suspected. The event resolved.

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6.4.2.4. Gastrointestinal disorders

6.4.2.4.1. Diarrhoea haemorrhagic, Haematochezia, Melaena, Rectal haemorrhage

During the period of this report, 10 cases were received with one the following MedDRA Preferred Terms: diarrhoea haemorrhagic (n=1), haematochezia (n=7), melaena (n=1) and/or rectal haemorrhage (n=3).

In case **B0619820A** rectal haemorrhage was reported together with idiopathic thrombocytopenic purpura. This case is described in section 6.4.2.1.1 on idiopathic thrombocytopenic purpura.

In case **B0643201A** haematochezia was reported in association with intussusception, this case is summarised in section 6.4.2.4.2 on intussusception.

In case **B0651961A** diarrhoea haemorrhagic and rectal haemorrhage were reported in association with intussusception, this case is summarised in section 6.4.2.4.2 on intussusception.

In case **B0663295A** haematochezia was reported together with anaphylactic reaction. This case is described in section 6.4.2.5.1 on anaphylactic reaction.

The other cases are summarised below.

Case **B0605572A** - MedDRA Preferred Term: Haematochezia

This case was reported by a physician and described the occurrence of blood in stools in a 2-month-old male. In August 2009 and October 2009, the subject received the 1st and 2nd doses of Rotarix and Infanrix hexa™. Two to 3 days after each vaccination, the subject experienced blood in stools. Since onset of the event until the time of reporting, the subject was under non-dairy diet to exclude food allergy. The event lasted 2 to 3 days.

Company comment: Intermittent episodes of bloody stool occurred after multiple vaccinations. No medical history and diagnostic tests results were provided. No type of bleeding and other symptoms were reported

Case **B0615474A** - MedDRA Preferred Terms: Haematochezia**,** Diarrhoea, Pyrexia

This case was reported by a physician and described the occurrence of bloody mucus in stool in a 3-month-old male who was vaccinated with Infanrix hexa™. The subject did not have history of blood in stools. Medical condition included a possible acute gastroenteritis. In September 2009, the subject received a dose of BCG vaccine. In October 2009, the subject received a first dose of Infanrix hexa™ and a first dose of Prevenar. First dose of Infanrix hexa™ was well tolerated. On 13 November 2009 the subject received the 2nd dose of Infanrix hexa™. On the evening, the subject experienced fever at 38 deg C, which was treated with paracetamol.

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On 14 November 2009, he presented with mild soft and bloody mucous stool which lasted five days. The subject was seen in an emergency service. Stool culture performed on the same day was negative. On that same day, fever was resolved. In December 2009, physical examination was normal. The physician considered soft and bloody mucous stool as possibly related to an acute gastroenteritis episode.

Company comment: A 3-month-old male subject experienced the event one day after vaccination with Infanrix hexa™. Acute gastroenteritis was suspected, but no details on symptoms, physical examination, investigations and treatment were reported.

Case **D0068600A** - MedDRA Preferred Terms: Haematochezia, Mucous stools, Faeces discoloured, Crying

This case was reported by the German regulatory authority and described the occurrence of bloody stools in a 3-month-old male subject who was vaccinated with the 2nd doses of Infanrix hexa™ and Synflorix™. The subject has no underlying or concurrent medical conditions or other risk factors. Less than one day post-vaccination the subject was weepy and experienced yellow coloured stool which contained mucus and was blood-tinged (bloody stools) for about two days. The subject was not hospitalised for the events. Blood count, blood coagulation parameters and ultrasound scan were normal. After about two days, on 02 September 2009, the events were resolved.

Company comment: A 3-month-old male subject experienced bloody stools on the same day as of multiple vaccinations. All investigations were normal. The event resolved spontaneously, no treatment reported.

Case **D0068909A** - MedDRA Preferred Terms: Haematochezia, Crying, Mucous stools, Restlessness,

This case was reported by a physician and described the occurrence of blood in stools as well as crying episodes in a nearly 4-month-old female less than one day after vaccination with the 2nd doses of Rotarix™, Infanrix hexa™ and Prevenar. First dose of Rotarix™ was well tolerated. The subject was examined ambulatory in a hospital. The subject had mucus and blood in stool. She was restless and treated with paracetamol. The following day the amount of blood increased, the subject was eating less, but was calm. She had no diarrhea, fever, vomiting, constipation or hard stool and no rhinitis or cough. Clinical examination was normal, without exanthema, petechiae or hematoma. Digital rectal examination showed no blood. Blood test including coagulation and stool test for pathologic germs was without pathologic findings: negative in culture for Salmonella, Shigella, Yersinia, Campylobacter, Staphylococcus, negative for dyspepsia coli including EPEC (culture + agglutination), Campylobacter antigen. Sonogram of abdomen showed no invagination, but meteorically enlarged intestine. No treatment was necessary. Blood in stool was resolved 4 days after the onset, the other events resolved on an unspecified date.

Company comment: A 4-month-old male subject experienced bloody stools on the same day as of multiple vaccinations. The event resolved spontaneously and did not required treatment.

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Case **B0671786A**- MedDRA Preferred Terms: Rectal haemorrhage, Abdominal pain, Haematochezia

This case was reported by a physician and described the occurrence of rectal bleeding in a 2-month-old female who was vaccinated with the 1st dose of Infanrix hexa™ and unspecified dose of Prevenar. Two days after vaccinations, the subject experienced colic and rectal bleeding. About 2 weeks after vaccination, the subject experienced bloody stools and rectal bleeding. The subject was hospitalised. Colic and rectal bleeding resolved (lasted for 2 weeks).

Company comment: Rectal haemorrhage and haematochezia occurred 2 days after multiple vaccinations. Medical history, results of any investigations, treatment and outcome are unknown.

Case **B0624719A** - MedDRA Preferred Terms: Melaena, Oesophagitis, Pyrexia, Vomiting, Irritability

This case was reported by the Italian regulatory authority and described the occurrence of melaena, oesophagitis, fever, vomiting and irritability in a 2-month-old male on the same day as vaccination on 8 October 2007 with an unspecified dose of Infanrix hexa™. The events were reported as resolved in 5 months.

Company comment: The subject experienced the event on the same days as of vaccination. Concurrent reported oesophagitis and vomiting suggest an infection of upper digestive tract. The case lacks data for medical assessment.

6.4.2.4.2. Intussusception

During the period of this report, four cases of intussusception have been received.

In case **B0663295A** intussusception was reported together with anaphylactic reaction, this case is summarised in section 6.4.2.5.1 on anaphylactic reaction.

The other cases are summarised below.

Case **B0643201A**- MedDRA Preferred Terms: Intussusception, Haematochezia, Peritoneal disorder, Gastrointestinal inflammation, Gastrointestinal hypomotility, Intestinal dilatation, Abdominal rigidity, Body temperature decreased, Hypotonic-hyporesponsive episode, Rash maculo-papular, Sepsis

This case was reported by the Poland regulatory authority and described the occurrence of suspected intussusception in a 9-week-old subject of unspecified gender who was vaccinated on 6 January 2010 with unspecified doses of Rotarix™, Infanrix hexa™ and Prevnar. On 11 January 2010, 5 days after vaccination, the subject experienced merging maculo-papular rash and hypotonic-hyporesponsive episode. Subsequently, the child was hospitalised. On admission, the child had decreased body temperature (35.9 deg. C).

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An ultrasonography showed dilated intestinal loops, intestinal hypomotility and traces of fluid in the peritoneum. The child was referred to the Infectious Disease Clinic because of suspected sepsis. During the first days of admission, the child was in a serious condition and experienced haematochezia, hard abdomen and intestinal hypomotility. No pathological flora was isolated from the blood culture. Because of the vaccination with Rotarix, the possibility of spontaneously resolved intussusception was considered.
At the time of reporting the events were improved.

Company comment: The events occurred 5 days after multiple vaccinations in a 9-week-old subject. Spontaneously resolved intussusception was considered.

Case **B0651961A**- MedDRA Preferred Terms: Intussusception, Rectal haemorrhage, Diarrhoea haemorrhagic, Lymphadenopathy, Pyrexia, Vomiting, Dyspepsia, Scar, Wound infection, Diarrhoea

This case was reported by a physician and described the occurrence of intussusception in a 6-month-old male who was vaccinated with Rotarix™, Infanrix hexa™ and Prevenar. The subject had no medical history. Previous and/or concurrent vaccination included Infanrix hexa™ and Prevenar given on 12 January 2010. On 5 February 2010, the subject received the 1st dose of Rotarix™. On 12 March 2010, the subject received unspecified doses of Infanrix hexa™ and Prevenar and the 2nd dose or Rotarix. On 1 May 2010, the subject experienced fever, vomiting, digestive discomfort (painful crises) proctorrhagia, blood diarrhea, ileo-caecal intussusception of 12 cm and lymphadenopathy (presence of lymph nodes confirmed via echography).CRP was 2.21. The subject was hospitalised and treated with injection of contrast product (enema administration) to reduce the invagination but it was only partially successful. Then, he was operated without any resection of the intestine. According to the paediatrician, this was a mechanical invagination due to the presence of lymph nodes. On 3 May 2010, the subject experienced fever. On 4 May 2010, the subject experienced diarrhoea. A stool analysis was performed and showed the presence of adenovirus (type40/41). Following the surgery, the subject developed wound infection. At the time of reporting, the events were resolved with sequelae (scar).

Company comment: This 10-month-old subject experienced intussusception 7months after multiple vaccinations, in the context of gastroenteritis.

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Case **B0656738A** - MedDRA Preferred Terms: Intussusception, Small intestinal resection, Vomiting, Colectomy, Abdominal pain

This case was reported by a nurse and described the occurrence of intussusception in a 10-month-old female who was vaccinated with Rotarix, Infanrix hexa™ and Prevenar. Previous and/or concurrent vaccination included unspecified dose Infanrix hexa™, Rotarix™ and Prevenar given on 20 August 2009 and on 21 September 2009. On 22 October 2009, the subject received unspecified doses of Infanrix hexa™ and Prevenar. On 12 May 2010, 7 months after vaccination with Infanrix hexa™ and Prevenar, 8 months after vaccination with Rotarix, the subject experienced vomiting with severe abdominal pain. She was admitted for gastroenteritis. On 13 May 2010, intussusception was diagnosed with barium enema; right hemicolectomy and a small bowel resection were done the same day. The subject was hospitalised 2 days in ICU and then ward. At the time of reporting, the events were resolved.

Company comment: This 10-month-old subject experienced intussusception 7months after multiple vaccinations, which make unlikely the causality of Infanrix hexa™.

6.4.2.4.3. General disorders and administration site conditions

6.4.2.4.4. Abscess sterile, Injection site abscess sterile and vaccination site abscess sterile

Five cases of abscess sterile (of which three cases in the same subject) as well as two cases coded with the MedDRA Preferred Terms injection site abscess sterile or vaccination site abscess sterile have been received during this reporting period. These cases are summarised below.

Cases **D0063315A**, **D0063315B** and **D0063315C** - MedDRA Preferred Term: Abscess sterile

These cases were reported by a physician and described the occurrence of sterile abscess in a male subject at 4, 6 and 16-months of age within some months after vaccination with the 2nd, 3rd and 4th dose of Infanrix hexa™. The subject had no disturbance of immune system. The first vaccination with Infanrix hexa™ as well as all other vaccinations were well tolerated. The first abscess discharged spontaneously with pus and resolved with sequelae (scar). The second and third times abscesses were opened by puncture to reduced scarring and discharged with pus.

Company comment: Case of recurrent sterile abscess at injection sites after vaccination with Infanrix hexa™.

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Case **D0068815A** - MedDRA Preferred Terms: Abscess sterile, Injection site swelling, Injection site induration, Scar, Malaise

This case was reported by a physician and described the occurrence of sterile abscess in a 17-month-old male who was vaccinated with Infanrix hexa™. The subject"s medical history included status post nephropyeloplasty. After the 1st dose of Infanrix hexa™ the subject was ill. On 11 January 2010 the subject received the 2nd dose of Infanrix hexa™ (left thigh). Within one year after vaccination, the subject experienced induration at injection site with afterwards abscess formation. Abscess was punctuated ambulatory and smear was analysed. Bacteria could not be detected. In the following a scar developed. At the time of reporting, the subject was in good health.

Company comment: This 17-month-old subject experienced injection site abscess sterile within one year after vaccination with Infanrix hexa™. No injection sites abscesses were reported at other vaccinations. The drainage of this abscess revealed sterile secretion.

Case **D0068941A** - MedDRA Preferred Terms: Abscess sterile, Injection site reaction, Injection site nodule, Injection site swelling

This case was reported by a physician and described the occurrence of possible sterile abscess in a 2-year-old male who was vaccinated with Infanrix hexa™. The subject"s medical history included severe injection site reaction(s) post-vaccination with the primary course of vaccination with Infanrix hexa™. The first three doses of Infanrix hexa™, were given on 13 February 2009, 20 March 2009 and 13 May 2009. On 30 July 2010 the subject received a booster with the fourth dose of Infanrix hexa™ (left thigh). Approximately four weeks post-vaccination, end of August 2010, the subject experienced very severe injection site reaction and possible sterile abscess at injection site. Sonography of the left thigh in the area of injection site, showed two structures which were overlapping or directly bordering on each other. The upper of these structures appears longitudinal oval, embedded about one cm deep, was distinctly hypoechogenic, surrounded by a thin hyperechogenic wall and has a size of 3.3 x 0.7 x 1.5 cm. After distal crossing the second of these structures was oval with mixed hypoechogenic content and with a size of 2.6 x 1.2 cm. No inner perfusion could be detected. The lower structure was consistent with possible injection site granuloma. For the upper structure injection site abscess could not be excluded completely, but sterile abscess was considered to be rather unlikely due to lack of accompanying fever, redness and pain. At the time of reporting, on 21 September 2010, the events were still ongoing.

Company comment: The subject experienced injection site reaction one month after vaccination with a booster dose of Infanrix hexa. Except injection site swelling, inflammatory signs were absent. Sonography revealed two structures that have been interpreted as possible granuloma and possible abscess.

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Case **D0067836A** - MedDRA Preferred Terms: Injection site abscess sterile, Injection site swelling

This case was reported by the German regulatory authority and described the occurrence of injection site abscess sterile in an 18-month-old female who was vaccinated with Infanrix hexa™. The subject was healthy and has no underlying or concurrent medical conditions or other risk factors. Previous and/or concurrent vaccinations with Priorix™ Tetra, Prevenar, and NeisVac-C given on unspecified dates, have been well tolerated. After previous vaccinations with Infanrix hexa™, given on an unknown date intramuscularly in the right thigh, the subject experienced late sterile abscess which was drained by incision. On 06 January 2010 the subject received a booster with the fourth dose of Infanrix hexa™ (left thigh). Approximately 34 days post-vaccination the subject experienced injection site swelling of about 5 cm at the left thigh anterolaterally that was diagnosed to be a sterile abscess at injection site. At first the subject was treated conservatively including local cooling and hydroxycitric acid topically. The events improved. On 17 March 2010 the abscess was opened by puncture with a drain tube. Discharge from sterile abscess showed a small amount of yellowish pus. The events resolved.

Company comment: The subject had a sterile abscess after an unspecified dose of Infanrix hexa™. The subject developed an injection site sterile abscess 34 days after a booster dose of Infanrix hexa™. The abscess required drainage which revealed a small amount of pus that was not analyzed. No treatment was reported.

Case **D0069205A** - MedDRA Preferred Terms: Vaccination site abscess sterile

This case was reported by the German regulatory authority and described the occurrence of vaccination site abscess sterile in a 10-month-old male who was vaccinated with Infanrix hexa™. The subject"s past medical history was not provided. Previous vaccination with the first two doses of Infanrix hexa™ given on 01 July 2010 and 23 July 2010, have been well tolerated. On 08 September 2010 the subject received the third dose of Infanrix hexa (left thigh). Approximately 23 days post-vaccination, on 01 October 2010, the subject experienced vaccination site abscess sterile. Diagnosis was confirmed by spontaneous perforation and discharge of pus. The subject was treated ambulatory, but was not hospitalised for the event. At the time of reporting, on 11 October 2010, the event was unresolved.

Company comment: Previous first two doses of Infanrix hexa™ at unknown sites were well tolerated. The abscess drained spontaneously with pus discharge. The analysis of the pus was not reported.

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6.4.2.4.5. Injection site necrosis

One case of injection site necrosis was received during the period of this report.

Case **D0069186A** - MedDRA Preferred Terms: Injection site necrosis, Injection site vesicles, Injection site erythema

This case was reported by a physician and described the occurrence of injection site necrosis in 11-week-old male who was vaccinated on 08 October 2010 with the first dose of Infanrix hexa™ (left thigh). The subject has no underlying or concurrent medical conditions or other risk factors. On 10 October 2010, the subject experienced an injection site blister about 2 Euro coin-sized with surrounding redness (injection site redness). The blister looked like a burn blister. When the blister was removed a central site of skin necrosis was found (injection site necrosis). The site was treated regularly like a burn blister. At the time of reporting the events was unresolved.

Company comment: The subject experienced injection site necrosis 2 days after administration of the first dose of Infanrix hexa™. There was a blister at the injection site which was removed and injection site necrosis observed. It is unclear whether necrosis was primary event or occurred as a result of blister removal.

6.4.2.4.6. Injection site nodule and Nodule

Twenty-six case reports of injection site nodule and 3 cases of nodule have been received during the period of this report.

Three cases met the criteria for „regulatory" seriousness. All 29 cases were spontaneously reported. The majority of cases lack data for adequate assessment e.g. specific site of injection when concurrent vaccines are given, and/or time to onset and/or time to outcome.

These cases are summarised in tabular format below (Tables 7 and 8). Cases with bolded event terms are also analysed/summarised in the relevant sub-sections of section 6.4 of this PSUR.

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Table 7 Summary information for complete data set, n=29

Patient age	Range (n=25)	months	1 to 24
	Median	months	3
Patient gender	Male	n	17
	Female	n	12
Report type	Spontaneous	n	29
Time to onset of event	Range		immediate' to 'months'
	Median		unable to be meaningfully calculated with the data received. 6/29 cases for which a TTO was provided occurred within 1 day
Outcome	Resolved	n	16
	Resolved with sequelae	n	1
	Improved	n	1
	Unresolved	n	7
	Unknown	n	4
Cases where concomitant vaccine was administered		n	9

Table 8 Case details for all 29 reports

Case ID	Age	Gender	Seriousness Fda	Events PT Comma Sep	Suspect Drugs PT Comma Sep	Time To Onset Since Last Dose	Case Outcome
B0606863A	20 Months	Male	Not serious	Injection site nodule, Injection site erythema, Injection site induration	Infanrix hexa	0 Weeks	Resolved
B0608567A	16 Months	Male	Not serious	Gait disturbance, Injected limb mobility decreased, Injection site inflammation, Injection site haemorrhage, Injection site pain, Injection site nodule	Infanrix hexa	2 Days	Improved
B0637196A	Infant	Female	Not serious	Erythema, Feeling hot, Injection site nodule, Injection site erythema, Pyrexia	Infanrix hexa, Infanrix-polio, Pneumococcal vaccines (Non-GSK)	1 Days	Resolved
B0647305A	8 Months	Female	Not serious	Nodule, Hypersensitivity, Pruritus	Infanrix hexa, Infanrix-polio-HIB,	2 Months	Unresolved

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Case ID	Age	Gender	Seriousness Fda	Events PT Comma Sep	Suspect Drugs PT Comma Sep	Time To Onset Since Last Dose	Case Outcome
					Pneumococcal vaccines (Non-GSK)		
B0649489A	21 Months	Male	Not serious	Pain, Erythema, Injection site nodule, Induration, Injection site scab, Skin warm, Mobility decreased, Pain in extremity, Pyrexia, Extensive swelling of vaccinated limb	Infanrix hexa	0 Days	Unknown
B0649610A	4 Months	Male	Not serious	Injection site pain, Injection site erythema, Injection site nodule	Infanrix hexa	0 Days	Resolved
B0649618A	2 Months	Male	Not serious	Injection site pain, Injection site erythema, Injection site nodule	Infanrix hexa	0 Days	Resolved
B0649651A	2 Months	Male	Not serious	Pyrexia, Local reaction, Nodule, Erythema	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	0 Days	Resolved
B0649673A	12 Months	Female	Not serious	Local reaction, Erythema, Nodule, Pyrexia	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	0 Days	Resolved
B0652412A	Infant	Female	Not serious	Injection site nodule, Injection site pruritus, Injection site reaction, Injection site erythema	Infanrix hexa, DTPa-Polio-HIB (Non-GSK)	0 Years	Unresolved
B0653484A	2 Months	Male	Not serious	Injection site nodule, Injection site swelling, Lymphadenopathy, Eczema, Injection site inflammation	Infanrix hexa, Infanrix-polio-HIB, Pneumococcal vaccines (Non-GSK)	Unknown	Unresolved
B0668555A	Infant	Female	Not serious	Injection site nodule, Injection site erythema	Infanrix hexa	See text	Unresolved
B0672492A	12 Months	Male	Not serious	Injection site nodule, Injection site pruritus, Injection site reaction	Infanrix-polio-HIB, Infanrix hexa	Months	Unresolved
B0680091A	Infant	Male	Not serious	Injection site nodule, Injection site pruritus, Injection site	Infanrix hexa, Infanrix-polio-HIB, Pneumococcal	Immediate	Unresolved

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Case ID	Age	Gender	Seriousness Fda	Events PT Comma Sep	Suspect Drugs PT Comma Sep	Time To Onset Since Last Dose	Case Outcome
				reaction	vaccines (Non-GSK)		
D0066316A	2 Months	Male	Not serious	Injection site nodule	Infanrix hexa	Unknown	Resolved
D0066318A	1 Months	Female	Not serious	Injection site nodule	Infanrix hexa	Unknown	Resolved
D0066319A	3 Months	Female	Not serious	Injection site nodule	Infanrix hexa	Unknown	Resolved
D0066320A	2 Months	Female	Not serious	Injection site nodule	Infanrix hexa	Unknown	Resolved
D0066321A	3 Months	Female	Not serious	Injection site nodule	Infanrix hexa	Unknown	Resolved
D0066322A	1 Months	Female	Not serious	Injection site nodule	Infanrix hexa	Unknown	Resolved
D0066323A	3 Months	Male	Not serious	Injection site nodule	Infanrix hexa	Unknown	Resolved
D0066324A	2 Months	Male	Not serious	Injection site nodule	Infanrix hexa	Unknown	Resolved
D0066325A	2 Months	Female	Not serious	Injection site nodule	Infanrix hexa	Unknown	Resolved
D0066326A	3 Months	Male	Not serious	Injection site nodule	Infanrix hexa, Synflorix	Unknown	Resolved
D0067489A	3 Years	Female	Not serious	Injection site nodule	Infanrix hexa	Unknown	Unknown
D0068654A	4 Months	Male	Not serious	Injection site nodule, Purulent discharge, Erythema, **Injection site abscess**	Infanrix hexa	Unknown	Resolved with Sequelae
D0068798A	3 Months	Male	Serious	**Injection site abscess**, **Incision site abscess**, Injection site reaction, Injection site induration, Injection site erythema, Injection site swelling, Injection site nodule	Infanrix hexa	Unknown	Unknown
D0068798B	4 Months	Male	Serious	**Injection site abscess**, **Incision site abscess**, Injection site induration, Injection site erythema, Injection site swelling, Injection site nodule	Infanrix hexa	Unknown	Unknown

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Case ID	Age	Gender	Seriousness Fda	Events PT Comma Sep	Suspect Drugs PT Comma Sep	Time To Onset Since Last Dose	Case Outcome
D0068941A	2 Years	Male	Serious	**Abscess sterile**, Injection site reaction, Injection site nodule, Injection site swelling	Infanrix hexa	4 Weeks	Unresolved

6.4.2.5. Immune system disorders

6.4.2.5.1. Anaphylactic reaction and anaphylactic shock

During the period of this report, four cases of anaphylactic reaction or anaphylactic shock have been reported.

Case **B0652232A** - MedDRA Preferred Term: Anaphylactic shock

This case was reported by the Spanish regulatory authority and described the occurrence of anaphylactic shock in a 2-year-old female who was vaccinated with the 1st dose of Infanrix hexa™ and unspecified dose of Menjugate (non-GSK). On 16 February 2009, less than one day after vaccination, the subject experienced anaphylactic shock. The subject was hospitalised. At the time of reporting, the event was resolved.

Company comment: This 2-year-old female subject experienced anaphylactic shock less than one day after multiple vaccinations. This report lacks important information such as anaphylaxis's symptoms and treatment.

Case **B0663295A** - MedDRA Preferred Terms: Anaphylactic reaction, Haematochezia, Intestinal obstruction, Intussusception, Somnolence, Pallor, Vomiting, Pulse abnormal, Capillary disorder

This case was reported by a physician and described the occurrence of anaphylaxis in a 6-month-old male who was vaccinated with unspecified dose of Infanrix hexa™ and unspecified dose of Rotarix. On 26 June 2010, 20 minutes after vaccination, the subject was mildly drowsy and pale. He was brought back home where he had 10 times clear yellowish vomiting. He had no diarrhea. Six hours after vaccination, the subject was markedly pale and drowsy. He was hospitalised. At admission, the subject was drowsy, pale, had a weak peripheral pulse and delayed capillary refill. The temperature was 37.6 degC, blood pressure 120/80 mmHg and pulse rate 130 beats/min. The subject was treated with intravenous fluid(s). Anaphylaxis was diagnosed, leading to treatment with adrenaline and antihistamine. The laboratory tests performed showed hematocrit 36%, white blood cell count 10700/mm3, neutrophils 60%, platelet count 300000/mm3 and normal electrolyte. On 27 June 2010, the subject experienced bilious vomiting and jelly stool. The abdomen x-ray showed abdominal obstruction and abdomen ultrasound revealed intussusception.

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The intussusception was closely reduced by medical air. The subject was treated with ceftriaxone sodium (Rocephin). On 28 June 2010, the subject was in a better condition and was discharged from hospital with oral antibiotics as treatment. At the time of reporting the events were resolved. The physician concluded this case as anaphylaxis due to Infanrix hexa™. He considered that the onset of the intussusception was too close to be related to vaccination.

Company comment: This 6-month-old male subject experienced the event 6 hours after multiple vaccinations. The reported symptoms of anaphylaxis are likely to be associated with the intussusception episode that was diagnosed within 24 hours after vaccination.

Case **B0664784A** - MedDRA Preferred Terms: Anaphylactic reaction, Agitation, Heart rate increased, Conjunctival hyperaemia, Urticaria, Crying

This case was reported by the Italian regulatory authority via a physician and described the occurrence of anaphylactic reaction in a 4-month-old male who was vaccinated with the 2nd dose of Infanrix hexa™ and Prevenar. On 2 July 2010, 1 hour after vaccination, the subject experienced anaphylactic reaction with widespread urticaria, agitation, accelerated heart rate, conjunctival redness and weeping. The subject was hospitalised and treated with chlorpheniramine (Clorfenamina) and cortisone.
On 2 July 2010, the events were resolved.

Company comment: Symptoms occurred 1 hour after multiple vaccinations. The reported symptoms provide insufficient evidence to confim the diagnosis of anaphylaxis.

Case **D0068761A** - MedDRA Preferred Terms: Anaphylactic reaction, Hypersensitivity, Dyspnoea, Urticaria, Angioedema, Bronchospasm, Stridor

This case was reported by a physician and also by the German regulatory authority and described the occurrence of anaphylaxis in a 30-month-old female who was vaccinated with a 4th dose of Infanrix hexa™. The first three doses of Infanrix hexa™ for basic immunisation on 15 May 2008, 16 July 2008 and 29 August 2008 were well tolerated. The subject‟s medical history included myocarditis in summer 2009 with cerebral edema, post-ischemic encephalopathy, cerebral convulsion and minimal response state. The subject was severely disabled after cerebral infarction and haemorrhage during cardiac assist therapy. The subject had no history of allergies to drugs. Concurrent medications included Spironolactone (Aldactone), Hydrochlorothiazide, acetylsalicylic acid (ASS), Topiramate (Topamax), Clobazam (Frisium), sodium valproate + valproic acid (Ergenyl chrono), Lamotrigine (Lamictal), macrogol + sodium chloride + sodium hydrogen carbonate + potassium chloride (Movicol junior), Baclofen, Melatonin, Sodium chloride (NaCl) and Omeprazole (Antra MUPS). On 24 August 2010, approximately 45 to 60 minutes after vaccination, the subject had a swollen face and was wheezing. The subject experienced anaphylaxis with severe dyspnea, generalized urticaria, quincke‟s edema and bronchoconstriction. None of the following symptoms or signs were present: hypotension, dizziness, syncope, nausea, vomiting, diarrhea, Coombs‟ positive haemolytic anemia, signs for bone marrow suppression, fever, arthropathy, lymphadenopathy, proteinuria, eosinophilia, skin rash or contact dermatitis. The subject received prednisone (Rectodelt) and an emergency physician was called.

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The emergency physician set up an intravenous line and administered volume, dimethindene maleate (Fenistil) and ranitidine hydrochloride (Ranitidin). Additionally the infant inhaled adrenaline (Adrenalin). After successful stabilisation, the subject was admitted to a pediatric intensive care unit. The treating paediatrician diagnosed dyspnea, inspiratory stridor, edema and urticaria over the body. The subject was diagnosed with allergic reaction grade III. In hospital the subject again received adrenaline and volume and additional prednisolone sodium succinate (Solu-Decortin) and oxygen via a mask. After several hours the events were resolved. On 25 August 2010 the subject was discharged from hospital without any symptoms. The physician considered the events were probably related to vaccination with Infanrix hexa™.

Company comment: This 30-month-old female subject experienced anaphylactic reaction after vaccination with the 4th dose of Infanrix hexa™. The reported symptoms are compatible with anaphylaxis as there is sufficient evidence to meet the case definition of anaphylaxis by the Brighton Collaboration criteria. Of note, several concurrent medications with unknown start date.

6.4.2.6. Infections and infestations

6.4.2.6.1. Abscess, Abscess limb, Incision site abscess, Injection site abscess, Vaccination site abscess

During the reporting period, 17 cases were received including one of the following MedDRA Preferred Terms: abscess (n=4), abscess limb (n=1), incision site abscess (n=5), injection site abscess (n=10) and/or vaccination site abscess (n=2).

These cases are summarised in the below tables. Cases with bolded event terms are also analysed/summarised in the relevant sub-sections of section 6.4 of this PSUR.

Table 9 Summary information for complete data set, n=17

Patient age	Range (n=16)		6 weeks to 2 years
	Median	months	4
Patient gender	Male	n	11
	Female	n	5
Report type	Spontaneous	n	17
Time to onset of event	Range		on the same day to 5 months
	Median	days	28
Outcome	Resolved	n	7
	Resolved with sequelae	n	3
	Improved	n	1
	Unknown	n	6
Cases where concomitant vaccine was administered		n	6

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Table 10 Case details for all 17 reports

Case ID	Age	Gender	Seriousness Fda	Events PT Comma Sep	Suspect Drugs PT Comma Sep	Time To Onset Since Last Dose	Case Outcome
B0600650A	19 Months	Male	Serious	Injection site abscess, Pain in extremity	Infanrix hexa	1 Months	Resolved
B0607303A	6 Weeks	Female	Not serious	Injection site abscess	Infanrix hexa	Unknown	Unknown
B0609130A	4 Months	Female	Not serious	Oxygen saturation decreased, Feeding disorder of infancy or early childhood, Injection site abscess, Crying, Pyrexia	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	0 Days	Unknown
B0622903A	14 Months	Male	Not serious	Abscess, Inflammation, Vomiting, Pyrexia	Priorix, Infanrix hexa, Meningococcal polysaccharide vaccine group C	5 Weeks	Resolved
B0639606A	3 Months	Male	Not serious	Abscess, Inflammation, Pain, Pyrexia	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	8 Days	Resolved
B0641879A	3 Months	Female	Serious	Erythema, Induration, Abscess, Pyrexia	Infanrix hexa	0 Days	Resolved
B0661002A	7 Months	Male	Serious	Injection site abscess	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	45 Days	Resolved
B0680202A	6 Months	Male	Serious	Injection site abscess, Injection site haematoma	Infanrix hexa	Days	Resolved
D0066615A	Infant	Male	Serious	Vaccination site abscess	Infanrix hexa, Synflorix	Unknown	Resolved
D0066818A	4 Months	Female	Serious	Abscess, Incision site abscess	Infanrix hexa	28 Days	Unknown
D0067672A	2 Years		Not serious	Injection site abscess	Infanrix hexa	23 Days	Unknown
D0067703A	10 Months	Male	Serious	Abscess limb, **Nodule on extremity**	Infanrix hexa	5 Months	Improved
D0068654A	4 Months	Male	Not serious	Injection site nodule, Purulent discharge, Erythema, Injection site abscess	Infanrix hexa	Unknown	Resolved with Sequelae
D0068798A	3 Months	Male	Serious	Injection site abscess, Incision site abscess, Injection site reaction, Injection site induration, Injection site erythema, Injection site swelling, Injection site nodule	Infanrix hexa	Unknown	Unknown

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Case ID	Age	Gender	Seriousness Fda	Events PT Comma Sep	Suspect Drugs PT Comma Sep	Time To Onset Since Last Dose	Case Outcome
D0068798B	4 Months	Male	Serious	Injection site abscess, Incision site abscess, Injection site induration, Injection site erythema, Injection site swelling, Injection site nodule	Infanrix hexa	Unknown	Unknown
D0068798C	20 Months	Male	Serious	Injection site abscess, Incision site abscess	Infanrix hexa	0 Years	Resolved with Sequelae
D0068928A	4 Months	Female	Serious	Vaccination site abscess, Incision site abscess, Staphylococcus test positive	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Unknown	Resolved with Sequelae

6.4.2.6.2. Cellulitis and injection site cellulitis

During the period under review, 7 serious cases have been received with the event cellulitis and 1 serious case was received with the event injection site cellulitis. These cases are summarised below.

Case **B0661012A** – MedDRA Preferred Terms: Cellulitis, Injection site erythema, Pyrexia, Injection site swelling

This case was reported by a physician and described the occurrence of phlegmon in a 2-year-old female who was vaccinated with the 4th dose of Infanrix hexa™. On 11 June 2010, 2 days after vaccination with Infanrix hexa™, the subject experienced redness and swelling at injection site and fever. CRP level was 32.8 mg/l. The subject was hospitalised and treated with antibiotics (Broad-spectrum antibiotic). At the time of reporting, all events were resolved.

Case **B0661014A**– MedDRA Preferred Terms: Cellulitis, Oedema peripheral, Erythema

This case was reported by a physician and by a regulatory authority and described the occurrence of phlegmon in a 23-month-old female after vaccination with the 4th dose of Infanrix hexa™ and the 2nd dose of Havrix™ 720. One day after vaccinations, the subject experienced erythema and swelling of the whole left upper arm. It was not known which vaccine was administered on which side. The subject was hospitalised and treated with antibiotics (Broad-spectrum antibiotic). CRP level was 21.1 mg/l. At the time of reporting, all the events were resolved.

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Case **B0661015A** – MedDRA Preferred Terms: Cellulitis, Erythema, Swelling

This case was reported by a physician and described the occurrence of phlegmon, erythema and swelling in the area of injection site (expansion until sternum) in a 2-year-old female less than 1 day after vaccination with an unspecified dose of Infanrix hexa™. The subject was hospitalised and treated with antibiotics (Broad-spectrum antibiotic). Laboratory results: WBC: 12.6, CRP: less than 8 mg/L. At the time of reporting, all the events were resolved.

Case **B0677146A** – MedDRA Preferred Term: Cellulitis

This case was reported by a physician and described the occurrence of cellulitis in an 18-month-old female 2 days after vaccination on 14 September 2010 with a 4th dose of Infanrix hexa™. The subject was hospitalised and discharged on 20 September 2010.

Case **D0067880A** – MedDRA Preferred Term: Cellulitis

This case was reported by the German regulatory authority and described the occurrence of phlegmon on the left thigh in a 22-month-old male 2 days after vaccination with the 4th dose of Infanrix hexa™ (left thigh). Previous vaccinations with the first three doses of Infanrix hexa™ were well tolerated. The subject was hospitalised for an unknown period of time. The event was confirmed by serology. After about six days the event was resolved.

Case **D0069118A** – MedDRA Preferred Terms: Cellulitis, Injection site erythema, Injection site swelling, Injection site warmth, Injection site induration

This case was reported by a regulatory authority and described the occurrence of phlegmon in a 3-year-old female who was vaccinated with Infanrix hexa™. Subject‟s father suffered from breathing complaints and psoriasis. The subject was the 3rd child of the family. Pregnancy was under strain of nicotine abuse. Birth and development were normal. Previous vaccinations with Infanrix hexa™ given on 3 August 2008 and 24 February 2009 were well tolerated. On 28 September 2010 the subject received the 3rd dose of Infanrix hexa™ (right upper arm). On 30 September 2010, the subject experienced phlegmon on right upper arm with significant redness, swelling, warmth and induration at injection site. The subject was hospitalised from 30 September 2010 till 5 October 2010 and treated by antibiosis with intravenous cefuroxime sodium (Cefuroxim) then switched to oral cefuroxime sodium. The upper arm was treated by coolin with hydroxychinolin. Blood sample showed mild monocytosis (0.07) and eosinophilia (0.06). White blood cell increased to 15.83gpt/l. Redness, swelling and induration improved. The subject was discharged from hospital on 5 October 2010 in stable general condition still with mild induration at injection site on right upper arm.

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Case **D0069190A** – MedDRA Preferred Terms: Cellulitis, Erythema, Oedema peripheral, Blister, Purulence, Skin warm, Ulcer, General physical health deterioration, Induration, Injection site erythema, Tympanic membrane hyperaemia, Vaccination complication

This case was reported by a physician via a regulatory authority and described the occurrence of phlegmon of arm in a 26-month-old female who was vaccinated with Infanrix hexa™. Previous vaccinations included Infanrix hexa™ given on 08 February 2010, 12 March 2010 and 24 April 2010, which were well tolerated. On 23 September 2010 the subject received the 4th dose of Infanrix hexa™ (right upper arm). Less than one day after vaccination, the subject experienced Ulcus cruris, purulent secretion, vaccination site warmth, vaccination site redness and vaccination site swelling, phlegmon of right upper arm. She did not develop fever. Bacterial superinfection was suspected. Due to staphylogenic phlegmon of right upper arm, the subject was hospitalised on 25 September 2010 for 3 days. On admission examination, the subject"s general condition was mildly reduced. Skin at right upper arm was warm, red and indurated. There were single partly opened blister which partly were weeping. Injection site showed redness without secretion. Eardrums at both sides showed redness. All other clinical physical examinations were normal. Body temperature 37.8degC, CRP 1.6mg/dl, Leukocyte 9.9 (Granulocyte 56%, Lymphocytes 35%). Possible superinfection and vaccination reaction at right upper arm were diagnosed. Wound smear was negative for Staphylococcus aureus and haemolytic Streptococcus. By differential diagnosis, bacterial superinfection has been excluded. The subject was treated with cefuroxime sodium (Cefuroxim) and octenisept bandages. Symptoms improved. On 27 September 2010, the subject was discharged from hospital in good general condition. There was one small area at skin, which was still mildly weeping.

Case **B0675146A** – MedDRA Prefered Terms: Injection site cellulitis, Injection site oedema, Blister, Injection site erythema, Injection site pain, Injection site induration, Injection site vesicles, Lymphadenopathy, Ecchymosis, C-reactive protein increased, Leukocytosis, Skin chapped

This case was reported by the French regulatory authority and described the occurrence of injection site cellulitis in a 17-month-old male who was vaccinated with Infanrix hexa™, and Meningitec (non-GSK). The subject had no known relevant medical history. First administration of Infanrix hexa™ in October 2009 was without reported adverse events. On 01 July 2010, the subject received booster doses of Infanrix hexa™ and Meningitec (unknown injection sites). On the same day in the evening, the subject presented with edema and phlyctena at injection site on right thigh. Size of edema increased thus the subject was taken to the emergency unit on 03 July 2010. On admission, he presented on right thigh with an erythema plaque of 15 cm long, painful, indurated and bullous at injection site associated with inguinal adenopathy (more than 1 cm of diameter). Left thigh was without local reaction and without palpable adenopathy. During the following hours, edema increased and extended over three quarter of right thigh with two or three phlyctenules. Ecchymotic aspect was noticed on peri-phlyctenules (coded ecchymosis at site). Post vaccinal cellulitis was diagnosed. The subject had neither fever nor abdominal pain. Lab tests revealed increased C-reactive protein at 25 mg/l and hyperleukocytosis at 11.4 G/L. Bacteriological tests performed on punctured phlyctenules showed no pathogenic microorganisms.

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The subject received one dose of intraveinous ceftriaxone sodium (Rocephine), then saccharomyces boulardii (Ultralevure) and amoxicillin trihydrate + potassium clavulanate (Augmentin) prescribed for 10 days.
On 08 July 2010, the subject returned to emergency unit. He had severe fever for 24 hours. On admission he presented with anal bleeding, diarrhea, candidiasis on buttocks and nasopharyngitis with both congested eardrums (all incidental events). At vaccine injection site on right thigh, skin was mildly indurated, without petechia or inflammation. Lab test showed decreased C-reactive protein level to 7 mg/L and normalisation of white blood cell count at 7 G/L. Blood culture was positive for coagulase negative staphylococcus (unspecified level). Augmentin was discontinued and the subject was treated with Rocephine firstly intravenously and then intramuscularly during 48 hours. On 21 July 2010, skin at edema area was a little crackled but with a normal colour. A mild induration persisted at injection site. The subject was well. On an unspecified date, injection site cellulitis resolved.

Company comment: In all described cases, the subjects were aged between 17 months and 3 years and received their booster dose of Infanrix hexa™. Six of them received antibiotics. In six cases, no causing agent of cellulitis was identified. In case D0067880A, cellulitis was confirmed by unspecified serology. In case B0675146A, a co-suspect vaccine was involved with unknown injection sites for both vaccines. Bacteriological tests were negative at the reaction site. Blood culture was positive for coagulase negative staphylococcus 8 days after vaccines administration.

6.4.2.6.3. Meningitis, Meningitis aseptic and meningitis pneumococcal

During the period under review, 3 cases were received with the MedDRA Preferred Terms meningitis (n=1), meningitis aseptic (n=1) or meningitis pneumococcal (n=1).

In case **D0068409A,** meningitis was reported together with Kawasaki"s disease. This case is described in section 6.4.2.10.1 on Kawasaki"s disease. Meningitis was likely suspected but no details were reported. The final diagnosis was Kawasaki"s disease. The other cases are described below.

Case **B0651993A-** MedDRA Preferred Term: Meningitis aseptic

This case was reported by the Spanish regulatory authority and described the occurrence of aseptic meningitis in an 18-month-old male 1 day after vaccination on 02 December 2008 with an unspecified dose of Infanrix hexa™. On 18 December 2008, the event was resolved.

Company comment: An 18-month-old subject developed aseptic meningitis 1 day after vaccination with unspecified dose of Infanrix hexa™. No data confirming this event were reported.

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Case **D0066195A**- MedDRA Preferred Terms: Meningitis pneumococcal, Pyrexia, Restlessness, Muscle spasms, Respiratory disorder, Salivary hypersecretion, Daydreaming, Hypertension, Hemiplegia, Cerebral haemorrhage, Motor dysfunction

This case was reported by a consumer, the subject‟s grandmother, via the GSK-sponsored internet site and described the occurrence of pneumococcal meningitis in a 4-month-old male who was vaccinated with Infanrix hexa™ and Synflorix™. The subject had received complete immunisation with two doses of Synflorix™. A physician or other health care professional has not verified this report. The subject was breast-feeding. On an unspecified date the subject received unspecified dose of Infanrix hexa™. In January 2010, at an unspecified time after vaccination with Infanrix hexa™, the subject experienced fever up to 39.5 degC and was treated with paracetamol. The subject was drinking normally. In the evening, at 21:30 the subject developed restlessness and cramps and was hospitalised.
Computerised tomogram was without findings. Meningitis was suspected and the subject treated accordingly. Because of respiration problems the subject received oxygen. In the morning at 05:00 respiration had stabilised. After lumbar puncture the subject was diagnosed with pneumococcal meningitis. The genotype was identified as C15. The subject was treated with phenobarbitone (Luminal) and antibiotics. Three days later the subject was in bad condition, with salivation, absent mind, high blood pressure and right sided paralysis. The subject was treated with heparin. On 18 January 2010 a magnetic resonance tomogram was performed and showed severe cerebral hemorrhage in the front of both halves of the brain. The subject had right-sided motor dysfunction. The subject was transferred to a neurochirurgic unit. Treatment included blood transfusions and other antibiotics, because inflammatory parameters had increased. At the time of reporting the outcome of the events was unspecified.

Company comment: A 4-month-old male subject experienced pneumococcal meningitis on unspecified time after vaccination with Infanrix hexa™ and Synflorix™. Based on CSF results, the subject was diagnosed with pneumococcal meningitis.

6.4.2.6.4. Sepsis

During the period of this report 4 cases of sepsis have been identified.

In case **B0643201A** suspected sepsis was reported in association with suspected intussusception. This case is described in more details in section 6.5.2.4.2 on intussusception. No data were available to confirm the diagnoses.

In case **D0064259A** the subject died. This case is described in more details in section 6.4.1 on cases with a fatal outcome. According to the autopsy report the cause of death was SIDS and viral infection. No data were available to confirm the diagnosis of sepsis.

In case **D0068409A** sepsis was reported together with Kawasaki‟s disease. This case is described in section 6.4.2.10.1 on Kawasaki‟s disease. Bacterial gastroenteritis and sepsis were suspected but not confirmed.

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Case **D0065893A** – MedDRA Preferred Terms: Ileus paralytic, Peritonitis, Ileostomy, Microcephaly, Inguinal hernia, Acute abdomen, General physical health deterioration, Ascites, Sepsis, Vomiting, Leukocytosis, Hyponatraemia, Muscle disorder

This case was reported by the Dutch regulatory authority and described the occurrence of paralytic ileus in a 3-month-old male who was vaccinated with Infanrix hexa™ and Prevenar. The subject was born prematurely at 28+1 weeks of gestation by caesarean section, because of maternal epilepsy and somnolence and suspicion of amniotic infection syndrome. After birth the subject had valproate embryopathy, dyspnoea syndrome, arterial hypotension, persistent ductus arteriosus which was closed by medication, persistent foramen ovale, apnea-bradycardia syndrome, conjunctivitis, possible infection and urinary transportation disorder grade 1. First dose of Infanrix hexa™ and Prevenar had been well tolerated. After second vaccination, on 20 May 2009, the subject was hospitalised with symptoms of gastroenteritis. Next day his general condition worsened, because of acute abdomen syndrome. Sonogram showed ileus with dilated intestinal loops. Laparotomy on 21 May 2009 showed no mechanic correlate of the symptoms, nor any pathology of the intestine. The subject had foul-smelling ascites and septic picture. Ileostomy was performed. Because of septic picture, antibiotic treatment with Ampicillin, tobramycin and metronidazole was started. No infective germs were found in stool and blood. On 25 May 2009 a gradual return to normal food was started. This was well tolerated at first, but on 28 May 2009 the subject again developed recurrent vomiting and leukocytosis which improved. Ampicillin trihydrate was stopped on 04 June 2009, tobramycin on 30 May 2009 and metronidazole on 02 June 2009. On 03 June 2009 the subject's condition again worsened, with dilated abdomen and vomiting. Inflammatory parameters increased and sonogram showed subileus. This improved after treatment with tobramycin, metronidazole and Unacid and after three days return to normal food was again started. Antibiotic treatment was stopped on 05 June 2009. Persisting hyponatremia was treated by oral NaCl. As no microbiological cause of subileus was found, biopsy was performed on 05 June 2009 which showed no sign for Hirschsprung disease. Inguinal hernia, found by sonogram on 05 June 2009, was removed. In sonogram, the side ventricles of brain were abnormal. The subject showed fluctuating muscle tone and was transferred to a neuropediatric unit on 22 June 2009. The subject was in good general condition on 03 July 2009.

Company comment: No etiological agent causing acute abdomen and ascitis were reported. Sepsis was suspected but not confirmed.

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6.4.2.7. Musculoskeletal and connective tissue disorders

6.4.2.7.1. Nodule on extremity

During the reporting period, two cases were reported with the MedDRA Preferred Term nodule on extremity.

Case **B0637004A** – MedDRA Preferred Terms: Nodule on extremity, Crying

This non-serious case was reported by the Italian regulatory authority and described the occurrence of thigh nodule in a 6-month-old male who was vaccinated with Infanrix hexa™ on 27 November 2009 (injection site unknown). On 12 February 2010, 77 days after vaccination with Infanrix hexa™, the subject experienced thigh nodule and persistent crying. The subject was treated with antibiotics. At the time of reporting, the events were resolved.

Company comment: This case lacks information on injection site of Infanrix hexa™.

In case **D0067703A** the event was reported together with abscess limb. This case was described in section 6.4.2.6.1 on abscess limb.

6.4.2.8. Nervous system disorders

6.4.2.8.1. Cerebral atrophy

During the period of this report, one case of cerebral atrophy was received.

Case **D0067158A** - MedDRA Preferred Terms: Convulsion, Partial seizures, Cerebral atrophy, Demyelination, Petechiae, Developmental delay, Schamberg's disease, Rhinitis

This serious case was reported by the Germany Regulatory Authority and described the occurrence of seizure in an infant male who was vaccinated with 3 doses of Infanrix hexa™, 3 doses of Prevenar, 3 doses of RotaTeq, 2 doses of Priorix™ Tetra and 1 dose of Menjugate. The subject's medical history included mother's insemination, cesarean section delivery at 36 + 3 weeks of pregnancy, HELLP syndrome during mother's pregnancy, postpartum hemorrhagic gastritis, hyperbilirubinemia, postpartum anemia, treated with transfusion. According to the report about a suspicion of vaccine damage, signed on 29 December 2009 by paediatrician, in August 2008, the subject developed for the first time petechiae. Haematological examinations of petechiae cause were missing. The subject was hospitalised due to first cerebral seizure, petechiae and serous rhinitis at the age of 7-months, in October 2008. Benign infant partial epilepsy Watanabe was suspected. Plasmatic coagulation disorder was excluded. Beginning of 2009, a stato-motoric developmental delay was suspected and confirmed in March 2009 during infant medical check-up, at the age of 11 months. Purpura pigmentosa progressive was diagnosed at that time. NMR tomography, performed at the age of 15 moths, in July 2009, showed mild increasing cerebral atrophy with wide inner and outer subarachnoid spaces. State of myelinization was considered to be like 11 months. Examinations of human genetics and molecular genetics in December 2009 were normal. The outcome of the events was unspecified.

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Company comment: This case describes a subject who was diagnosed with cerebral atrophy and suspected Watanabe epilepsy after multiple vaccinations. The subject received complete vaccinations according to his age. The reported subject's conditions (postpartum hemorrhagic gastritis, hyperbilirubinemia, postpartum anemia, treated with transfusion and suspected epilepsy) might have contributed to an observed psychomotor retardation.

6.4.2.8.2. Cerebral haemorrhage

During the period of this PSUR, two cases of cerebral haemorrhage were received. They are described below.

Case **B0666511A** - MedDRA Preferred Terms: Cerebral haemorrhage, Hemiparesis, Lethargy, Convulsion, Crying, Nervousness, Tension.

This serious case was reported by a physician and described the occurrence of brain hemorrhage in a 4-month-old female who was vaccinated with the 2nd doses of Infanrix hexa™ and Prevenar. Less than one month after first vaccinations, the subject cried a lot, she was jumpy and easily startled. One day after vaccination with the 2nd doses, the subject experienced lethargy, right-sided hemiparesis and brain hemorrhage. The subject was hospitalised. NMR of brain showed left side cerebral hemorrhage involving capsula interna and basal nuclei. The subject was treated with hydration therapy, intravenous fluids and corticosteroid. According to the follow-up information, motion awkwardness and paresis of right hand have decreased and the leg had a full motion. Seizure did not recur. At the time of reporting, the events were resolved with sequelae.

Company comment: A 4-month-old subject experienced cerebral haemorrhage 1 day after multiple vaccinations. Provided information is limited only to NMR findings and did not provide results of other tests. Such short time to onset makes vaccinations as uncertain cause of this event. Information on investigation of other causes of haemorrhage like infection diseases, coagulation disorders were not provided.

The second case **D0066195A** was reported by a consumer and described a 4-month-old subject who experienced cerebral haemorrhage in the context of pneumococcal meningitis. This case is described in more details in section 6.4.2.6.3 on meningitis.

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6.4.2.8.3. Seizures

Atonic seizures, Clonic convulsion, Clonus, Convulsion, Convulsions local, Febrile convulsion, Grand mal convulsion, Myoclonus, Partial seizures, Tonic convulsion

During the reporting period, 117 individual case reports were received including one of the following MedDRA Preferred Terms: atonic seizures (n=1), clonic convulsion (n=1), clonus (n=1), convulsion (n=55), convulsions local (n=1), febrile convulsion (n=54), grand mal convulsion (n=18), myoclonus (n=4), partial seizures (n=3) and/or tonic convulsion (n=3). In some instances more than one MedDRA Preferred Terms was included to describe the same event.

Note compared to the previous PSURs epilepsy, infantile spasms, petit mal epilepsy and status epilepticus are described separately from the other types of seizures.

These cases are summarised in the below tables.

Table 11 Summary information for complete data set, n=117

Patient age (n=114)	Range	months	1-36
	Median	months	5
Patient gender (n=112)	Male	n	54
	Female	n	58
Report type	Spontaneous	n	117
Type of convulsion*	Febrile	n	82
	Afebrile	n	35
Time to onset of event (n=108)	Range		less than 1 day to 3 weeks
	Median	days	same day
Outcome	Resolved	n	81
	Resolved with sequelae	n	3
	Improved	n	5
	Fatal	n	1
	Unresolved	n	5
	Unknown	n	22
Cases where concomitant vaccine was administered		n	92

*note that some febrile seizures were described with the MedDRA Preferred Terms 'Convulsion' and 'Pyrexia' rather than the Preferred Term 'Febrile convulsion'.

Subject age was provided in 114 reports included in the analysis and ranged from 1 month to 3 years with a median of 5 months. Subject gender was provided in 112 reports and included 54 males and 58 females. TTO was provided in 108 reports and ranged from less than 1 day to 3 weeks (median: less than 1 day).

Epilepsy, Petit mal epilepsy, Infantile spasms, Status epilepticus

During this reporting period 11 cases of epilepsy, 4 cases of petit mal epilepsy, 2 cases of infantile spasm and 4 cases of status epilepticus were reported.

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These cases are summarised in the below tables. Cases with bolded event terms are also analysed/summarised in the relevant sub-sections of section 6.4 of this PSUR.

Table 12 Summary information for complete data set, n=117

Patient age (n=)	Range	months	2-32
	Median	months	5
Patient gender (n=19)	Male	n	8
	Female	n	11
Report type	Spontaneous	n	19
Time to onset of event (n=19)	Range		same day to 16 months
	Median	days	1
Outcome	Resolved	n	9
	Resolved with sequelae	n	2
	Improved	n	2
	Unresolved	n	3
	Unknown	n	3
Cases where concomitant vaccine was administered		n	14

Table 13 Cases of epilepsy (n=11) and petit mal epilepsy (n=2) identified during the reporting period

Case ID	Age	Gender	Suspects	Events PT Comma Sep	Case Outcome	Comments
B0607020A	5M	Male	Infanrix hexa	Epilepsy	Resolved	Normal EEG and biochemistry
B0636914A	5M	Female	Infanrix hexa, Prevenar	Loss of consciousness, **Cyanosis**, Epilepsy, Hypotonia, Asthenia, Areflexia, Pyrexia	Resolved	Normal EEG
B0642185A	15M	Female	Infanrix hexa, Prevenar	Altered state of consciousness, **Gaze palsy**, **Tonic convulsion**, **Convulsion**, Epilepsy, Gastroenteritis, **Febrile convulsion**, Hypertonia, Ear infection, Gastritis, Nasopharyngitis, Hypotonia, Body temperature increased, Vomiting, Diarrhoea, Pyrexia	Unknown	Normal EEG
B0645066A	12M	Female	Infanrix hexa, Meningitec	Epilepsy, **Partial seizures**, Cerebrovascular disorder, Apnoea, Joint hyperextension, Pyrexia	Improved	EEG showed epileptic focus, positive family epilepsy history, the subject's aunt
B0657965A	4M	Female	Infanrix hexa	Epilepsy, Loss of consciousness, **Convulsions local**, Methylmalonic aciduria,	Resolved with sequela	No EEG, epilepsy was considered as a part of metabolic

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Case ID	Age	Gender	Suspects	Events PT Comma Sep	Case Outcome	Comments
				Vitamin B12 deficiency		syndrome
B0675844A	13M	Female	Infanrix hexa, Prevenar	**Febrile convulsion**, Depressed level of consciousness, **Convulsion**, Epilepsy, Vaccination complication, Fatigue, Crying, Chills, Somnolence, Pyrexia	Unresolved	No EEG, epilepsy not confirmed, periventricular leukomalacia on NMR probably perinatal.
B0677130A	4M	Male	Infanrix hexa, Prevenar, Rotarix	Epilepsy, **Convulsion**, **Cyanosis**, Musculoskeletal stiffness	Resolved	EEG normal
B0677923A	32M	Male	Infanrix hexa	**Meningitis haemophilus**, Osteomyelitis, Epilepsy, Muscular weakness, Balance disorder, Gait disturbance, Muscle rigidity, Pyrexia, Vomiting, Mastoiditis, Subdural effusion, **Vaccination failure**	Unresolved	No EEG result, no clear description of convulsion
B0680077A	3M	Female	Infanrix hexa, Prevenar	Epilepsy, Psychomotor retardation, Hypotonia	Unresolved	Several EEG examinations were performed and only one showed unspecified abnormalities
D0064824A	3M	Female	Infanrix hexa, RotaTeq	**Convulsion**, Dyskinesia, Dissociation, Fatigue, Epilepsy	Improved	Normal EEG, epilepsy was ruled out
D0068399A	5M	Female	Infanrix hexa	Autism, Epilepsy, Developmental delay	Unresolved	It was reported that diagnose confirmed, but no data provided.
B0664846A	10M	Male	Infanrix hexa, Prevenar	Petit mal epilepsy, Hypotonia, Irritability	Resolved	Medical history included epilepsy, cerebellar hypoplasia and partial agenesis of corpus callosum
B0670341A	13M	Male	Infanrix hexa, Prevenar	Petit mal epilepsy, Irritability, Eye rolling	Resolved with Sequelae	No clear epileptic pattern on EEG

In only 4 cases out of these 13 reports diagnosis of epilepsy can be considered as confirmed. In case B0645066A a family origin of epilepsy has also to be considered. In case B0657965A epilepsy was considered as a part of metabolic disturbance. In case

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D0068399A, it was reported that diagnosis was confirmed by several examination, but data were not provided. In case (B0664846A), the subject was diagnosed with epilepsy before vaccination.

Table 14 Cases of status epilepticus (n=4) identified during the reporting period

Case ID	Age	Gender	Suspects	Events PT Comma Sep	Case Outcome	Comments
B0641899A	2M	Male	Infanrix hexa	Status epilepticus, **Grand mal convulsion**, Loss of consciousness, **Cyanosis**, Muscle spasms, Somnolence, Pyrexia	Resolved	Normal EEG and other investigations.
B0665503A	16M	Female	Infanrix hexa, Meningitec	Status epilepticus, Hypotonia, **Grand mal convulsion**, Pyrexia	Resolved	Normal EEG and other investigations
B0677766A	5M	Female	Infanrix hexa, Prevnar	**Retinal haemorrhage**, Traumatic brain injury, Child maltreatment syndrome, Status epilepticus, Depressed level of consciousness, **Convulsion**, Subdural effusion, Oligodipsia, Staring, Vomiting, Diarrhoea	Resolved	The diagnosis of shaken baby syndrome was considered
D0068402A	8W	Male	Infanrix hexa, Prevnar	**Febrile convulsion**, Status epilepticus, Fatigue, Restlessness, Staring, Body temperature increased	Resolved	Normal EEG

Table 15 Cases of infantile spasms (n=2) identified during the reporting period

Case ID	Age	Gender	Suspects	Events PT Comma Sep	Case Outcome	Comments
B0613669A	2M	Male	Infanrix-polio-HIB, Infanrix hexa	Infantile spasms, **Gaze palsy**, Muscle spasms, Sleep disorder, Condition aggravated, Motor dysfunction, Hypertonia	Resolved	Asymmetric atypical hypsarrhythmia on EEG
D0067330A	7M	Female	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	Infantile spasms, **Clonic convulsion**, Gastroenteritis rotavirus, Bronchitis	Unknown	Positive family history of epilepsy, typical West syndrome on EEG

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6.4.2.8.4. Encephalitis and encephalopathy

During the period of this PSUR, two cases case were reported with the MedDRA Preferred Terms encephalitis and/or encephalopathy.

Case **B0649288A** - MedDRA Preferred Terms: Encephalopathy, Altered state of consciousness, Encephalitis, Hypotonia, Hyperreflexia

This case was reported by the Italian Regulatory Authority and described the occurrence of encephalopathy in a 4-month-old female who was vaccinated with unspecified doses of Infanrix hexa™ and Prevenar. Four days after vaccination, the subject experienced aseptic encephalopathy. The subject was hospitalized. The diagnosis was: axial hypotonia with hyperreflexia of patellae. The sensibility could be partially stimulated (to pain). The subject was treated with ceftriaxone, corticosteroids, and antiviral medication. The subject"s 24-hour monitoring showed no abnormality (oxygen saturation, heart rate and ECG). NMR and lumbar puncture did not show any abnormality also. Other investigations: PCR was negative to HSV2, EBV, CMV, HSV1, HHV6 and HHV8. At the 13th days of hospitalization the baby began to follow the physiokinesis-therapy.

Company comment: A 4-month-old subject experienced hypotonia and hyperreflexia of patellae 4 days after multiple vaccinations. All investigations resulted in normal findings. No symptoms of acute inflammation and/or involvement of central nervous system were reported.

Case **B0678021A** - MedDRA Preferred Terms: Encephalopathy, Decreased eye contact, Psychomotor skills impaired, Speech disorder developmental, Developmental delay, Motor dysfunction, Gait disturbance, Dysstasia, Indifference, Cognitive disorder, Crying, Decreased appetite

This case was reported by the Italian Regulatory Authority and described the occurrence of encephalopathy in a 3-month-old male on the same day as vaccination with Infanrix hexa™ on 16 June 2006. Vaccination history included the 2nd and 3rd doses of Infanrix hexa™ given on 28 July 2006 and 5 February 2007, an unspecified dose of Priorix on 21 November 2007 and an unspecified dose of Prevenar given on 12 March 2008. The subject also developed the following symptoms: inconsolable crying, refusing food, loss of eye contact, slowing psychomotor development each vaccine injection, loss of empathy, lack of language development, delayed walking, regression of motor skills, loss of ability to walk and stand up alone, indifference to the environment and for social interaction, lack of maturation of cognitive functions. At the time of follow-up, the outcome of the event was unresolved.

Company comment: A 4-month-old subject experienced encephalopathy less than 1 day after vaccination. Neither symptoms nor laboratory investigation performed at that time were reported. The subject received further Infanrix hexa™ vaccinations as well as other vaccines: Prevenar, Priorix, but not according to a schedule. The case lacks data on subject medical and family history, results of genetic investigation.

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6.4.2.8.5. Hemiparesis and Hemiplegia

During the reporting period one case of hemiparesis and one case of hemiplegia were reported. Both cases **B0666511A** and **D0066195A** were reported together with cerebral haemorrhage. These cases were described in section 6.4.2.8.2 on cerebral haemorrhage.

6.4.2.9. Skin and subcutaneous tissue disorders

6.4.2.9.1. Erythema multiforme

One case of erythema multiforme was received during the reporting period.

Case **B0616513A** – MedDRA Preferred Term: Erythema multiforme

This serious case was reported by a physician via sales representative and described the occurrence of erythema multiforme in a 1-month-old male 2 days after vaccination on 4 December 2009 with unspecified doses of Infanrix hexa™, Prevenar and RotaTeq. At the time of reporting the event was improved.

Company comment: A 1-month-old subject developed erythema multiforme 2 days after multiple vaccinations. This case lacks data on the subject's medical history, data confirming the diagnosis (biopsy), and other possible diagnosis.

6.4.2.9.2. Henoch-Schonlein purpura

One case of Henoch-Schonlein purpura (HSP) was received during the period of this report.

Case **D0067815A** – MedDRA Preferred Terms: Henoch-Schonlein purpura, Pyrexia, Nausea, Vomiting, Decreased appetite, Myalgia, Arthralgia, Erythema nodosum, Malaise, Gait disturbance, Rash, Oedema peripheral, Pain in extremity, Off label use

This serious case was reported by a physician and described the occurrence of Henoch-Schonlein purpura in a 7-year-old male who received on 25 May 2010 the 5th dose of Infanrix hexa™ (right deltoid). There were no concurrent medications, no concurrent medical conditions or any other risk factors. One day after vaccination the subject experienced fever (below 38 deg C), nausea, vomiting and was not eating for 3 days. Nausea and vomiting resolved. Afterward the subject experienced myalgia and arthralgia and, on the left leg, two foci of erythema nodosum. The subject was not feeling well and was limping. The subject experienced rash on right arm with increase to left lower leg and swelling of left ankle joint. The subject was in good general condition with no pain in stomach and no complaints. On the dorsal left lower leg were HSP haemorrhages. The swollen left ankle joint was tender on pressure. At admission to emergency hospital the subject showed no fever. Urine was without pathological findings. On 25 June 2010, HSP was resolved.

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Company comment: A 7-year-old subject experienced HSP unspecified time after vaccination with 5th dose of Infanrix hexa™. Infanrix hexa™ is not indicated at this age. Reported gastrointestinal symptoms one day after vaccination could be another plausible cause of this event. The case lacks laboratory data to confirm the diagnosis.

6.4.2.9.3. Petechiae

During the reporting period 31 cases of petechiae were received.

Summary information for the complete set of reports is shown in the below tables. Cases with bolded events terms are also analysed/summarised in the relevant sub-sections of section 6.4 of this PSUR.

Tabel 16 Summary information for complete data set, n=117

Patient age (n=29)	Range	months	2-15
	Median	months	3
Patient gender (n=30)	Male	n	13
	Female	n	17
Report type	Spontaneous	n	31
Time to onset of event (n=28)	Range	days	0-150
	Median	days	less than 1 day
Outcome	Resolved	n	19
	Improved	n	1
	Unresolved	n	5
	Unknown	n	6
Cases where concomitant vaccine was administered		n	26

Tabel 17 Cases of petechiae identified during the reporting period

Case ID	Age	Gender	Seriousness Fda	Events PT Comma Sep	Suspect Drugs PT Comma Sep	Time To Onset Since Last Dose	Case Outcome
B0601844A	2 Months	Female	Not serious	Petechiae, Oedema peripheral, Urticaria, Injection site induration, Rash erythematous	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	2 Hours	Unresolved
B0622905A	89 Days	Male	Not serious	Crying, Pyrexia, Skin discolouration, Petechiae, Swelling	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	5 Hours	Resolved
B0627290A	3 Months	Female	Serious	Depressed level of consciousness, Respiratory disorder, Petechiae, Hypotonia, Somnolence, Diarrhoea, Crying, Pyrexia, Pallor	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	2 Hours	Resolved

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Case ID	Age	Gender	Seriousness Fda	Events PT Comma Sep	Suspect Drugs PT Comma Sep	Time To Onset Since Last Dose	Case Outcome
B0628345A	5 Months	Male	Not serious	Petechiae	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	6 Days	Resolved
B0630575A	3 Months	Female	Not serious	Skin discolouration, Petechiae, Swelling, Skin warm, Pyrexia, Crying	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	5 Hours	Resolved
B0630988A	12 Months	Female	Serious	**Thrombocytopenic purpura**, Viral infection, Pyrexia, Rash, Petechiae, Ecchymosis	Infanrix hexa, MMR vaccine (Non-GSK)	15 Days	Resolved
B0634231A	2 Months	Female	Serious	Petechiae	Infanrix hexa, Rotavirus vaccine (Non-GSK)	3 Hours	Resolved
B0636568A	4 Months	Male	Not serious	Petechiae, Oedema peripheral, Skin discolouration, Pyrexia, Crying	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	6 Days	Resolved
B0638020A	7 Months	Female	Not serious	Petechiae	Infanrix hexa, Synflorix	4 Days	Resolved
B0648028A	3 Months	Female	Serious	Leukocytosis, Lymphadenopathy, Pain in extremity, Petechiae, Condition aggravated	Infanrix hexa, Rotavirus vaccine, Bacillus Calmette-Guerin Vaccine (Non-GSK)	46 Days	Unknown
B0651929A	11 Months	Male	Not serious	Rash, Petechiae	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	0 Days	Resolved
B0652855A	2 Months	Female	Serious	**Purpura**, Petechiae, **Thrombocytopenia**	Rotavirus vaccine, Infanrix hexa, Pneumococcal vaccines (Non-GSK)	6 Days	Unknown
B0656703A	2 Months	Male	Serious	**Idiopathic thrombocytopenic purpura**, Petechiae, Abnormal behaviour, **Purpura**	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	8 Days	Resolved
B0657766A	11 Months	Female	Not serious	Petechiae	Infanrix hexa	10 Minutes	Resolved
B0668854A	3 Months	Male	Serious	Petechiae, Erythema, Crying	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	0 Days	Resolved

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Case ID	Age	Gender	Seriousness Fda	Events PT Comma Sep	Suspect Drugs PT Comma Sep	Time To Onset Since Last Dose	Case Outcome
B0673408A	2 Months	Female	Not serious	Petechiae, Crying, Somnolence	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	3 Minutes	Resolved
B0679687A	2 Months	Female	Not serious	Hyperaemia, Irritability, Petechiae, Food aversion	Infanrix hexa	0 Days	Resolved
D0066805A	12 Months	Female	Serious	**Idiopathic thrombocytopenic purpura**, Haematoma, Petechiae, Mouth haemorrhage	Priorix Tetra, Infanrix hexa	19 Days	Unresolved
D0066937A	4 Months	Female	Serious	Erythema, Swelling, Petechiae, General physical health deterioration, Fluid intake reduced, Crying, Agitation, Lividity, Rash macular	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	2 Minutes	Unknown
D0066939A	Child	Unknown	Not serious	Erythema, Swelling, Petechiae	Infanrix hexa	Unknown	Unknown
D0067158A	Infant	Male	Serious	**Convulsion**, **Partial seizures**, **Cerebral atrophy**, Demyelination, Petechiae, Developmental delay, Schamberg's disease, Rhinitis	Infanrix hexa, Priorix Tetra, Rotavirus vaccine (Non-GSK), Pneumococcal vaccines (Non-GSK), Meningococcal polysaccharide vaccine group C (Non-GSK)	86 Days	Unresolved
D0067175A	4 Months	Female	Serious	**Idiopathic thrombocytopenic purpura**, **Thrombocytopenia**, Petechiae	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	31 Days	Resolved

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Case ID	Age	Gender	Seriousness Fda	Events PT Comma Sep	Suspect Drugs PT Comma Sep	Time To Onset Since Last Dose	Case Outcome
D0067177A	15 Months	Female	Serious	**Thrombocytopenia**, **Idiopathic thrombocytopenic purpura**, Gastroenteritis, Petechiae, Haematoma, Vomiting, Diarrhoea, Injection site inflammation, Injection site induration, Incorrect route of drug administration	Infanrix hexa, Priorix Tetra, Pneumococcal vaccines (Non-GSK)	0 Days	Unresolved
D0067257A	3 Months	Female	Serious	Petechiae, Rash, Injection site induration, Injection site erythema, Pyrexia	Infanrix hexa, Synflorix	0 Days	Unknown
D0068471A	8 Months	Male	Serious	**Idiopathic thrombocytopenic purpura**, Petechiae, Haematoma, Upper respiratory tract infection, Rhinitis, Pyrexia, Constipation, Hypochromic anaemia	Infanrix-polio-HIB, Infanrix hexa, Pneumococcal vaccines (Non-GSK)	5 Months	Unresolved
D0068563A	7 Months	Male	Serious	B precursor type acute leukaemia, Anaemia, White blood cell disorder, Neutropenia, Decreased appetite, Body temperature increased, Asthenia, Fatigue, Infection, Weight decreased, Lymphadenopathy, Indifference, Cough, Rhinitis, Pallor, Petechiae, Hepatosplenomegaly, Viral test positive, Bronchitis	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	4 Days	Unknown
D0068602A	3 Months	Male	Not serious	Rash erythematous, Petechiae, Restlessness, Screaming, Swelling, Vomiting, Decreased appetite	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	5 Minutes	Resolved

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Case ID	Age	Gender	Seriousness Fda	Events PT Comma Sep	Suspect Drugs PT Comma Sep	Time To Onset Since Last Dose	Case Outcome
D0068680A	3 Months	Male	Not serious	Petechiae, Crying, Oedema peripheral, Erythema	Infanrix hexa	0 Days	Resolved
D0068750A	3 Months	Male	Serious	Petechiae, Haematoma	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	0 Days	Improved
D0068961A	4 Months	Male	Serious	Petechiae, Pyrexia, Febrile infection, Rhinitis, Leukocytosis, **Thrombocytosis**, Crying, Restlessness, Bacterial infection	Infanrix hexa	0 Days	Resolved
D0069114A	4 Months	Female	Not serious	Petechiae, Pyrexia	Infanrix hexa, Pneumococcal vaccines (Non-GSK)	1 Days	Resolved

6.4.2.9.4. Purpura

During the reporting period 7 cases of purpura have been received.

In cases **B0619820A**, **B0652855A** and **B0656703A** idiopathic thrombocytopenic purpura, thrombocytopenia or thrombocytopenic purpura was reported as well. These cases are described in section 6.4.2.1.1 on thrombocytopenia. The other cases are described below.

Case **B0651934A** – MedDRA Preferred Terms: Vasculitis, Purpura

This serious case was reported by the Italian regulatory authority and described the occurrence of vasculitis and purpura in a 4-month-old female on the same day as vaccination with Infanrix hexa™. The events were resolved.

Case **D0063497A** – MedDRA Preferred Term: Purpura

This non-serious case was reported by a physician, via a sales representative, and described the occurrence of purpura on right leg in an approximately 2.5-month-old female 3 days after vaccination with Infanrix hexa™ (left thigh) and RotaTeq (oral). At the time of reporting the event was improved.

Case **D0067173A** – MedDRA Preferred Terms: Purpura, Pyrexia

This non-serious case was reported by the German regulatory authority and described the occurrence of purpura and fever in a 4-month-old male 10 days after vaccination with a 2nd dose of Infanrix hexa™ (left thigh) and Prevenar (right thigh). Thrombocytopenia was excluded. At the time of reporting the outcome of the events was unspecified.

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Case **D0068231A** – MedDRA Preferred Terms: Purpura, Oedema peripheral, Haemostasis

This non-serious case was reported by a physician and described the occurrence of purpura in a 3-month-old female 10 minutes after vaccination who was vaccinated with a 1st dose of Infanrix hexa™ (left upper thigh). Ten days after vaccination the subject experienced fresh large extended purpura (petechia-like of blue colour) below application site, that resolved 2 days later. The subject also developed oedema at back of foot. At the time of reporting all events were resolved. The same case was received via the German regulatory authority. The subject was healthy. The subject experienced fresh extended purpura on left leg below vaccination site over lower leg. Differential diagnose included circular stasis caused by holding or nappy approximately 45 minutes after vaccination. At the time of reporting the events were resolved.

6.4.2.9.5. Subcutaneous nodule

Two non-serious cases of subcutaneous nodule have been received during the reporting period.

Case **B0669691A** – MedDRA Preferred Terms: Hyperaemia, Pyrexia, Injection site pain, Oedema, Subcutaneous nodule, Gait disturbance, Irritability

This case was reported by the Italian regulatory authority and described the occurrence of hyperemia at injection site, fever (38 deg. C), injection site pain, edema, small subcutaneous nodule, difficulty with gait and irritability in a 15-month-old male less than 1 day after vaccination with a 3rd dose of Infanrix hexa™ and Meningitec. At the time of reporting the events were improved.

Case **B0672162A** – MedDRA Preferred Terms: Subcutaneous nodule, Injection site reaction, Pyrexia

This case was reported by the Italian a regulatory authority and described the occurrence of persistent subcutaneous nodule in the right thigh, injection site reaction (local reaction at the legs) and fever (39.5 deg C) for 3 days in a 14-month-old male on the same day as vaccination with a 3rd dose of Infanrix hexa™ and Prevenar (unknown thighs). The subject was treated with paracetamol and ibuprofen. At the time of reporting, the outcome of the events was unspecified.

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6.4.2.10. Vascular disorders

6.4.2.10.1. Kawasaki's disease

Five serious cases of Kawasaki"s disease were reported during the period under review and summarised below.

Case **B0616059A** - MedDRA Preferred Terms: Kawasaki's disease, Macrophage activation, Pyrexia, Irritability, Rash erythematous, Oedema peripheral, Pain in extremity, Hepatic function abnormal, Hypoalbuminaemia, Serum ferritin increased, Anaemia, Histiocytosis haematophagic, Rash.

This case was reported by the Italian Regulatory Authority and described the occurrence of Kawasaki disease in a 3-month-old female who was vaccinated with unspecified doses of Infanrix hexa™ and Prevenar on 08 January 2008. One day after vaccination, the subject experienced fever up to 40 C with irritability, erythematous rash on face and legs. The subject started a treatment with antibiotics and was hospitalised. There the subject also experienced bilateral tumefaction with pain at feet. The subject experienced polymorphous rash, peripheral oedema and peripheral erythema. Initial tests showed progressive increase of inflammation index, liver dysfunction, hypoalbuminemia, ferritin increase. An infective etiology of the adverse events was ruled out based on the following tests: EchoCG, cranial and total body CT, CSF analysis, bone marrow analysis and concentration of vanilmandelic and homovanilmandelic acids in urine.

The suspect of Kawasaki's disease was substantiated by the following interventions, performed on 19 February 2008: immunoglobulin infusion and ASA (acetylsalicylic acid) without any improvement of the symptoms. The subject received hemotransfusion due to an anaemia. It was followed by a high-dose therapy with steroids that lead to a rapid improvement in symptoms and clinical data. Steroid therapy was quickly reduced and withdrawn. After 48 hours from the suspension of the steroid therapy, the subject experienced reoccurrence of high fever and was hospitalised. The physicians defined the diagnosis of secondary macrophage activation syndrome in the context of an atypical form of Kawasaki's disease. The subject was treated with high dose steroids and cyclosporine. This led to rapid improvement in symptoms. On 03 March 2008, the subject was discharged from hospital, in a good general condition. Then the subject was monitored periodically, always with good clinical results.

Company comments: The subject experienced fever, irritability and rash one day after multiple vaccinations. Laboratory tests showed inflammation, however no focus was identified. Treatment with immunoglobulin and aspirin was unsuccessful that makes diagnosis of Kawasaki disease doubtful.

Case **B0653827A** – MedDRA Preferred Terms: Kawasaki"s disease, Oedema peripheral, Rash maculo-papular, Conjunctivitis, Rash, Cheilitis, Pyrexia

This case was reported by the Italian Regulatory Authority as suspected Kawasaki disease, however during follow-up information received after DLP of this PSUR the Kawasaki disease was not confirmed.

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Case **B0657560A** – MedDRA Preferred Terms: Rash maculo-papular, Conjunctivitis, Oedema peripheral, Kawasaki's disease, Pyrexia

This case was reported by the Italian regulatory authority and described the occurrence of maculo-papular exanthema in a 11-month-old male who was vaccinated with unspecified doses of Infanrix hexa™ and Prevenar on 20 April 2010. One day after vaccination, the subject experienced maculo-papular exanthema at back and lower limbs, conjunctivitis, edema of hand, pedal edema and fever (>39 deg.C). Kawasaki disease was considered. The subject was hospitalised and treated with cephalosporins. On 24 April 2010, the events were resolved.

Company comments: The subject experienced fever, rash oedema and conjunctivitis one day after multiple vaccinations. Event resolved 4 days after treatment with antibiotic. Short duration of symptoms (less than 5 days) and response to antibiotic treatment makes reported diagnosis of Kawasaki disease doubtful.

Case **D0066913A** - MedDRA Preferred Terms: Kawasaki's disease, Pyrexia, Interstitial lung disease, Crying, Oligodipsia, Faeces discoloured, Dermatitis diaper, Rash, Conjunctival hyperaemia, Cheilitis, Chapped lips, Skin exfoliation, Anaemia, Thrombocytosis, Hepatic enzyme increased

This case was reported by a physician and described the occurrence of Kawasaki syndrome in a 4-month-old female who was vaccinated with the 1st doses of Infanrix hexa™ and Prevenar. Concomitant medications included antibiotics as needed, as recent family anamnesis included infection of URTI of the sister some days ago. Approximately 3 days post vaccinations, on 07 June 2009, the subject experienced persistent fever up to 40 degC. The subject showed no signs of infection, but CRP increased. The subject was hospitalised for 16 days and diagnosed with Kawasaki syndrome, interstitial pneumonia right, decreased fluid intake and diaper rash. Suspected meningitis was excluded. On admission the subject was in decreased general condition and good nutritional condition. Body temperature was 37.9 degC. The subject was crying and whimpering and showed mild signs of meningeal disorder. The skin was pale and marbled.Laboratory examinations showed increased inflammatory parameters. In combination with clinical signs bacterial infection was suspected and intravenous antibiotic treatment with cefuroxime was started. Thoracic X-rays, performed on 08 and 10 June 2009 showed interstitial pneumonia right lower lobe with spotted extensive pulmonary infiltration due to pneumonia in the lower right pulmonary field. Urinalysis was normal. Blood and CSF cultures were sterile. During course of hospitalisation general condition deteriorated further, laboratory infection parameters worsened and high fever up to 40.3 degC persisted. On 09 June 2009 the subject experienced greenish stools. Test for occult blood was positive one time, but follow-up tests for occult blood were negative. Microbiological stool examinations showed no pathologic findings. Abdominal and cranial sonography was normal. Because of persistent high fever antibiotic treatment was changed to cefotaxime, Certomycin, erythromycin, Unacid, in combination with antimycotic prophylaxis with nystatin. Due to intermittent exanthema, conjunctival injection, lip redness and lip tension (cracked lips), as well as antibiotic resistant fever the subject was diagnosed with possible Kawasaki syndrome. She was treated with normal immunoglobulin and aspirin. Antibiotic treatments were discontinued. Fever resolved and

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general condition improved. The subject showed increased skin exfoliation on hands and feet. Laboratory examinations showed anemia, thrombocytosis and increase in liver values, which were seen within the scope of Kawasaki syndrome and treatment with aspirin. Multiple EchoCG and ECG, performed for controls, showed no conspicuous findings.

Company comments: The reported events are compatible with typical Kawasaki's disease. No coronary abnormalities were observed. Recent URTI in family could not be ruled out as a possible cause of Kawasaki's disease.

Case **D0068409A** - MedDRA Preferred Terms: Kawasaki's disease, Leukocytosis, Meningitis, Gastroenteritis bacterial, Sepsis, Anaemia, Pyrexia, General physical health deterioration, Hyperaesthesia, Crying, Abnormal faeces, Lymphadenopathy, Pain, Acute tonsillitis, Sinus tachycardia, Rash, Chapped lips, Hypotension, Dysplasia, Dry throat, Lip disorder, Conjunctivitis, Hypoalbuminaemia

This case was reported by a physician via the German regulatory authority and described the occurrence of Kawasaki's disease in a 4-month-old subject who was vaccinated with the 2nd doses of Infanrix hexa™ and Prevenar on 09 July 2010. Four days later, the subject was presented to a doctor with high fever without signs of an infection. Laboratory test showed leukocytosis of 19.700. The subject was hospitalised. The subject did not develop cough, rhinitis, diarrhea or vomiting. Fluid intake was well. Maternal concurrent medical condition included rheumatoid arthritis and psoriasis. On admission, general condition was reduced, skin showed no exanthema. Skeleton, eyes, ears, oral cavity, heart, respiration, abdomen and genitals were without pathological findings. Central nervous system was without pathological finding despite of sensitiveness to touch and crying fits. Inflammatory values were increased. Urine test and X-ray of thorax were normal. By differential diagnosis, bacterial gastroenteritis and sepsis was suspected. The subject was treated with cefotaxime for 2 days. The subject developed painful cervical lymph node swelling at right side. There were just solitary stipples at tonsils (angina follicularis). Treatment was changed to clindamycin and cefuroxime for 5 days. Due to recurrent tachycardia during sleep, ECG was performed and showed only sinus tachycardia. EchoCG and sonography of abdomen showed normal results. Values of CRP further increased. The subject was additionally treated with fosfomycin for 3 days. The subject developed small spot exanthema on trunk and dry chapped lips. Fever remained already since 5 days, which could not be resolved by antibiotics. Therefore, Kawasaki's syndrome was diagnosed. The subject was treated with normal immunoglobulin and aspirin. General condition improved fast. Echocardiography excluded coronary ectasia. Thirty hours after treatment with immunoglobulin, the subject's general condition again decreased and second dose of immunoglobulin was administered. The subject was transferred to another hospital for further medical care treatment. First episode of Kawasaki vasculitis on 13 July 2010 and recurrent Kawasaki vasculitis on 20 and 24 July 2010 as well as dysplastic pinna (right more than left sided) was diagnosed. On 04 August 2010, the subject was discharged in good general condition. Fever had not recurred. Recently cardiologic examinations resulted normal. No cardiac manifestations of Kawasaki-syndrome could be identified.

Company comment: The reported events are compatible with typical Kawasaki's disease.

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6.5. Follow-Up Data

Relevant follow-up information was received on fatal cases subsequent to their inclusion in PSUR #14. This information was taken into account for the O/E analysis of sudden deaths. CIOMS forms are presented in Appendix 5B.

In case **B0580597A** the autopsy report was received and confirmed SUDI.

In case **B0590738A** cause of death was probably due to underlying conditions.

For cases **B0598135A** and **D0061280A** SIDS was confirmed by autopsy report.

In case **D0061486A** death was due to cardiac failure (probably of genetic origin).

For case **D0062778A** SIDS was not confirmed, cause of death was reported as severe respiratory infection and myocarditis.

No new data has been received for case **B0591078A**.

Of note case **D0038393A** received in 2001 was published in the literature.

7. STUDIES

In line with the Addendum to ICH E2C [2], only studies with findings that have potential impact on product safety information are included in Sections 7.1 and 7.3. These sections do not contain a complete listing of all studies completed or reviewed in the reporting period.

7.1. Newly-Analysed Studies

Three new corporate studies relevant to the safety of Infanrix hexa™ were completed and analysed during the period of this report.

Study #**112157** (DTPa-HBV-IPV=Hib-MenC-TT-002 PRI): A phase II, open-label, randomised, multicentre study to evaluate the safety and immunogenicity of GSK Biologicals‟ DTPa-HBV-IPV/Hib-MenC-TT vaccine co-administered with GSK Biologicals‟ 10-valent pneumococcal conjugate vaccine in healthy infants when administered as a three-dose primary vaccination course at 2, 3 and 4 months of age. The observed incidence of solicited and unsolicited adverse events was in the same range in the 3 groups, i.e. “Hepta” (candidate heptavalent vaccine), “HexaMnC” (Infanrix hexa™ co-administered with conjugate meningococcal vaccine (Menjugate), and “HexaPn” [Infanrix hexa™ co-administered with conjugate pneumococcal vaccine (Synflorix)]; all the vaccines administered in the study were well tolerated. One SAE (thrombocytopenia) reported for a subject in the Hepta group was considered by the investigator to have a potential causal relationship to vaccination. All serious adverse events reported during the study resolved without sequelae.

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Study #**110142** (10-PN-PD-DIT-027 PRI): A phase III randomized, single-blind, controlled study to demonstrate the non-inferiority of co-administration of GSK Biological 10-valent pneumococcal conjugate vaccine with Pediacel™ versus co-administration with Infanrix hexa™, when administered to infants as a three-dose primary vaccination course during the first six months of life and as a booster dose at 11-13 months of age. This study was conducted with 3 parallel groups: "10Pn-Hexa" group received 10Pn-PD-DIT and Infanrix hexa™, "10Pn-PDC" group received 10Pn-PD-DIT and Pediacel and "Prev-PDC" group received Prevenar and Pediacel. The incidences of grade 3 solicited local and general adverse events were low in all study groups. The percentage of doses followed by unsolicited adverse events was in the same range in all groups. Grade 3 unsolicited adverse events with causal relationship to vaccination were rarely reported. No fatal SAEs were reported in this study up to the data lock point. Up to the data lock point, SAEs after primary vaccination were reported in 32 subjects (17 subjects in the 10Pn-Hexa group, 5 subjects in the 10Pn-PDC group and 10 subjects in the Prev-PDC group).One of these SAEs reported for a subject in the 10Pn-Hexa group (apparent life threatening event) was assessed by the investigator to be causally related to vaccination.

Study #**111654** (10-PN-PD-DIT-048): A phase III, multi-centre, double-blind, randomised study to assess the non-inferiority of a commercial lot of GlaxoSmithKline (GSK) Biologicals 10-valent pneumococcal conjugate (10Pn-PD-DiT) vaccine compared to a clinical phase III vaccine lot, when given as a three-dose primary immunization course. This study was conducted with 2 parallel groups: the "Clin" group received the phase 3 clinical lot of 10Pn-PD-DIT with Infanrix hexa™ or Infanrix-IPV/Hib and HRV, the "Com" group received the commercial lot of 10Pn-PD-DIT with Infanrix hexa™ or Infanrix-IPV/Hib and HRV. All subjects were concomitantly administered a dose of Infanrix hexa™. The following results are supportive of an acceptable safety profile of the clinical phase III:
Unsolicited adverse events:
The percentage of doses followed by at least one unsolicited symptom in the 31-day post-vaccination period was 16.2% in the Clin group and 17.0% in the Com group. The most frequently reported unsolicited AE in each group was upper respiratory tract infection (5.0% in the Clin group and 6.0% in the Com group). The percentage of doses followed by at least one unsolicited symptom considered by the investigator to be causally related to vaccination and the percentage of doses with grade 3 unsolicited AEs in the 31-day post-vaccination period was at most 1.0% in both groups. No grade 3 unsolicited AEs were considered by the investigator to be causally related to vaccination.
Serious adverse events:
No fatal SAEs were reported in this study.
A total of 36 non-fatal SAEs were reported for 25 (5.4%) out of 466 vaccinated subjects: 18 subjects (7.7%) in the Clin group and 7 subjects (3.0%) in the Com group.
No SAEs were considered by the investigator to be causally related to vaccination.
One SAE did not resolve (spinal muscular atrophy) and one SAE (tuberculous meningitis) was still ongoing at the end of this study.

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7.2. Targeted Safety Studies

This section provides an update on any planned, ongoing or completed targeted safety studies involving Infanrix hexa™ in the reporting period. Targeted safety studies are those specifically planned or conducted to examine an actual or hypothetical safety concern (Vol 9A, Section 6.3.8.b) in a product marketed anywhere in the world. This includes any GSK-sponsored, and when applicable, GSK-supported pharmacoepidemiology study or clinical trial conducted anywhere in the world with the aim of identifying or quantifying a safety hazard. Although all clinical trials collect safety information as a matter of routine, only those initiated to examine a specific safety concern are considered a targeted safety study.

There are no targeted safety studies for Infanrix hexa.

7.3. Published Safety Studies

Study #**217744/100** (DTPa-HBV-IPV-100) is currently in press in Southeast Asian J Trop Med Pub Health 2011; 42(1).

This study was an open, multicentre, post-marketing surveillance (PMS) study to assess the safety and reactogenicity of GlaxoSmithKline Biologicals‟ DTPa-IPV/Hib vaccine administered at 3 and 4 months of age and DTPa-HBV-IPV/Hib vaccine (Infanrix hexa™.) administered at 5 months of age, as primary vaccination course, followed by administration of GSK Biologicals‟ DTPa-IPV/Hib vaccine at 18 months of age in healthy infants who received hepatitis B vaccine at birth and at one month of age. Both study vaccines were well tolerated and demonstrated a good safety profile. Two SAEs (febrile convulsions and exanthema subitum) were reported by one subject after administration of the booster dose that were considered by the investigator to have causal relationship to the study vaccine. Both events were resolved during the course of the study.

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8. OTHER INFORMATION

8.1. Efficacy Related Information

During the period of this report, there were 28 cases where the MedDRA Preferred Terms could potentially correspond to lack of efficacy (LOE) of the pertussis, hepatitis B or Hib component.

8.1.1. Pertussis

Twenty-one cases including the event pertussis were identified during the reporting period. A total of 12 reports were received from Germany, 5 from Ireland, 2 from France, 1 from Italy and 1 from Austria. Seventeen were reported as serious and 4 as non-serious.

From these 21 cases (see below table), 13 were laboratory-confirmed either by positive PCR (n=9) or serological testing (n=4). In the 8 remaining cases, clinical signs and symptoms of pertussis were present (n=2) or no data was available, i.e. pertussis was reported with no further description of the case (n=6).

Table 18 Cases of pertussis during the reporting period

Case ID	Age	Gender	Events PT Comma Sep	Seriousness Fda	Case Outcome	Test
B0603739A	17 Months	Male	Pertussis, Cough, Hypochromasia, Leukocytosis, Regurgitation, Vaccination failure	Serious	Resolved	serology
B0650143A	Infant	Unknown	Pertussis	Not serious	Worse	no data
B0668296A	2 Months	Female	Pertussis, Apnoeic attack, Cough, Gastrooesophageal reflux disease, Inflammation	Serious	Improved	clinical
B0674120A*	1 Years		Pertussis, Vaccination failure	Serious	Unknown	PCR
B0675100A*	1 Years		Pertussis, Vaccination failure	Serious	Unknown	PCR
B0675102A*	1 Years		Pertussis, Vaccination failure	Serious	Unknown	PCR
B0675103A*	2 Years		Pertussis, Vaccination failure	Serious	Unknown	PCR
B0675104A*	2 Years		Pertussis, Vaccination failure	Serious	Unknown	PCR
B0675234A	12 Months	Male	Pertussis, Cough, Salivary hypersecretion, Vaccination failure	Serious	Resolved	PCR

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Case ID	Age	Gender	Events PT Comma Sep	Seriousness Fda	Case Outcome	Test
D0063484A	Child	Female	Pertussis, Vaccination failure, Inappropriate schedule of drug administration	Serious	Resolved	no data
D0063511A	Child	Male	Pertussis, Vaccination failure, Inappropriate schedule of drug administration	Serious	Resolved	no data
D0063525A	Child	Female	Pertussis, Vaccination failure, Inappropriate schedule of drug administration	Serious	Resolved	no data
D0065887A	5 Years	Female	Pertussis, Cough, Vaccination failure	Serious	Resolved	serology
D0066535A	5 Years	Female	Pertussis, Vaccination failure	Serious	Improved	PCR
D0067293A	8 Months	Male	Pertussis, Cough, Bronchitis	Not serious	Unresolved	PCR
D0067933A	4 Months	Female	Pertussis	Not serious	Resolved	clinical
D0067934A	14 Months	Female	Pertussis, Vaccination failure	Serious	Resolved	no data
D0068073A	8 Months	Female	Pertussis, Cough	Not serious	Unknown	PCR
D0068650A	Child		Pertussis, Vaccination failure	Serious	Unknown	no data
D0068825A	10 Years	Male	Pertussis, Vaccination failure	Serious	Unknown	serology
D0069119A	7 Years	Female	Pertussis, Cough, Sneezing, Vaccination failure	Serious	Unknown	serology

*note that these 5 cases were reported in a literature article which describes a community pertussis outbreak that occurred in a small town located in the northwest of Ireland. The extent and development of this outbreak, together with the clinical presentation and also laboratory confirmation supported the hypothesis that most cases were likely to be pertussis.

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8.1.2. Diphtheria

During the period covered by this PSUR no case has been identified where the MedDRA Preferred Term could correspond to a lack of effect of the diphtheria component.

8.1.3. Haemophilus influenza type b

During the reporting period 6 cases have been identified that could correspond to LOE of the Hib component.

Case **B0660183A** was reported by a consumer and described the occurrence of *Haemophilus influenza* type b in a male subject of unspecified age at an unspecified time after vaccination with an unspecified dose of Infanrix hexa™.

Case **B0653461A** was reported by a healthcare professional and described the occurrence of *Haemophilus influenzae* serotype b in a 3-year-old subject at an unspecified time after vaccination with Infanrix Hexa™ and Hiberix™. The subject received a 3rd dose of Infanrix hexa™ on 2 October 2007 and an unspecified dose of Hiberix™ on 11 April 2008.

Case **B0653464A** was reported by a healthcare professional and described the occurrence of *Haemophilus influenzae* serotype b in a 7-month-old female 36 days after vaccination with a 3rd dose of Infanrix hexa™. Blood culture was positive after 24 hours incubation. Gram stain was Gram negative bacilli detected in Aerobic bottle and showed growth of *Haemophilus Influenzae* type B. The microbiology report confirmed that the isolate was serotyped as B.

Case **B0675363A** was reported by a healthcare professional and described a 3-year-old male who received a 3rd dose of Infanrix hexa™ on 27 December 2007 and a dose of Hiberix on 18 June 2008 and developed *Haemophilus influenzae* serotype b 3 years after vaccination with Infanrix hexa™ and 2 years after vaccination with Hiberix™. Blood culture showed *Haemophilus influenzae* serotype b.

Case **D0066769A** was reported by a consumer (presumably the subject's mother) and described the occurrence of *Haemophilus influenza* in a 2-year-old female 13 months after the 4th dose of Infanrix hexa™ on 12 January 2009. On 5 March 2010, a test for *Haemophilus influenza* bacteria in throat was positive.

Case **B0677923A** was reported by a physician and described the occurrence of Hib meningitis breakthrough with osteomyelitis, muscle weakness, balance disorder, walking problems, muscular rigidity, fever and vomiting in a 2-year-old male 16 months after vaccination with the 4th dose of Infanrix hexa™. Relevant tests were performed: computerized tomogram of brain showed meningitis and subdural effusion, lumbar puncture (CSF culture) was *Haemophilus influenzae* positive and blood culture which also was *Haemophilus influenzae* positive presented following results: haemoglobin 11.1 g/dl; white blood cells 7.570; neutrophils 66 %; lymphocytes 29.5 %; and thrombocytes 399.000 10^9/l. Then white blood cells, C-reactive protein and sedimentation rate was elevated.

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8.1.4. Hepatitis B

During the reporting period 1 case has been identified that could correspond to a lack of effect of the hepatitis B component.

Case **D0069123A** was reported by a physician and described the occurrence of negative hepatitis b antibody in a 3-year-old male who was vaccinated with Infanrix hexa™. It was reported that the subject's father (living apart) was hepatitis b positive. In September 2008 the subject received the 4th dose of Infanrix hexa™. Approximately on October 2010, 2 years after vaccination with Infanrix hexa™, a test for Anti-HBs antibody titre was less 10 (hepatitis b antibody negative).

8.1.5. Conclusion of cases of potential lack of efficacy

During the period of this PSUR, 28 cases were identified where the MedDRA Preferred Terms could potentially correspond to a lack of effect of the Hib, pertussis or hepatitis B component.

The table below shows the number of cases and respective reporting frequencies as reported during this PSUR and the previous PSUR periods.

Table 19 Reporting rate of cases that could potentially correspond to lack of efficacy

	PSUR #14		PSUR #15	
Disease	number of cases	reporting rate per 100,000 doses distributed	number of cases	reporting rate per 100,000 doses distributed
Pertussis	24	0.21	21	0.18
Haemophilus influenza	1	0.01	6	0.05
Diphtheria	0	0.00	0	0.00
Hepatitis B	1	0.01	1	0.01

There has been no unusual level of reports of lack of efficacy, which might represent a significant hazard to the treated population.

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8.2. Late-breaking information

There has been no new important information received after the data lock point.

8.3. EU Risk Management Plan

There is no specific risk management plan in place for Infanrix hexa.

8.4. Benefit Risk Analysis

During the PSUR reporting period, no separate risk-benefit analysis has been conducted.

9. OVERALL SAFETY EVALUATION

9.1. Signal Management

GSK employs a routine, pro-active process for identifying safety signals[1] with three main components:

Ongoing awareness and review of important individual cases, including all reports with a fatal outcome.

Systematic, regular and proactive review of aggregate safety data. This includes trend analysis to detect increased frequency of reporting and quantitative methodologies to detect drug interactions and signals in overdose/medication errors, paediatrics and the elderly.

Systematic, regular review of the literature.

A holistic approach is used so that all relevant data sources are interrogated when evaluating safety signals e.g. external sources, clinical studies, epidemiological studies, pre-clinical information.

All signals identified are evaluated; however, priority is given for serious events, particularly events reported with disproportionately high frequency, DMEs[2], and events that if found to be causally related to the vaccine could significantly affect the benefit-risk profile.

Following evaluation of the signal, appropriate action is agreed. The options include continuing routine proactive pharmacovigilance, defining further work to better understand the risk, or recommendation of a label change and/or amendment to the Risk Management Plan (RMP).

GSK is able to detect issues of potential concern promptly and, where appropriate, communicate them expeditiously to regulators outside the PSUR process. Actions taken on these issues are then reflected in the PSUR to ensure information is communicated appropriately to all regulatory authorities.

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[1]A safety signal is defined as a report or reports of an event with an unknown causal relationship to treatment that is recognised as worthy of further exploration and continued surveillance (CIOMS VI).

[2] Designated Medical Events: medically important events that are generally associated with drug toxicity.

Table 20 presents the reporting frequency of the 10 most frequently reported events for Infanrix hexa™ arising from spontaneous reporting including regulatory and consumer reports. For this analysis both serious and non-serious events reported were taken into account, from launch up to the data lock point of this safety update report. Listed events are in bold.

Table 20 Overview of the 10 most frequently spontaneously reported events for Infanrix hexa™. Events in bold are listed in CSI version 10.

Event SOC	Event PT	Number Of Events[1]	Reporting frequency per 100,000 doses distributed
General disorders and administration site conditions	**Pyrexia**	3560	5.87
Nervous system disorders	**Crying**	1113	1.84
General disorders and administration site conditions	**Injection site erythema**	975	1.61
General disorders and administration site conditions	**Injection site swelling**	826	1.36
Injury, poisoning and procedural complications	Inappropriate schedule of drug administration	589	0.97
Nervous system disorders	**Hypotonia**	529	0.87
Vascular disorders	Pallor	461	0.76
Skin and subcutaneous tissue disorders	Erythema	446	0.74
General disorders and administration site conditions	**Injection site induration**	420	0.69
General disorders and administration site conditions	**Injection site reaction**	416	0.69

1. Including regulatory non serious and consumer reports, but excluding clinical trial cases.

All these top 10 events were reported with a frequency between 0.69 to 5.87 per 100,000 doses distributed.

Since the last PSUR the top 10 events has not significantly changed in the reporting frequency except for inappropriate schedule of drug administration, which is now part of the top 10 events. This is mainly related to cases received from France reported via a solicited interview or market research (see section on medication errors).

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9.2. Adverse events of interest

The cumulative count of an event since launch if provided in the following sections is based on the count of MedDRA PTs from cases originating from spontaneous reporting (including non-medically verified and regulatory non-serious cases).

9.2.1. Cases with a fatal outcome

During the period covered by this report 14 fatal cases were identified.

9.2.1.1. Cases of Sudden Death (SD)

Ten cases suggestive of sudden deaths (sudden infant death syndrome: SIDS and sudden unexpected death in infancy: SUDI) were identified during the period covered by this PSUR. A cumulative review of Sudden Death since launch has been performed. Follow-up information is taken into account.

Table 21 shows the number of cases as reported during the different PSUR periods linked to the patient exposure of each period.

Table 21 Reporting rate of SD since launch per PSUR period

PSUR #	period	time period	number of doses sold doses	number of SD as reported in the different PSURs	reporting rate per 100,000 doses distributed
15	23oct09-22oct10	1Y	11981722	10	0.08
14	23oct08-22oct09	1Y	11496552	12	0.10
13	23oct07-22oct08	1Y	10067611	7	0.07
12	23oct06-22oct07	1Y	8621066	6	0.07
11	23oct05-22oct06	1Y	7166964	9	0.13
10	23apr05-22oct05	6M	2282686	2	0.09
9*	23oct00-22apr05	4 1/2Y	9681894	18	0.19
8	23apr04-22oct04	6M	1386298	1	0.07
7	23oct03-22apr04	6M	1246906	5	0.40
6	23apr03-22oct03	6M	1247422	4	0.32
5	23oct02-22apr03	6M	1041975	1	0.10
4	23apr02-22oct02	6M	998814	0	0.00
3	23oct01-22apr02	6M	772137	1	0.13
2	23apr01-22oct01	6M	1050000	1	0.10
1	23oct00-22apr01	6M	430000	0	0.00

*Note that this PSUR covers 4 years and a half and comprises data since launch

This table shows that the reporting frequency of SD is relatively stable over time.

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Observed/Expected Analysis of SD

INTRODUCTION

Regarding the PSUR#14 sent in December 2009, EMA requested that "*The MAH should try to collect relevant and recent data of background incidences rates of sudden death in other European countries.*"

METHODS

1- Literature research

In order to collect relevant and recent data, a literature review of sudden death or sudden infant death was performed for Europe. The search of the literature was made in PubMed and Embase using simultaneously the key words "sudden infant death" or "sudden death", "incidence rate" and "Europe" without restriction on dates. However for SIDS, only publications after 1990"s were selected due to the effect of „Back to Sleep" campaign performed in several European countries. Publications were limited to those published in French and English languages. The bibliographies of identified studies and reviews were searched to identify additional studies of interest. The German Federal Statistical Office was also consulted on line. The search was made in November 2010.

2- Observed Expected Analysis

To estimate the expected numbers, the incidence rate of SID was considered homogenous within each age (ie. over 1st or 2d year of life); therefore the expected number over any day was linearly extrapolated (ie. 1/365) from the prevalence per birth cohort.

The number of cases expected to occur within a predetermined risk period following vaccination (*Ne*) for children under 1 year of age and those between 1 and 2 years of age is derived from the following formula:

$$Ne = Inc \times Nbc \times RiskPeriod \times \alpha$$

where

Inc = the incidence of the disease in the first or second year of life

0.454 per 1,000 live births for < 1 year olds

0.062 per 1,000 live births for 1<2 year olds

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Nbc = the number of doses of vaccine sold since launch (assumption: proportion of adverse events by age is representative for the actual age distribution at vaccination).

Risk Period = adjustement from a predetermined risk period (Days/365)

α = healthy vaccinee correction factor (taken here to be 0.8 based on various case-control studies of SIDS or SUID).

RESULT

Literature research

The tables below present the background incidence rate of Sudden Death or Infant Sudden Death in Europe. The incidence rates of Sudden Death in the table 22 are not all directly comparable since they may refer to different age groups and/or different periods.

Table 22 Incidence rate of Sudden Death per 100,000 person-years

Country/Population	Time period	Age (years)	Number of Sudden Deaths	Incidence Rate (/100,000 py)	Author
Sweden. 6-year retrospective study; necropsy records. Population aged of 1-20 years	1974-1979	1- 20	31	1.15	Molander, 1982
UK. 10-year retrospective study; death certificate. Population resident aged of 1-20 years.	1985-1994	1- 20	270	3.3	Wren, 2000
Germany. Data from the German Federal Statistical Office (ICD code R95-R99).	2007 2008	1-5	38 42	5.5 6.2	German Federal Statistical Office (on line)

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Table 23 Incidence rate of Sudden Infant Death (<1 year of age) per 1,000 live births

Country/Population	Time period	Incidence Rate (/1,000 live birth)	Author
Data from the European Concerted Action on Sids. Case-control studies of SIDS done in 20 regions in Europe.	1992-1996	European range: 0.17 – 1.3 (median: 0.6)	Carpenter, 2004
Ireland. Data from National Sudden Infant Death Register.	1993-1997	0.80	Mehanni, 2000
Austria. Prospective study. Data from autopsy records in the Tyrol.	1994-1998	0.4	Kiechl-Kohlendorfer, 2001
Italy. Data from mortality registry of the 15 health districts in the Lombardy region.	1990-2000	0.13-0.54	Montomoli, 2004
Sweden. Data from the Medical Birth Registry of Sweden.	1999	0.30	Alm, 2001
Sweden. Literature review of Scandinavian studies.	2004	0.2-0.3	Wennergren, 2004
Sweden. Data from the Medical Birth Register of Sweden from 1997-2005.	2005	0.23	Mollborg, 2010
France. National statistics from CepiDc-Inserm	2005	0.32	Aouba, 2008
Germany. Data extracted from the Federal Health Monitoring of Germany (ICD code R95).	2005 2007	0.43 0.33	Nennstiel-Ratzel, 2010
Germany. Data from the German Federal Statistical Office (ICD code R95-R99).	2007 2008	0.44 0.45	German Federal Statistical Office (on line).

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Observed/Expected Analysis of Sudden Deaths (SD)

Given the attention that has been given to the occurrence of sudden deaths in children in the second year of life within 14 days of the administration of hexavalent vaccines, the Company evaluated whether the number of sudden deaths reported in this age group exceeded the number one could expect to occur by coincidence.

Since the distribution of the age at which subjects are vaccinated is unknown, the Company assumed that the proportion of adverse events by age is representative for the actual age distribution at vaccination. It can thus be estimated that 90.6% of all recipients of Infanrix hexa™ were in their first year of life, and 9.4% were in their second year of life. Therefore the number of doses (since launch) was estimated to be 54,927,729 and 5,698,904 respectively. Given that Germany is the main country where Infanrix hexa™ doses are distributed (close to 30% only in Germany); It was assumed that the incidence of sudden death observed in Germany is representative for the entire population of Infanrix hexa™ recipients (German Federal Bureau of Statistics, Statistisches Bundesamt; incidence rate in 1st year of life: 0.454/1,000 live births; second year: 0.062/1,000 live births, data 2008). A healthy vaccinee correction factor (taken here to be 0.8 based on various case-control studies of SIDS or SUID) was applied.

The results of this analysis are present in the below table that shows the number of sudden deaths that could be expected to occur by chance within a range of days post-vaccination.

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Table 24 Cumulative number of O/E cases SD following Infanrix hexa™, first and second year of life, Oct 00 - Dec 10

	1st year of life		2nd year of life	
Time since vaccination	Observed	Expected	Observed	Expected
Less than 1 day	10	54.7	1	0.8
1 day	20	109.3	2	1.5
2 days	33	164.0	3	2.3
3 days	42	218.6	3	3.1
4 days	49	273.3	3	3.9
5 days	50	327.9	3	4.6
6 days	50	382.6	3	5.4
7 days	51	437.3	4	6.2
8 days	52	491.9	5	7.0
9 days	54	546.6	5	7.7
13 days	54	765.2	6	10.8
15 days	55	874.5	6	12.4
16 days	56	929.2	6	13.2
18 days	57	1038.5	6	14.7
19 days	58	1093.1	6	15.5

This analysis shows that the number of sudden death cases reported within 19 days of Infanrix hexa™ vaccination is below the number of cases expected for this time period in children under 2 years of age except when death occurred during the first three days after vaccination in the second year of life where the observed death number is almost equal to the number expected.

The Company will continue to monitor these cases and their reporting frequencies.

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Limitations

There are several limitations for Observed/Expected analyses, and several levels of uncertainty. The major factors affecting O/E analyses are related to:

- Underreporting, reporting biases, and incomplete case details.
- Uncertainty on the number of subjects actually vaccinated.
- No age stratification within the two age groups.

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9.2.2. Other adverse events of interest

9.2.2.1. Blood and lymphatic system disorders

9.2.2.1.1. Idiopathic thrombocytopenic purpura, Thrombocytopenia, Thrombocytopenic purpura

During the period of this PSUR eleven serious cases including the event idiopathic thrombocytopenic purpura (n=6), thrombocytopenia (n=6) or thrombocytopenic purpura (n=1) were identified. The immune character of the events was confirmed only in one case of warm type haemolytic anaemia. In two cases B0619820A and D0067175A negative re-challenge was observed.

Since launch, 63 cases of autoimmune thrombocytopenia, idiopathic thrombocytopenic purpura, thrombocytopenia and thrombocytopenic purpura have been received corresponding to a reporting frequency of 0.10 per 100,000 doses distributed.

Thrombocytopenia is a listed event.

The Company will continue monitoring this event closely.

9.2.2.2. Cardiac disorders

9.2.2.2.1. Cyanosis

Fifty cases including the MedDRA Preferred Term cyanosis were identified during the period of this report. Most cases (45/50) were reported in association with a concurrent condition likely to have caused cyanosis such as convulsions, HHE, hypotonia, hypertonia, apnoea, dyspnoea, ALTE, and syncope. In the remaining 5 cases no clear pattern of events suggestive of a clinical condition or syndrome could be identified.

Since launch, 224 cases have been received corresponding to a reporting frequency of 0.37 per 100,000 doses distributed.

The information received in these cases does not provide evidence of a specific safety signal.

9.2.2.3. Eye disorders

9.2.2.3.1. Gaze palsy

Twenty four cases with the MedDRA Preferred Term gaze palsy were received during the period of this report. It concerned 15 males, 9 females, aged between 1 month and 2 years (median: 5.5 months). Time to onset ranged between less than 1 day to 7 days (median: less than 1 day). Outcome was reported as resolved in 19 cases, unresolved in 1 case and unknown in 4 cases. In all cases this event was reported in association with concurrent events, mostly convulsions (17).

The information received in these cases does not provide evidence of a specific safety signal.

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9.2.2.3.2. Retinal haemorrhage

Two cases with the MedDRA Preferred Term retinal haemorrhage were reported during this PSUR period. In one case B0636708A child maltreatment syndrome was suspected. In the second case B0677766A the event was reported in the context of status epilepticus.

The information received in these cases does not provide evidence of a safety signal.

9.2.2.4. Gastrointestinal disorders

9.2.2.4.1. Diarrhoea haemorrhagic, Haematochezia, Melaena, Rectal haemorrhage

During the period of this report, 10 cases were received with one the following MedDRA Preferred Terms: diarrhoea haemorrhagic (n=1), haematochezia (n=7), melaena (n=1) and/or rectal haemorrhage (n=3). In case B0619820A rectal haemorrhage was reported as a symptom of ITP. In tree cases (B0643201A, B0651961A and B0663295A) haematochezia was reported in association with intussusception. In cases B0615474A and B0624719A, the subjects developed concurrent acute gastroenteritis or oesophagitis. In cases D0068600A and D0068909A investigations were normal and the events resolved spontaneously. In cases B0605572A and B0671786A insufficient data was provided for medical assessment.

The information received in these cases does not provide evidence of a specific safety signal.

9.2.2.4.2. Intussusception

During the period of this report, four cases with the MedDRA Preferred Term intussusception have been received. In one case the symptoms likely occurred 20 minutes after vaccination, in 2 cases the event was observed from 2.5 to 7 months after vaccination and likely related to gastroenteritis, and in one case**,** intussusception was suspected but not confirmed.

The information received in these cases does not provide evidence of a specific safety signal.

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9.2.2.5. General disorders and administration site conditions

9.2.2.5.1. Abscess sterile, Injection site abscess sterile and vaccination site abscess sterile

Five cases with the MedDRA Preferred Term abscess sterile as well as two cases coded with the MedDRA Preferred Terms injection site abscess sterile or vaccination site abscess sterile have been received during this reporting period. Cases D0063315A, D0063315B and D0063315C described recurrent sterile abscess at injection sites after vaccination with Infanrix hexa™ in the same subject. In case D0068815A, the subject experienced the event within one year after vaccination with sterile secretion. In case D0068941A, the subject experienced injection site reaction one month after vaccination and sonography revealed two structures that have been interpreted as possible granuloma and possible abscess. In two cases D0067836A and D0069205A, abscesses were drained and revealed pus that were not analyzed.

Since launch, 31 cases of abscess sterile, injection site abscess sterile and vaccination site abscess sterile have been received corresponding to a reporting frequency of 0.05 per 100,000 doses distributed.

The information received in these cases does not provide evidence of a specific safety signal.

9.2.2.5.2. Injection site necrosis

One case with the MedDRA Preferred Term injection site necrosis was identified during the period covered by this report. The event was observed 2 days after vaccination after removal of injection site blister.

Since launch, 8 cases of injection site necrosis have been received corresponding to a reporting frequency of 0.01 per 100,000 doses distributed.

The information received in these cases does not provide evidence of a specific safety signal.

9.2.2.5.3. Injection site nodule and Nodule

Twenty-six cases with the MedDRA Preferred Term injection site nodule and 3 cases with the MedDRA Preferred Term nodule have been received during the period of this report, corresponding to a reporting frequency of 0.24 per 100,000 doses distributed.

Three cases met the criteria for „regulatory" seriousness. The majority of cases lack data for adequate assessment e.g. specific site of injection when concurrent vaccines are given, and/or time to onset and/or time to outcome.

Since launch, 136 cases of injection site nodule and nodule have been received corresponding to a reporting frequency of 0.22 per 100,000 doses distributed.

The Company will continue monitoring this event closely.

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9.2.2.6. Immune system disorders

9.2.2.6.1. Anaphylactic reaction and anaphylactic shock

Four cases with the MedDRA Preferred Term anaphylactic reaction and/or anaphylactic shock were identified during the period covered by this report. In three cases the subjects received multiple vaccinations and in the forth case the subject had multiple concurrent therapies with unspecified start date.

Only one of these (D0068761A) met sufficient criteria in order to confirm true anaphylaxis (Anaphylaxis: Case definition and guidelines for data collection, analysis, and presentation of immunization safety data The Brighton Collaboration Anaphylaxis Working Group. Vaccine 25 (2007) 5675-5684).

Since launch, 17 cases of anaphylactic reaction and anaphylactic shock have been received corresponding to a reporting frequency of 0.03 per 100,000 doses distributed. The company will continue to monitor cases of anaphylactic reaction and anaphylactic shock.

9.2.2.7. Infections and infestations

9.2.2.7.1. Abscess, Abscess limb, Incision site abscess, Injection site abscess, Vaccination site abscess

During the reporting period, 17 cases were received including one of the following MedDRA Preferred Terms: abscess (n=4), abscess limb (n=1), incision site abscess (n=5), injection site abscess (n=10) and/or vaccination site abscess (n=2).

These cases feature 11 males, 5 females and 1 unknown gender with a median age of 4 months (range: from 6 weeks to 2 years, n=16). At time of reporting, events resolved in 7 cases, resolved with sequelae in 3 cases, improved in 1 case, were unknown in 6 cases. Only in one case D0068928A the causing agent of injection site abscess *Staphylococcal aureus* was found. In case B0545354A *Stapylococcal septicaemia* was detected after the 3rd attempt of abscess drainage. The abscess was treated with antibiotics in 9 cases (B0607303A, B0609130A, B0622903A, B0639606A, B0641879A, B0680202A, D0066818A, D0068798A, D0068798B) and surgery or drainage in 2 cases (B0661002A, B0600650A).

There is no concentration of these cases by batch, supportive of a manufacturing issue.

Since launch, 116 cases have been received corresponding to a reporting frequency of 0.19 per 100,000 doses distributed.

The Company will continue to monitor all cases of abscess and injection site abscess.

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9.2.2.7.2. Cellulitis and Injection site cellulitis

During the period under review 7 cases with the MedDRA Preferred Tem "Cellulitis" and 1 case with the MedDRA Preferred Tem "Injection site cellulitis" were received. In all described cases, the subjects were aged between 17 months and 3 years and received their booster dose of Infanrix hexa™. Six of them received antibiotics. In six cases, no causing agent of cellulitis was identified. In case D0067880A, cellulitis was confirmed by unspecified serology. In case B0675146A, a co-suspect vaccine was involved with unknown injection sites for both vaccines. Bacteriological tests were negative at the reaction site. Blood culture was positive for coagulase negative staphylococcus 8 days after vaccines administration.

Since launch, 35 cases have been received corresponding to a reporting frequency of 0.06 per 100,000 doses distributed.

These reports do not constitute a safety signal.

9.2.2.7.3. Meningitis, Meningitis aseptic, Meningitis pneumococcal

During the period under review, 3 cases were received with the MedDRA Preferred Terms "Meningitis" (n=1), "Meningitis aseptic" (n=1) and "Meningitis pneumococcal" (n=1). In case D0068409A, meningitis was suspected but the final diagnosis was Kawasaki"s disease. In case B0651993A of aseptic meningitis no data confirming this event were reported. In the last case D0066195A**,** a 4-month-old subject experienced pneumococcal meningitis, confirmed CSF results.

These reports do not constitute a safety signal.

9.2.2.7.4. Sepsis

Four cases were reported with the MedDRA Preferred Term sepsis during the period of this report. None of these 4 cases provide sufficient information to confirm sepsis by bacteriaemia.

Since launch, 28 cases have been received corresponding to a reporting frequency of 0.05 per 100,000 doses distributed.

These reports do not constitute a safety signal.

9.2.2.8. Musculoskeletal and connective tissue disorders

9.2.2.8.1. Nodule on extremity

During the reporting period, two cases were reported with the MedDRA Preferred Term nodule on extremity. One case lacks information on the Infanrix hexa™ injection site, in the other case, the event was reported together with abscess.

These reports do not constitute a safety signal.

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9.2.2.9. Nervous system disorders

9.2.2.9.1. Seizures

Atonic seizures, Clonic convulsion, Clonus, Convulsion, Convulsions local, Febrile convulsuion, Grand mal convulsion, Myoclonus, Partial seizures, Tonic convulsion

During the reporting period, 117 individual case reports, 82 febrile and 35 afebrile convulsions, were received including one of the following MedDRA Preferred Terms: atonic seizures (n=1), clonic convulsion (n=1), clonus (n=1), convulsion (n=55), convulsions local (n=1), febrile convulsion (n=54), grand mal convulsion (n=18), myoclonus (n=4), partial seizures (n=3) and/or tonic convulsion (n=3).

Subject age was provided in 114 reports included in the analysis and ranged from 1 month to 3 years with a median of 5 months. Subject gender was provided in 112 reports and included 54 males and 58 females. TTO was provided in 108 reports and ranged from less than 1 day to 3 weeks (median: less than 1 day).

The reporting frequency and the pattern of the cases did not deviate from the last PSUR reporting period.

Convulsions (with or without) fever is included in the current Core Safety Information for Infanrix hexa™

These cases do not raise a safety signal.

Epilepsy, Infantile spasms, Petit mal epilepsy, Status epilepticus

During this reporting period 11 cases of epilepsy, 4 cases of petit mal epilepsy, 2 cases of infantile spasm and 4 cases of status epilepticus were reported.

In only 4 cases out of the 13 reports of epilepsy and petit mal epilepsy diagnosis of epilepsy can be considered as confirmed. In case B0645066A a family origin of epilepsy has also to be also considered. In case B0657965A epilepsy was considered as a part of metabolic disturbance.In case D0068399A, it was reported that diagnosis was confirmed by several examination, but data were not provided. In case (B0664846A), the subject was diagnosed with epilepsy before vaccination.

In three of the four cases of status epilepticus EEG was reported as normal and in one case the diagnosis of shaken baby was considered.

These cases do not raise a safety signal.

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9.2.2.9.2. Cerebral atrophy

During the period of this report, 1 case with the MedDRA Preferred Term cerebral atrophy was identified. In this case (D0067158A) the subject was diagnosed with cerebral atrophy on NMR and suspected Watanabe epilepsy after multiple vaccinations. The reported subject"s conditions (postpartum hemorrhagic gastritis, hyperbilirubinemia, postpartum anemia, treated with transfusion and suspected epilepsy) might have contributed to an observed psychomotor retardation.

Since launch 6 cases of cerebral atrophy have been received, corresponding to a reporting frequency of 0.01 per 100,000 doses distributed.

This case does not raise a safety signal.

9.2.2.9.3. Cerebral haemorrhage

Two reports received during this PSUR period with the MedDRA Preferred Terms cerebral haemorrhage.

In one case B0666511A the subject experienced haemorrhage one day after multiple vaccinations. The case lacks information on investigation of other causes of haemorrhage like infection diseases, coagulation disorders. The second case D0066195 reported this event in the context of pneumococcal meningitis.

Since launch, 5 cases have been received with cerebral haemorrhage, corresponding to a reporting frequency of 0.01 per 100,000 doses distributed.

These cases do not raise a safety signal.

9.2.2.9.4. Encephalitis and Encephalopathy

During the period of this PSUR, two cases case were reported with the MedDRA Preferred Terms encephalitis and/or encephalopathy.

In one case the subject was hospitalized due to suspicion of meningitis 4 days after multiple vaccinations. However, all investigations resulted in normal findings. Reported data are insufficient to support a diagnosis of encephalitis. In the second case (B0678021A) the subject experienced progressive psychomotor retardation, but no information on cause investigation was reported.

Since launch, 29 cases of encephalitis and/or encephalopathy have been received, corresponding to a reporting frequency of 0.05 per 100,000 doses distributed.

The Company will continue to monitor important neurological events, including encephalitis and encephalopathy.

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9.2.2.10. Skin and subcutaneous tissue disorders

9.2.2.10.1. Erythema multiforme

During the period of this report, one case with the MedDRA Preferred Term erythema multiforme has been identified. No data confirming this diagnosis were provided.

The information received in this case does not constitute a safety signal.

Since launch, 13 cases were received corresponding to a reporting frequency of 0.02 per 100,000 doses distributed.

The Company will continue to monitor cases of erythema multiforme.

9.2.2.10.2. Henoch-Schonlein purpura

During the period of this report, one case with the MedDRA Preferred Term Henoch-Schonlein purpura was received.

The case lacks details on laboratory confirmation of the diagnosis.

Since launch, 5 cases were received corresponding to a reporting frequency of 0.01 per 100,000 doses distributed.

The Company will continue to monitor cases of Henoch-Schonlein purpura.

9.2.2.10.3. Petechiae

During the period covered by this report 31 cases were identified with the MedDRA Preferred Term petechiae.

In 26 cases the subjects received multiple vaccinations. In 8 cases petechiae were observed together with purpura, thrombobocytopenia,and/or IPT. In 4 cases petechiae were reported as a single event. In the other cases, petechiae were mainly associated with other signs and symptoms, and give no indication of a specific safety signal.

Since launch, 132 cases were received corresponding to a reporting frequency of 0.22 per 100,000 doses distributed.

The Company will continue to monitor cases of petechiae.

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9.2.2.10.4. Purpura

During the period of this report, seven cases with the MedDRA Preferred Term purpura were received.

In cases B0619820A, B0652855A and B0656703A idiopathic thrombocytopenic purpura, thrombocytopenia or thrombocytopenic purpura was reported as well. In cases B0651934A and D0068231A purpura was observed within on the same day as vaccination and resolved spontaneously without treatment. Cases D0063497A and D0067173A lack information for medical assessment.

The information received in these cases does not constitute a specific safety signal.

Since launch, 28 cases were received corresponding to a reporting frequency of 0.05 per 100,000 doses distributed.

The company will continue to monitor cases of purpura.

9.2.2.10.5. Subcutaneous nodule

Two non-serious cases with the MedDRA Preferred Term “Subcutaneous nodule” have been received during the reporting period. In both cases the event was observed shortly after vaccination in the context of other injection site reaction.

The information received in these cases does not constitute a specific safety signal.

9.2.2.11. Vascular disorders

9.2.2.11.1. Kawasaki’s disease

Five serious cases with the MedDRA Preferred Term “Kawasaki‟s disease” were reported during the period under review. In one case B0653827A the event was ruled out according to the follow-up information. In two cases B0616059A and B0657560A reported information is incompatible with the diagnosis of Kawasaki‟s disease. The remaining two cases D0066913A and D0068409A are compatible with typical Kawasaki‟s disease, but none of the subjects develop cardiac complications.

Based on the individual case history assessment no safety signal was identified.

Since launch, 18 cases were received corresponding to a reporting frequency of 0.03 per 100,000 doses distributed.

The information received in these cases does not provide evidence of a specific safety signal.

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9.3. Areas of Regulatory Interest

Areas of regulatory interest (specifically Drug Interactions, Overdose and Medication Errors, Abuse Potential, Pregnancy and Lactation, Use in Children) routinely monitored throughout the product lifecycle and during the period of the PSUR are presented below. Note that non-medically verified reports and non-serious reports received from regulatory authorities are included in these analyses.

9.3.1. Drug interactions

No cases of potential drug interactions have been received during the reporting period.

Most of the spontaneous cases reported during the period of this report include co-administration with other vaccines (mostly pneumococcal vaccines). Vaccination with pneumococcal vaccines is standard practice in the countries where most reports originated (Germany and Italy).

No relevant findings were noticed as regards the co-administration profile of the vaccine. No cluster of events suggestive of potential interaction was found.

No new important safety information regarding drug interactions has been identified in the time period.

9.3.2. Overdose and Medication Errors

A total of 687 cases of potential overdose and/or reports of medication error have been received during the reporting period. Non-medically verified and regulatory non-serious cases are included in this analysis.

In view of the varying ways in which reports of overdose and medication error are described and coded, there is often much overlap between these concepts.

9.3.2.1. Overdose

“Overdose” is defined as more than the recommended dose of vaccine administered at the same occasion (either two vaccine doses administered too soon one after each other or two vaccines with overlapping components accidentally co-administered.)

A total of 17 non-serious cases of overdose and accidental overdose have been identified in the current time period.

Adverse events were reported in 6 cases: irritability in cases B0649576A and B0677762A; gait disturbance, joint stiffness, pyrexia and injection site reaction in case B0651926A; pyrexia in cases B0663536A and B0675106A and pyrexia and restlessness in case B0666873A.

No new important safety information regarding overdose has been identified during the time period.

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9.3.2.2. Medication Errors

In addition to cases with overdose and accidental overdose, 670 cases involving medication errors have been identified in the current time period. From these reports, 638 were reported with no adverse events and 32 with adverse events. An overview per category of maladministration is presented in the below table. Note that a case can contain more than one PT related to maladministration.

Table 25 Overview per category of maladministration

Category of maladministration (MedDRA PT)	Number Of Events
Inappropriate schedule of drug administration	342
Wrong drug administered	227
Wrong technique in drug usage process	90
Incorrect storage of drug	31
Incorrect dose administered	25
Underdose	23
Incorrect product storage	17
Off label use	13
Overdose	13
Drug administration error	11
Incorrect route of drug administration	10
Expired drug administered	7
Accidental overdose	5
Drug dispensing error	2
Accidental exposure	1
Drug administered at inappropriate site	1
Medication error	1

Eighty-two percent of the medication errors cases were reported from France (551 cases). The majority of the cases concerned mainly the following:

- Inappropriate schedule of drug administration: cases where Infanrix hexa™ administration was reported not following the locally recommended vaccination schedule (most of the time the interval between two consecutive doses was too short or the subject was outside the normal range of the vaccination schedule.

- Wrong drug administered: another vaccine should have been administered.

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Of these 551 cases of medication errors reported from France, the majority were reported via a solicited interview or market research.

Indeed, on the request of the CEPS (Comité économique des produits de santé, French authority in charge of drug price in France) and following the reimbursement of Infanrix hexa™ in France, two studies were requested by the authorities in order to evaluate the evolution of hepatitis B vaccinal status in infants and to evaluate the acceptability of hepatitis B vaccine.

One study consists of interviewing parents on vaccination (PopCorn) or physicians (Praline). These studies are handled by the French pharmacoepidemiological department and are subcontracted to a company called Kappa Santé. These studies are run on 3 years.

The other study is a market study (Vaccinoscopie) handled by the marketing department and subcontracted to a company called Institut des mamans. The objective is to obtain information about vaccinal coverage, age of vaccination, compliance with the French vaccinal recommendations. The Institut des mamans has a panel of mothers who answered via internet to questions on vaccination of their children.

Adverse events were reported in 32 cases. Cases with bolded event terms are also analysed/summarised in the relevant sub-sections of section 6.4 of this PSUR.

Table 26 Cases reported following medication errors

Case ID	Age	Gender	Seriousness Fda	Events PT Comma Sep	Case Outcome
B0605673A	3 Months	Unknown	Serious	**Febrile convulsion**, Wrong technique in drug usage process	Resolved
B0625276A	2 Months	Male	Not serious	Diarrhoea, Decreased appetite, Pyrexia, Incorrect route of drug administration, Inappropriate schedule of drug administration	Resolved
B0638208A	2 Months	Unknown	Not serious	Pyrexia, Incorrect storage of drug	Resolved
B0642250A	2 Months	Female	Not serious	Incorrect storage of drug, Inappropriate schedule of drug administration, Wrong drug administered	Not Applicable
B0643578A	4 Months	Female	Not serious	Wrong drug administered, Pyrexia, Restlessness	Resolved
B0648514A	4 Months	Male	Not serious	Pyrexia, Irritability, Wrong technique in drug usage process	Unresolved

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Case ID	Age	Gender	Seriousness Fda	Events PT Comma Sep	Case Outcome
B0659288A		Female	Not serious	Laceration, Accidental exposure, Product quality issue	Unknown
B0660461A	2 Months	Female	Not serious	Injection site reaction, Wrong drug administered	Unknown
B0661515A	6 Years	Female	Not serious	Injection site inflammation, Injection site induration, Injection site pruritus, Injection site erythema, Inappropriate schedule of drug administration	Unresolved
B0662189A		Male	Not serious	Pyrexia, Wrong technique in drug usage process	Resolved
B0670363A	2 Months	Female	Not serious	Injection site erythema, Injection site swelling, Crying, Wrong technique in drug usage process	Resolved
B0673318A	2 Months	Female	Not serious	Pyrexia, Injection site erythema, Injection site induration, Incorrect storage of drug	Resolved
B0673893A	6 Months	Female	Not serious	Pyrexia, Wrong technique in drug usage process	Unknown
B0676832A	Child	Male	Not serious	Pyrexia, Wrong technique in drug usage process	Resolved
B0676833A	Child	Female	Not serious	Injection site induration, Pyrexia, Wrong technique in drug usage process	Resolved
B0680257A		Unknown	Not serious	Injection site erythema, Injection site swelling, Wrong technique in drug usage process	Unknown
D0063484A	Child	Female	Serious	**Pertussis**, Vaccination failure, Inappropriate schedule of drug administration	Resolved
D0063511A	Child	Male	Serious	**Pertussis**, Vaccination failure, Inappropriate schedule of drug administration	Resolved

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Case ID	Age	Gender	Seriousness Fda	Events PT Comma Sep	Case Outcome
D0063525A	Child	Female	Serious	**Pertussis**, Vaccination failure, Inappropriate schedule of drug administration	Resolved
D0063921A	10 Years	Female	Not serious	Injection site erythema, Injection site pain, Off label use	Resolved
D0066271A		Unknown	Not serious	Wrong technique in drug usage process, Injection site reaction, Injection site swelling	Unknown
D0066916A	5 Months	Female	Not serious	Erythema, Incorrect route of drug administration	Unknown
D0067001A	27 Years	Male	Not serious	Injection site pain, Off label use	Resolved
D0067177A	15 Months	Female	Serious	**Thrombocytopenia**, **Idiopathic thrombocytopenic purpura**, Gastroenteritis, **Petechiae**, Haematoma, Vomiting, Diarrhoea, Injection site inflammation, Injection site induration, Incorrect route of drug administration	Unresolved
D0067375A	29 Days	Male	Not serious	Pyrexia, Agitation, Fatigue, Drug administration error	Resolved
D0067600A	27 Years	Male	Not serious	Inappropriate schedule of drug administration, Injection site erythema	Resolved
D0067815A	7 Years	Male	Serious	**Henoch-Schonlein purpura**, Pyrexia, Nausea, Vomiting, Decreased appetite, Myalgia, Arthralgia, Erythema nodosum, Malaise, Gait disturbance, Rash, Oedema peripheral, Pain in extremity, Off label use	Resolved
D0068256A	3 Months	Female	Not serious	Injection site swelling, Inappropriate schedule of drug administration	Unknown

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Case ID	Age	Gender	Seriousness Fda	Events PT Comma Sep	Case Outcome
D0068575A	4 Months	Male	Serious	Haematoma, Injection site discolouration, Injection site vesicles, Incorrect route of drug administration	Resolved
D0068800A	24 Months	Male	Not serious	Incorrect dose administered, Abnormal behaviour	Resolved
D0069059A	4 Months	Male	Serious	Warm type haemolytic anaemia, **Thrombocytopenia**, Jugular vein thrombosis, Jaundice acholuric, Incorrect route of drug administration	Unresolved
D0069153A	6 Months	Female	Not serious	Pyrexia, Infection, Inappropriate schedule of drug administration	Unknown

No new important safety information regarding medication errors has been identified during the time period.

9.3.3. Abuse or misuse

Not applicable to vaccines.

9.3.4. Pregnancy and Lactation

9.3.4.1. Pregnancy

All cases involving a pregnant patient are included. In addition, the search strategy includes a broad selection of MedDRA PTs suggesting exposure *in utero* or via breast feeding or indicative of birth defects (e.g. congenital or hereditary disorders). Thus the search retrieves cases where pregnancy outcome is abnormal, normal or unknown. Cases involving females over 60 years of age and adult males (where the case was not reported as a partner pregnancy) have been excluded. Note that this search does not include the entire SMQ for „Adverse Pregnancy Outcome/Reproductive Toxicity (incl neonatal disorders)"; furthermore, it includes some terms that are not in the SMQ.

One case possibly related to administration during pregnancy has been received during the reporting period and since launch.

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Case **B0606306A** was reported by a physician and was a prospective report of pregnancy in a 28-year-old female who was vaccinated with Infanrix hexa™ while she was pregnant (23 weeks of amenorrhea). Upon follow-up received on 04 October 2010: nothing in particular occurred during pregnancy and delivery, for the mother and the baby.

No new important safety information regarding use in pregnancy has been identified during the time period.

9.3.4.2. Lactation

No cases have been received during the reporting period where Infanrix hexa was known to have been given to lactating mothers.

9.3.5. Special Patient Groups

No new important safety information related to use in the children, elderly or organ impaired patients has been identified in the reporting period.

9.3.6. Effects of long-term treatment

Not applicable to vaccines.

9.3.7. Patient/Consumer and other non-healthcare professional reports.

The events of interest described in section 6.5 within the PSUR review period include all cases (irrespective of source, seriousness and listedness). Non-healthcare professional reports are therefore discussed in section 6.5. Separate Line Listings and Summary Tabulations are provided as appendices for consumer reports as per guideline E2C(R1).

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10. CONCLUSION

From the review of data received during the reporting period and presented in this PSUR, it has been concluded that the safety profile of Infanrix hexa™ is adequately reflected in the Reference Safety Information.

No further amendments to RSI are considered necessary at this time.

The benefit/risk profile of Infanrix hexa™ continues to be favourable.

The Company will continue to monitor all cases of thrombocytopenia, injection site nodule and nodule, anaphylaxis, abscess and injection site abscess, important neurological events including encephalitis and encephalopathy, erythema multiforme, Henoch-Schonlein purpura, petechiae and purpura.

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11. REFERENCES

Guideline on Conduct of Pharmacovigilance for Medicines Used by the Paediatric Population, EMEA/CHMP/PhVWP/235910/2005, effective January 2007.

Guideline on the Exposure to Medicinal Products During Pregnancy: Need for Post-Authorisation Data, EMEA/CHMP/313666/2005, May 2006.

ICH Harmonised Tripartite Guideline for Clinical Safety Data Management Periodic Safety Update Reports for Marketed Drugs E2C(R1), 6 November 1996.

Addendum to ICH E2C Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs, ICH Harmonised Tripartite Guideline, 6 February 2003.

Volume 9A of the Rules Governing Medicinal Products in the European Union – Guidelines on Pharmacovigilance for Medicinal Products for Human Use, September 2008.

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APPENDIX 1A : WORLDWIDE MARKETING AUTHORISATION STATUS

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APPENDIX 1A WORLDWIDE MARKETING AUTHORISATION STATUS

	Country			Tradename	Approval	Launch	Launch comment
DTPa-HBV-IPV+Hib	Albania	pc	L	INFANRIX HEXA	25-Mar-09		Planned to be launched
DTPa-HBV-IPV+Hib	Argentina	c	L	INFANRIX HEXA	15-May-01		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Aruba		L	INFANRIX HEXA	20-Feb-02		Not applicable
DTPa-HBV-IPV+Hib	Australia	c	L	INFANRIX HEXA	26-Nov-01		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Austria	c	L	INFANRIX HEXA	23-Oct-00	30/03/2001	Launched
DTPa-HBV-IPV+Hib	Azerbajian	c	L	INFANRIX HEXA	01-Dec-08		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Bahrain	c	L	INFANRIX HEXA	01-Aug-05		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Bangladesh	c	L	INFANRIX HEXA	09-Sep-08		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Belgium	c	L	INFANRIX HEXA	23-Oct-00	01/09/2002	Launched
DTPa-HBV-IPV+Hib	Brazil	c	L	INFANRIX HEXA	02-Apr-01		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Bulgaria		L	INFANRIX HEXA	23-Oct-00		Not applicable
DTPa-HBV-IPV+Hib	Canada	c	L	INFANRIX HEXA	28-May-04		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Chile	c	L	INFANRIX HEXA	26-Mar-02		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Colombia	c	L	INFANRIX HEXA	23-Feb-00		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Costa Rica	c	L	INFANRIX HEXA	02-Oct-01		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Croatia	c	L	INFANRIX HEXA	18-Nov-04		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Curacao		L	INFANRIX HEXA	28-Sep-01		Not applicable
DTPa-HBV-IPV+Hib	Cyprus	c	L	INFANRIX HEXA	23-Oct-00	31/10/2003	Launched
DTPa-HBV-IPV+Hib	Czech Republic		L	INFANRIX HEXA	23-Oct-00	01/11/2003	Not applicable
DTPa-HBV-IPV+Hib	Denmark	pc	L	INFANRIX HEXA	23-Oct-00		Planned to be launched
DTPa-HBV-IPV+Hib	Dominican Republic	c	L	INFANRIX HEXA	22-Oct-01		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Ecuador	c	L	INFANRIX HEXA	07-Feb-03		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	El Salvador	c	L	INFANRIX HEXA	11-Feb-03		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Estonia	c	L	INFANRIX HEXA	23-Oct-00	01/03/2004	Launched
DTPa-HBV-IPV+Hib	Finland		L	INFANRIX HEXA	23-Oct-00		Not applicable
DTPa-HBV-IPV+Hib	France	c	L	INFANRIX HEXA	23-Oct-00	15/05/2002	Launched
DTPa-HBV-IPV+Hib	Georgia	c	L	INFANRIX HEXA	04-Mar-09		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Germany	c	L	INFANRIX HEXA	23-Oct-00	21/10/2000	Launched

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	Country			Tradename	Approval	Launch	Launch comment
DTPa-HBV-IPV+Hib	Greece		L	INFANRIX HEXA	23-Oct-00	01/11/2001	Not applicable
DTPa-HBV-IPV+Hib	Guatemala	c	L	INFANRIX HEXA	09-Apr-02		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Haiti	c	L	INFANRIX HEXA	25-Jun-08		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Honduras	c	L	INFANRIX HEXA	06-Jun-02		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Hong Kong	c	L	INFANRIX HEXA	26-Nov-01		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Hungary		L	INFANRIX HEXA	23-Oct-00		Not applicable
DTPa-HBV-IPV+Hib	Iceland		L	INFANRIX HEXA	23-Oct-00		Not applicable
DTPa-HBV-IPV+Hib	Ireland	c	L	INFANRIX HEXA	23-Oct-00		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Israel		L	INFANRIX HEXA	01-Aug-05		Not applicable
DTPa-HBV-IPV+Hib	Italy	c	L	INFANRIX HEXA	23-Oct-00	21/02/2001	Launched
DTPa-HBV-IPV+Hib	Ivory Coast		L	INFANRIX HEXA	14-Jun-02		Not applicable
DTPa-HBV-IPV+Hib	Jamaica	c	L	INFANRIX HEXA	19-Jul-01		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Jordan	c	L	INFANRIX HEXA	30-Mar-05		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Kazakhstan		L	INFANRIX HEXA	16-Jan-09		Not applicable
DTPa-HBV-IPV+Hib	Kenya	c	L	INFANRIX HEXA	06-Dec-01		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Latvia	pc	L	INFANRIX HEXA	23-Oct-00		Planned to be launched
DTPa-HBV-IPV+Hib	Lebanon	c	L	INFANRIX HEXA	25-Mar-09		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Lithuania		L	INFANRIX HEXA	23-Oct-00		Not applicable
DTPa-HBV-IPV+Hib	Luxembourg	c	L	INFANRIX HEXA	23-Oct-00	31/12/2000	Launched
DTPa-HBV-IPV+Hib	Macedonia		L	INFANRIX HEXA	26-Apr-10		Not applicable
DTPa-HBV-IPV+Hib	Madagascar	c	L	INFANRIX HEXA	11-Feb-08	01/03/2008	Launched
DTPa-HBV-IPV+Hib	Malaysia	c	L	INFANRIX HEXA	06-Jan-06		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Malta	c	L	INFANRIX HEXA	23-Oct-00	01/11/2001	Launched
DTPa-HBV-IPV+Hib	Mauritius	c	L	INFANRIX HEXA	22-May-06		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Mexico	c	L	INFANRIX HEXA	15-Dec-00		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Moldova	c	L	INFANRIX HEXA	12-May-03		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Morocco	c	L	INFANRIX HEXA	06-Oct-03		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Myanmar		L	INFANRIX HEXA	26-May-10		Not applicable
DTPa-HBV-IPV+Hib	Namibia	c	L	INFANRIX HEXA	07-Apr-06		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Netherlands	c	L	INFANRIX HEXA	23-Oct-00	30/01/2005	Launched
DTPa-HBV-IPV+Hib	New Zealand	c	L	INFANRIX HEXA	24-Apr-01		Launch could be assumed as having happened not less than 3

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	Country			Tradename	Approval	Launch	Launch comment
							months after approval.
DTPa-HBV-IPV+Hib	Nicaragua	c	L	INFANRIX HEXA	02-Apr-02		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Norway		L	INFANRIX HEXA	13-Aug-01		Not applicable
DTPa-HBV-IPV+Hib	Pakistan	c	L	INFANRIX HEXA	22-Nov-02		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Panama	c	L	INFANRIX HEXA	22-Apr-02		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Peru	c	L	INFANRIX HEXA	06-May-03		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Philippines	c	L	INFANRIX HEXA	03-Oct-02		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Poland	c	L	INFANRIX HEXA	23-Oct-00	06/02/2004	Launched
DTPa-HBV-IPV+Hib	Portugal		L	INFANRIX HEXA	23-Oct-00		Not applicable
DTPa-HBV-IPV+Hib	Romania	c	L	INFANRIX HEXA	23-Oct-00		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Saudi Arabia	c	L	INFANRIX HEXA	03-Oct-05		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Serbia	pc	L	INFANRIX HEXA	20-Mar-09		Planned to be launched
DTPa-HBV-IPV+Hib	Singapore	c	L	INFANRIX HEXA	07-May-03		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Slovakia	c	L	INFANRIX HEXA	23-Oct-00	13/12/2004	Launched
DTPa-HBV-IPV+Hib	Slovenia	c	L	INFANRIX HEXA	23-Oct-00		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	South Africa	c	L	INFANRIX HEXA	07-Apr-06		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Spain	c	L	INFANRIX HEXA	23-Oct-00	01/06/2001	Launched
DTPa-HBV-IPV+Hib	Sri Lanka	c	L	INFANRIX HEXA	04-Jul-05		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Sweden	c	L	INFANRIX HEXA	23-Oct-00	01/12/2001	Launched
DTPa-HBV-IPV+Hib	Switzerland	c	L	INFANRIX HEXA	02-Oct-00		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Taiwan	c	L	INFANRIX HEXA	14-Oct-04		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Thailand	c	L	INFANRIX HEXA	13-Sep-02		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Trinidad and Tobago	c	L	INFANRIX HEXA	24-Sep-01		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Tunisia		L	INFANRIX HEXA	20-Aug-05		Not applicable
DTPa-HBV-IPV+Hib	UK		L	INFANRIX HEXA	23-Oct-00		Not applicable
DTPa-HBV-IPV+Hib	Ukraine	c	L	INFANRIX HEXA	12-Nov-02		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	United Arab Emirates	c	L	INFANRIX HEXA	18-Sep-06		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Venezuela	c	L	INFANRIX HEXA	11-Jul-02		Launch could be assumed as having happened not less than 3 months after approval.

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	Country			Tradename	Approval	Launch	Launch comment
DTPa-HBV-IPV+Hib	Vietnam	c	L	INFANRIX HEXA	19-Sep-05		Launch could be assumed as having happened not less than 3 months after approval.
DTPa-HBV-IPV+Hib	Yemen		L	INFANRIX HEXA	11-Aug-08		Not applicable

Commercialized column	
pc	planned commercialized
c	commercialized
(empty)	not commercialized and not planned

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APPENDIX 1B : IMPORTANT NEW SAFETY INFORMATION COMMUNICATED TO HEALTHCARE PROFESSIONALS

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APPENDIX 1B WITHDRAWN AUTHORISATION STATUS

	Country	Date of cancellation	Reason for cancellation
DTPa HBV IPV Hib	Uruguay	24/03/2009	Cancelled because not marketed

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APPENDIX 2A : REFERENCE SAFETY INFORMATION AT THE BEGINNING OF THE REPORTING PERIOD

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Active Name: Combined diphtheria, tetanus, pertussis (acellular), hepatitis B, poliomyelitis (inactivated) and *Haemophilus influenzae* type b vaccine
Version Number: 009
Version Date: 23-Nov-07

GLOBAL DATASHEET

Combined diphtheria, tetanus, pertussis (acellular), hepatitis B, poliomyelitis (inactivated) and *Haemophilus influenzae* type b vaccine

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Active Name: Combined diphtheria, tetanus, pertussis (acellular), hepatitis B, poliomyelitis (inactivated) and *Haemophilus influenzae* type b vaccine
Version Number: 009
Version Date: 23-Nov-07

GLOBAL PRESCRIBER INFORMATION

TITLE

Combined diphtheria-tetanus-acellular pertussis, hepatitis B, enhanced inactivated polio vaccine and *Haemophilus influenzae* type b vaccine.

SCOPE

Trade Name(s)

Infanrix hexa

Formulation, Strength and Device* (*if appropriate)

Infanrix hexa contains diphtheria toxoid, tetanus toxoid, three purified pertussis antigens [pertussis toxoid (PT), filamentous hemagglutinin (FHA) and pertactin (PRN; 69 kiloDalton outer membrane protein)] and the purified major surface antigen (HBsAg) of the hepatitis B virus (HBV) and purified polyribosyl-ribitol-phosphate capsular polysaccharide (PRP) of *Haemophilus influenzae* type b (Hib), covalently bound to tetanus toxoid, adsorbed onto aluminium salts. It also contains three types of inactivated polio viruses (type 1: Mahoney strain; type 2: MEF-1 strain; type 3: Saukett strain).

The tetanus and diphtheria toxoids are obtained by formaldehyde treatment of purified *Corynebacterium diphtheriae* and *Clostridium tetani* toxins. The acellular pertussis vaccine components are obtained by extraction and purification from phase I *Bordetella pertussis* cultures, followed by irreversible detoxification of the pertussis toxin by glutaraldehyde and formaldehyde treatment, and formaldehyde treatment of FHA and PRN. The diphtheria toxoid, tetanus toxoid and acellular pertussis components are adsorbed onto aluminium salts. The DTPa-HBV-IPV components are formulated in saline.

The surface antigen of the HBV is produced by culture of genetically-engineered yeast cells (*Saccharomyces cerevisiae*) which carry the gene coding for the major surface antigen of the HBV. This HBsAg expressed in yeast cells is purified by several physico-chemical steps. The HBsAg assembles spontaneously, in the absence of chemical treatment, into spherical particles of 20 nm in average diameter containing non-glycosylated HBsAg polypeptide and a lipid matrix consisting mainly of phospholipids. Extensive tests have demonstrated that these particles display the characteristic properties of the natural HBsAg.

The three polioviruses are cultivated on a continuous VERO cell line, purified and inactivated with formaldehyde.

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The Hib polysaccharide is prepared from Hib, strain 20,752 and after activation with cyanogen bromide and derivatisation with an adipic hydrazide spacer is coupled to tetanus toxoid via carbodiimide condensation. After purification the conjugate is adsorbed on aluminium salt, and then lyophilised in the presence of lactose as stabiliser.

Infanrix hexa meets the World Health Organisation requirements for manufacture of biological substances, of diphtheria, tetanus, pertussis and combined vaccines, of hepatitis B vaccines made by recombinant DNA techniques, of inactivated poliomyelitis vaccines and of Hib conjugate vaccines.

A 0.5 ml dose of the vaccine contains not less than 30 IU of adsorbed diphtheria toxoid, not less than 40 IU of adsorbed tetanus toxoid, 25 mcg of adsorbed PT, 25 mcg of adsorbed FHA, 8 mcg of adsorbed pertactin, 10 mcg of adsorbed recombinant HBsAg protein, 40 D-antigen units of type 1 (Mahoney), 8 D-antigen units of type 2 (MEF-1) and 32 D-antigen units of type 3 (Saukett) of the polio virus. It also contains 10 mcg of adsorbed purified capsular polysaccharide of Hib (PRP) covalently bound to 20-40 mcg tetanus toxoid (T).

Excipients

Lactose

Sodium chloride (NaCl)

Aluminium hydroxide

Aluminium phosphate

Medium 199 (as stabilizer including amino acids, mineral salts and vitamins)

Water for injections

It is mandatory for local product information to state the complete list of excipients for all locally marketed presentations.

Residues (optional)

Potassium chloride

Disodium phosphate

Monopotassium phosphate

Polysorbate 20 and 80

Glycine

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Formaldehyde

Neomycin sulphate

Polymyxin B sulphate

CLINICAL INFORMATION [1]

Indications

Infanrix hexa is indicated for primary and booster vaccination of infants against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and *Haemophilus influenza* type b.

Dosage and Administration

- Primary vaccination

The primary vaccination schedule consists of three doses of 0.5 ml (such as 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months) or two doses (such as 3, 5 months). There should be an interval of at least 1 month between doses. The Expanded Program on Immunisation schedule (at 6, 10, 14 weeks of age) may only be used if a dose of hepatitis B vaccine has been given at birth.

Locally established immunoprophylactic measures against hepatitis B should be maintained. Where a dose of hepatitis B vaccine is given at birth, Infanrix hexa can be used as a replacement for supplementary doses of hepatitis B vaccine from the age of 6 weeks. If a second dose of hepatitis B vaccine is required before this age, monovalent hepatitis B vaccine should be used.

- Booster vaccination:

After a vaccination with 2 doses (e.g. 3, 5 months) of Infanrix hexa a booster dose must be given at least 6 months after the last priming dose, preferably between 11 and 13 months of age.

After vaccination with 3 doses (e.g. 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months) of Infanrix hexa a booster dose may be given at least 6 months after the last priming dose and preferably before 18 months of age.

Booster doses should be given in accordance with the official recommendations.

Infanrix hexa can be considered for the booster if the composition is in accordance with the official recommendations.

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Other combinations of antigens have been studied in clinical trials following primary vaccination with Infanrix hexa and may be used for a booster dose: diphtheria, tetanus, acellular pertussis (DTPa), diphtheria, tetanus, acellular pertussis, *Haemophilus influenzae* type b (DTPa/Hib), diphtheria, tetanus, acellular pertussis, inactivated poliomyelitis, *Haemophilus influenzae* type b (DTPa-IPV/Hib) and diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliomyelitis, *Haemophilus influenzae* type b (DTPa-HBV-IPV/Hib).

Infanrix hexa is for deep intramuscular injection.

Contraindications

Hypersensitivity to the active substances or to any of the excipients or residues. (see Excipients and Residues)

Hypersensitivity after previous administration of diphtheria, tetanus, pertussis, hepatitis B, polio or Hib vaccines.

Infanrix hexa is contra-indicated if the child has experienced an encephalopathy of unknown aetiology, occurring within 7 days following previous vaccination with pertussis containing vaccine. In these circumstances pertussis vaccination should be discontinued and the vaccination course should be continued with diphtheria-tetanus, hepatitis B, inactivated polio and Hib vaccines.

Warnings and Precautions

As with other vaccines, administration of Infanrix hexa should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor infection is not a contra-indication.

Vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable events) and a clinical examination.

If any of the following events are known to have occurred in temporal relation to receipt of pertussis-containing vaccine, the decision to give further doses of pertussis-containing vaccines should be carefully considered :

Temperature of ≥ 40.0°C within 48 hours, not due to another identifiable cause.

Collapse or shock-like state (hypotonic-hyporesponsiveness episode) within 48 hours of vaccination.

Persistent, inconsolable crying lasting ≥ 3 hours, occurring within 48 hours of vaccination.

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Convulsions with or without fever, occurring within 3 days of vaccination.

There may be circumstances, such as a high incidence of pertussis, when the potential benefits outweigh possible risks.

In children with progressive neurological disorders, including infantile spasms, uncontrolled epilepsy or progressive encephalopathy, it is better to defer pertussis (Pa or Pw) immunization until the condition is corrected or stable. However, the decision to give pertussis vaccine must be made on an individual basis after careful consideration of the risks and benefits.As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

Infanrix hexa should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects.

Infanrix hexa should under no circumstances be administered intravascularly or intradermally.

Infanrix hexa contains traces of neomycin and polymyxin. The vaccine should be used with caution in patients with known hypersensitivity to one of these antibiotics.

Infanrix hexa will not prevent disease caused by pathogens other than *Corynebacterium diphtheriae*, *Clostridium tetani*, *Bordetella pertussis*, hepatitis B virus, poliovirus or *Haemophilus influenzae* type b. However, it can be expected that hepatitis D will be prevented by immunisation as hepatitis D (caused by the delta agent) does not occur in the absence of hepatitis B infection.

A protective immune response may not be elicited in all vaccinees (see section Pharmacodynamic effects).

A history of febrile convulsions, a family history of convulsions or Sudden Infant Death Syndrome (SIDS) do not constitute contraindications for the use of Infanrix hexa. Vaccinees with a history of febrile convulsions should be closely followed up as such adverse events may occur within 2 to 3 days post vaccination.

Human Immunodeficiency Virus (HIV) infection is not considered as a contra-indication. The expected immunological response may not be obtained after vaccination of immunosuppressed patients.

Since the HIB capsular polysaccharide antigen is excreted in the urine a positive urine test can be observed within 1-2 weeks following vaccination. Other tests should be performed in order to confirm HIB infection during this period.

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Limited data in 169 premature infants indicate that *Infanrix hexa* can be given to premature children. However, a lower immune response may be observed and the level of clinical protection remains unknown.

The potential risk of apnoea and the need for respiratory monitoring for 48-72h should be considered when administering the primary immunization series to very premature infants (born < 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed.

Interactions

There are insufficient data with regard to the efficacy and safety of simultaneous administration of Infanrix hexa and Measles-Mumps-Rubella vaccine to allow any recommendation to be made.

Data on concomitant administration of Infanrix hexa with Prevenar (pneumococcal saccharide conjugated vaccine, adsorbed) have shown no clinically relevant interference in the antibody response to each of the individual antigens when given as a 3 dose primary vaccination.

However, high incidence of fever (> 39.5°C) was reported in infants receiving Infanrix Hexa and Prevenar compared to infants receiving the hexavalent vaccine alone.

Antipyretic treatment should be initiated according to local treatment guidelines.

As with other vaccines it may be expected that in patients receiving immunosuppressive therapy, an adequate response may not be achieved.

Pregnancy and Lactation

Pregnancy

As Infanrix hexa is not intended for use in adults, adequate human data on use during pregnancy and adequate animal reproduction studies are not available.

Lactation

As Infanrix hexa is not intended for use in adults, adequate human data on use during lactation and adequate animal reproduction studies are not available.

Ability to perform tasks that require judgement, motor or cognitive skills

The vaccine is unlikely to produce an effect on the ability to drive and use machines.

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Adverse Reactions

- Clinical trials:

The safety profile presented below is based on data from more than 16,000 subjects.

As has been observed for DTPa and DTPa-containing combinations, an increase in local reactogenicity and fever was reported after booster vaccination with Infanrix hexa with respect to the primary course.

Frequencies per dose are defined as follows:

Very common: ≥ 10%

Common: ≥ 1% and < 10%

Uncommon: ≥ 0.1% and < 1%

Rare: ≥ 0.01% and < 0.1%

Very rare: < 0.01%

Infections and infestations

Uncommon: upper respiratory tract infection

Metabolism and nutrition disorders

Very common: appetite lost

Psychiatric disorders:

Very common: irritability, crying abnormal, restlessness

Common: nervousness

Nervous system disorders:

Uncommon: somnolence

Very rare: convulsions (with or without fever)

Respiratory, thoracic and mediastinal disorders

Uncommon: cough*

Rare: bronchitis

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Gastrointestinal disorders:

Common: vomiting, diarrhoea

Skin and subcutaneous tissue disorders

Common: pruritus*

Rare: rash

Very rare: dermatitis, urticaria*

General disorders and administration site conditions:

Very common: pain, redness, local swelling at the injection site (≤ 50 mm), fever ≥ 38°C, fatigue

Common: local swelling at the injection site (> 50 mm)**, fever >39.5°C, injection site reactions, including induration

Uncommon: diffuse swelling of the injected limb, sometimes involving the adjacent joint**

- Post-Marketing Surveillance:

Blood and lymphatic system disorders

Lymphadenopathy, thrombocytopenia

Immune system disorders

Allergic reactions (including anaphylactic and anaphylactoid reactions)

Nervous system disorders:

Collapse or shock-like state (hypotonic-hyporesponsiveness episode)

Respiratory, thoracic and mediastinal disorders:

Apnoea* *[see section "Warnings and Precautions" for apnoea in very premature infants (≤ 28 weeks of gestation)]*

Skin and subcutaneous tissue disorders

Angioneurotic oedema*

General disorders and administration site conditions:

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Extensive swelling reactions, swelling of the entire injected limb**, vesicles at the injection site

* observed with other GSK DTPa-containing vaccines

** Children primed with acellular pertussis vaccines are more likely to experience swelling reactions after booster administration in comparison with children primed with whole cell vaccines. These reactions resolve over an average of 4 days.

- Experience with hepatitis B vaccine:

Meningitis, mimicking serum sickness, paralysis, encephalitis, encephalopathy, neuropathy, neuritis, hypotension, vasculitis, lichen planus, erythema multiforme, arthritis, muscular weakness have been reported during post-marketing surveillance following GlaxoSmithKline Biologicals" hepatitis B vaccine in infants < 2 years old. The causal relationship to the vaccine has not been established.

Overdosage

Insufficient data are available.

Clinical Pharmacology

Pharmacodynamics

ATC Code

Pharmaco-therapeutic group: Bacterial and viral vaccines combined, ATC code J07CA09

Pharmacodynamic Effects

Result obtained in the clinical studies for each of the components are summarised in the tables below :

Percentage of subjects with antibody titres ≥ assay cut-off one month after primary vaccination with Infanrix hexa

Antibody (cut-off)	**Two doses**	**Three doses**			
	3-5 months N= 530 (4 studies)	**2-3-4 months N= 196 (2 studies)**	**2-4-6 months N= 1693 (6 studies)**	**3-4-5 months N= 1055 (6 studies)**	**6-10-14 weeks N= 265 (1 study)**
	%	**%**	**%**	**%**	**%**
Anti-diphtheria (0.1 IU/ml) †	98.0	100.0	99.8	99.7	99.2

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Anti-tetanus (0.1 IU/ml) †	100.0	100.0	100.0	100.0	99.6
Anti-PT (5 EL.U/ml)	99.5	100.0	100.0	99.8	99.6
Anti-FHA (5 EL.U/ml)	99.7	100.0	100.0	100.0	100.0
Anti-PRN (5 EL.U/ml)	99.0	100.0	100.0	99.7	98.9
Anti-HBs (10 mIU/ml) †	96.8	99.5	98.9	98.0	98.5*
Anti-Polio type 1 (1/8 dilution) †	99.4	100.0	99.9	99.7	99.6
Anti-Polio type 2 (1/8 dilution) †	96.3	97.8	99.3	98.9	95.7
Anti-Polio type 3 (1/8 dilution) †	98.8	100.0	99.7	99.7	99.6
Anti-PRP (0.15 µg/ml) †	91.7	96.4	96.6	96.8	97.4

* in a subgroup of infants not administered hepatitis B vaccine at birth, 77.7% of subjects had anti-HBs titres ≥ 10 mIU/ml
† cut-off accepted as indicative of protection

Percentage of subjects with antibody titres ≥ assay cut-off one month after booster vaccination with Infanrix hexa

Antibody (cut-off)	**Booster vaccination at 11 months of age following a 3-5 month primary course N=532 (3 studies)**	**Booster vaccination during the second year of life following a three dose primary course N= 2009 (12 studies)**
	%	**%**
Anti-diphtheria (0.1 IU/ml) †	100.0	99.9
Anti-tetanus (0.1 IU/ml) †	100.0	99.9
Anti-PT (5 EL.U/ml)	100.0	99.9
Anti-FHA (5 EL.U/ml)	100.0	99.9
Anti-PRN (5 EL.U/ml)	99.2	99.5
Anti-HBs (10 mIU/ml) †	98.9	98.4
Anti-Polio type 1 (1/8 dilution) †	99.8	99.9
Anti-Polio type 2 (1/8 dilution) †	99.4	99.9
Anti-Polio type 3 (1/8 dilution) †	99.2	99.9

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Anti-PRP (0.15 µg/ml) †	99.6	99.7

† cut-off accepted as indicative of protection

As the immune response to pertussis antigens following Infanrix hexa administration is equivalent to that of Infanrix™, the protective efficacy of the two vaccines is expected to be equivalent.

The protective efficacy of the pertussis component of Infanrix™ against WHO-defined typical pertussis (≥ 21 days of paroxysmal cough) was demonstrated in:

- a prospective blinded household contact study performed in Germany (3, 4, 5 months schedule). Based on data collected from secondary contacts in households where there was an index case with typical pertussis, the protective efficacy of the vaccine was 88.7%.

- a NIH sponsored efficacy study performed in Italy (2, 4, 6 months schedule). The vaccine efficacy was found to be 84%. In a follow-up of the same cohort, the efficacy was confirmed up to 60 months after completion of primary vaccination without administration of a booster dose of pertussis.

Results of long term follow-up in Sweden demonstrate that acellular pertussis vaccines are highly efficacious in infants when adminsitered according to the 3 and 5 months primary vaccination schedule, with a booster dose administered at approximately 12 months. However, data indicate that protection against pertussis may be waning at 7-8 years of age. This suggests that a second booster dose of pertussis vaccine is warranted in children aged 5-7 years who have previously been vaccinated following this schedule.

Protective immunity against hepatitis B has been shown to persist for at least 3.5 years in more than 90% of children administered four doses of *Infanrix hexa*. Antibody levels were not different from what was observed in a parallel cohort administered monovalent hepatitis B vaccine.

The effectiveness of the GlaxoSmithKline Biologicals' Hib component (when combined with DTPa, or DTPa-IPV or DTPa-HBV-IPV) has been and continues to be investigated via an extensive post-marketing surveillance study conducted in Germany. Over a 4.5 year follow-up period, the effectiveness of DTPa/Hib or DTPa-IPV/Hib vaccines was 96.7% for a full primary series and 98.5% for a booster dose (irrespective of priming). Over a three year follow-up period, the effectiveness of hexavalent vaccines was 92.8% for a full primary series and 100% for a booster dose.

Clinical Studies

See section "*Pharmacodynamic effects*".

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NON-CLINICAL INFORMATION

Preclinical data reveal no special hazard for humans based on conventional studies of safety, specific toxicity, repeated dose toxicity and compatibility of ingredients.

PHARMACEUTICAL INFORMATION

Shelf-Life

The expiry date of the vaccine is indicated on the label and packaging. The date for last use corresponds to the first day of the month mentioned.

The shelf-life is 36 months.

Storage

Infanrix hexa should be stored at +2°C to +8°C. Protect from light.

During transport, recommended conditions of storage must be respected.

The DTPa-HBV-IPV suspension and the reconstituted vaccine must not be frozen. Discard if it has been frozen.

Nature and Contents of Container

The DTPa-HBV-IPV component is presented as a turbid white suspension in a syringe. Upon storage, a white deposit and clear supernatant can be observed.

The lyophilised Hib vaccine is presented as a white pellet in a glass vial or in a glass vial with Bioset®.

The vials and syringes are made of neutral glass type I, which conforms to European Pharmacopoeia Requirements.

Vial and syringe with or without needles in packs of 1, 10, 20 and 50.

Vial with Bioset® and syringe with or without needle in packs of 1, 10, 20 and 50

Incompatibilities

Infanrix hexa should not be mixed with other vaccines in the same syringe.

Use and Handling

<u>Wording for vial and syringe</u>

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The DTPa-HBV-IPV suspension should be well shaken in order to obtain a homogeneous turbid white suspension. The DTPa-HBV-IPV suspension and the Hib powder should be inspected visually for any foreign particulate matter and/or variation of physical aspect. In the event of either being observed, discard the container.

The vaccine is reconstituted by adding the contents of the syringe to the vial containing the Hib powder. It is good clinical practice to only inject a vaccine when it has reached room temperature. In addition, a vial at room temperature ensures sufficient elasticity of the rubber closure to minimise any coring of rubber particles. To achieve this, the vial should be kept at room temperature (25 ± 3 °C) for at least five minutes before connecting the syringe and reconstituting the vaccine.

The reconstituted vaccine presents as a slightly more cloudy suspension than the liquid component alone. This is normal and does not impair the performance of the vaccine. In the event of other variation being observed, discard the vaccine.

After reconstitution, the vaccine should be injected promptly. However the vaccine may be kept for up to 8 hours at room temperature (21°C).

Wording for vial with Bioset® and syringe

The DTPa-HBV-IPV suspension should be well shaken in order to obtain a homogeneous turbid white suspension. The DTPa-HBV-IPV suspension and the Hib powder should be inspected visually for any foreign particulate matter and/or variation of physical aspect. In the event of either being observed, discard the container.

The vaccine is reconstituted by adding the contents of the syringe to the vial containing the Hib powder. It is good clinical practice to only inject a vaccine when it has reached room temperature. In addition, a vial at room temperature ensures sufficient elasticity of the rubber closure to minimise any coring of rubber particles. To achieve this, the vial should be kept at room temperature (25 ± 3 °C) for at least five minutes before connecting the syringe and reconstituting the vaccine.

1. For reconstitution, remove while twisting the cover from the vial with the Bioset® cap containing the Hib component and remove the cap from the syringe.

2. Connect the syringe (without the needle) onto the vial with the Bioset® cap and push it downwards – without pushing on the stopper - until syringe „clicks" into position.

3. Inject the liquid contained in the syringe into the vial and shake carefully until the Hib powder is completely dissolved.

4. Aspirate the reconstituted vaccine back into syringe and then unscrew the syringe from the empty vial with the Bioset® cap.

5. Affix a needle on the syringe for administering the vaccine.

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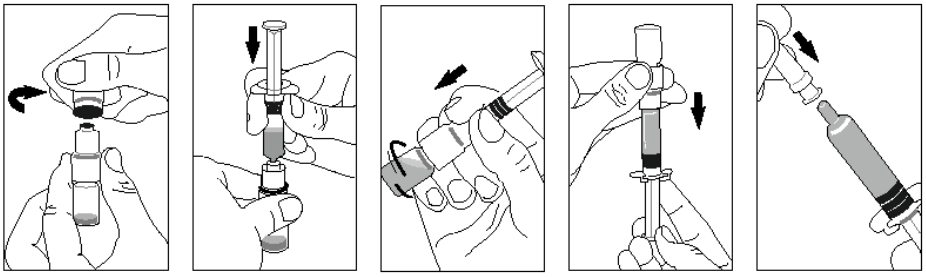

The reconstituted vaccine presents as a slightly more cloudy suspension than the liquid component alone. This is normal and does not impair the performance of the vaccine. In the event of other variation being observed, discard the vaccine.

After reconstitution, the vaccine should be injected promptly. However the vaccine may be kept for up to 8 hours at room temperature (21°C).

REFERENCES

[1] European Base dossier June 1999 – Part I – Expert Report on the Clinical Documentation; Revision of the Global Data Sheet document December 2005

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Active Name: Combined diphtheria, tetanus, pertussis (acellular), hepatitis B, poliomyelitis (inactivated) and *Haemophilus influenzae* type b vaccine
Version Number: 009
Version Date: 23-Nov-07

GLOBAL PATIENT LEAFLET

Read all of this leaflet carefully before your child starts receiving this vaccine.

- Keep this leaflet until your child has finished the complete vaccination course. You may need to read it again.
- If you have any further questions, ask your doctor or your pharmacist.
- This vaccine has been prescribed for your child. Do not pass it on to others.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

TITLE

Diphtheria (D), tetanus (T), pertussis (acellular, component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and Haemophilus type b (HIB) conjugate vaccine (adsorbed).

Trade Name of the product

Infanrix hexa, Powder and suspension for suspension for injection

Formulation and strength

Infanrix hexa contains immunogenic agents that will stimulate an immune response to diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and *Haemophilus* type b. Infanrix hexa is presented as a powder and a suspension for injection (1 dose of 0.5 ml) to be reconstituted before vaccination.

Excipients

The other ingredients in Infanrix hexa are:

Hib powder: lactose anhydrous

DTPa-HBV-IPV suspension: sodium chloride (NaCl), aluminium hydroxide, aluminium phosphate and water for injections, Medium 199 (as stabilizer including amino acids, mineral salt and vitamins).

Residues (optional)

Potassium chloride, disodium phosphate, monopotassium phosphate, polysorbate 20 and 80, glycine, formaldehyde, neomycin sulphate, polymyxin B sulphate

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Active Name: Combined diphtheria, tetanus, pertussis (acellular), hepatitis B, poliomyelitis (inactivated) and *Haemophilus influenzae* type b vaccine
Version Number: 009
Version Date: 23-Nov-07

WHAT INFANRIX HEXA IS AND WHAT IT IS USED FOR

The diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliomyelitis (DTPa-HBV-IPV) component is a white, slightly milky liquid presented in a prefilled syringe (0.5 ml).

The Hib component is a white powder presented in a glass vial or in a glass vial with Bioset®.

Both components must be mixed together before your child receives the vaccine. The mixed appearance is a white, slightly milky liquid.

Infanrix hexa is available in packs of 1, 10, 20 and 50 with or without needles.

Infanrix hexa is a vaccine used in children to prevent six diseases: diphtheria, tetanus (lockjaw), pertussis (whooping cough), hepatitis B, poliomyelitis (Polio) and *Haemophilus influenzae* type b. The vaccine works by causing the body to produce its own protection (antibodies) against these diseases.

- **Diphtheria**: Diphtheria mainly affects the airways and sometimes the skin. Generally the airways become inflamed (swollen) causing severe breathing difficulties and sometimes suffocation. The bacteria also release a toxin (poison), which can cause nerve damage, heart problems, and even death.

- **Tetanus** (Lockjaw): Tetanus bacteria enter the body through cuts, scratches or wounds in the skin. Wounds that are especially prone to infection are burns, fractures, deep wounds or wounds contaminated with soil, dust, horse manure/dung or wood splinters. The bacteria release a toxin (poison), which can cause muscle stiffness, painful muscle spasms, fits and even death. The muscle spasms can be strong enough to cause bone fractures of the spine.

- **Pertussis** (Whooping cough): Pertussis is a highly infectious illness. The disease affects the airways causing severe spells of coughing that may interfere with normal breathing. The coughing is often accompanied by a “whooping” sound, hence the common name “whooping cough”. The cough may last for 1-2 months or longer. Pertussis can also cause ear infections, bronchitis which may last a long time, pneumonia, fits, brain damage and even death.

- **Hepatitis B**: Hepatitis B is caused by the hepatitis B virus. It causes the liver to become swollen (inflamed). The virus is found in body fluids such as blood, semen, vaginal secretions, or saliva (spit) of infected people.

- **Poliomyelitis** (Polio): Poliomyelitis, sometimes called simply “polio” is a viral infection that can have variable effects. Often it causes only a mild illness but in some people it causes permanent damage or even death. In its severest form, polio infection causes paralysis of the muscles (muscles cannot move), including those

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muscles needed for breathing and walking. The limbs affected by the disease may be painfully deformed.

- **Haemophilus influenzae** type b (Hib): Hib infection most frequently causes brain inflammation (swelling). There will be some type of serious complications such as: mental retardation, cerebral palsy, deafness, epilepsy or partial blindness. Hib infection also causes inflammation of the throat. It occasionally causes death by suffocation. Less commonly, the bacteria can also infect the blood, heart, lungs, bones, joints, and tissues of the eyes and mouth.

Vaccination is the best way to protect against these diseases. None of the components in the vaccine are infectious.

BEFORE YOUR CHILD RECEIVES INFANRIX HEXA

Infanrix hexa should not be given:

- if your child has previously had any allergic reaction to Infanrix hexa, or any ingredient contained in this vaccine. The active substances and other ingredients in Infanrix hexa are listed at the beginning of the leaflet. Signs of an allergic reaction may include itchy skin rash, shortness of breath and swelling of the face or tongue.
- if your child has previously had an allergic reaction to any vaccine against diphtheria, tetanus, pertussis (whooping cough), hepatitis B, poliomyelitis or *Haemophilus influenzae* type b diseases.
- if your child experienced problems of the nervous system within 7 days after previous vaccination with a vaccine against pertussis (whooping cough) disease.

Take special care with Infanrix hexa:

- if your child has a severe infection with a high temperature (over 38°C). A minor infection such as a cold should not be a problem, but talk to your doctor first.
- if after previously having Infanrix hexa or another vaccine against pertussis (whooping cough) disease, your child had any problems, especially:
  - A high temperature (over 40°C) within 48 hours of vaccination
  - A collapse or shock-like state within 48 hours of vaccination
  - Persistent crying lasting 3 hours or more within 48 hours of vaccination
  - Seizures/fits with or without a high temperature within 3 days of vaccination
- if your child is suffering from neurological disorders, including infantile spasms, uncontrolled epilepsy or progressive encephalopathy (disease of brain)
- if your child has a bleeding problem or bruises easily
- if your child has a tendency to seizures/fits due to a fever, or if there is a history in the family of this
- if your child has breathing difficulties, please contact your doctor. This may be more common in the first three days following vaccination if your child is born prematurely (before or at 28 weeks of pregnancy).

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Using other medicines or vaccines

Please tell your doctor if your child is taking or has recently taken any other medicines, including medicines obtained without a prescription or has recently received any other vaccine.

Important information about some of the ingredients of Infanrix hexa

Please tell your doctor if your child has had an allergic reaction to neomycin or polymyxin (antibiotics).

HOW INFANRIX HEXA IS GIVEN

Your child will receive a total of three or two injections with an interval of at least one month between each one. Each injection is given on a separate visit. You will be informed by the doctor or nurse when you should come back for subsequent injections.

If additional injections or "booster" are necessary, the doctor will tell you.

If your child misses a scheduled injection, talk to your doctor and arrange another visit.

Make sure your child finishes the complete vaccination course of three or two injections. If not, your child may not be fully protected against the diseases.

The doctor will give Infanrix hexa as an injection into the muscle.

POSSIBLE SIDE EFFECTS

Like all medicines, Infanrix hexa can cause side effects, although not everybody gets them.

Side effects that may occur are the following:

- **Very common** (more than 1 in 10 doses of vaccine):
  - Loss of appetite
  - Restlessness, unusual crying, irritability
  - Pain, redness and swelling at the injection site
  - Fever (≥38°C)
  - Tiredness
- **Common** (up to 1 in 10 doses of vaccine):
  - Nervousness
  - Vomiting, diarrhoea
  - Fever (>39.5°C)
  - Hard lump at the injection site
  - Itching

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- **Uncommon** (up to 1 in 100 doses of vaccine):
  - Upper respiratory tract infection
  - Sleepiness
  - Cough
- **Rare** (up to 1 in 1000 doses of vaccine):
  - Bronchitis
  - Rash
- **Very Rare** (less than 1 in 10.000 doses of vaccine):
  Side effects occurred very rarely during clinical trials or routine use of the vaccine or with other diphtheria, tetanus and pertussis containing vaccines include:
  - As with all injectable vaccines, there is an extremely small risk of severe allergic reactions. These can be recognised by:
    - Itchy rash of the hands and feet
    - Swelling of the eyes and face
    - Difficulty in breathing or swallowing

    These reactions will usually occur before leaving the doctor‟s surgery. However, if your child gets any of these symptoms you should contact a doctor urgently.
  - Swollen glands in the neck, armpit or groin
  - Bleeding or bruising more easily than normal
  - Collapse or periods of unconsciousness, lack of awareness, seizures or fits (with or without fever) which usually occur within 2 to 3 days after vaccination
  - Temporarily stopping breathing
  - Swelling of the entire injected limb
  - Blister at the injection site
  - Hives

If your child gets side effects
If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

HOW TO STORE INFANRIX HEXA

Store in a refrigerator (2°C – 8°C).

Store in the original package in order to protect from light.

Do not freeze. Freezing destroys the vaccine.

Keep out of the reach and sight of children.

Do not use Infanrix hexa after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

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Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

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APPENDIX 2B : REFERENCE SAFETY INFORMATION AT THE END OF THE REPORTING PERIOD

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Active Name: Combined diphtheria, tetanus, pertussis (acellular), hepatitis B, poliomyelitis (inactivated) and *Haemophilus influenzae* type b vaccine
Version Number: 010
Version Date: 21 Oct 2010

GLOBAL DATASHEET

Combined diphtheria, tetanus, pertussis (acellular), hepatitis B, poliomyelitis (inactivated) and *Haemophilus influenzae* type b vaccine

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Active Name: Combined diphtheria, tetanus, pertussis (acellular), hepatitis B, poliomyelitis (inactivated) and *Haemophilus influenzae* type b vaccine
Version Number: 010
Version Date: 21 Oct 2010

GLOBAL PRESCRIBER INFORMATION

TITLE

Combined diphtheria-tetanus-acellular pertussis, hepatitis B, enhanced inactivated polio vaccine and *Haemophilus influenzae* type b vaccine.

SCOPE

Trade Name(s)

Infanrix hexa

Formulation and Strength

Powder and suspension for suspension for injection.

1 dose (0.5 ml) contains:

Diphtheria toxoid[1]	not less than 30 International units
Tetanus toxoid[1]	not less than 40 International units
Bordetella pertussis antigens	
Pertussis toxoid[1]	25 micrograms
Filamentous Haemagglutinin[1]	25 micrograms
Pertactin[1]	8 micrograms
Hepatitis B surface antigen[2,3]	10 micrograms
Poliovirus (inactivated)	
type 1 (Mahoney strain)[4]	40 D-antigen unit
type 2 (MEF-1 strain)[4]	8 D-antigen unit
type 3 (Saukett strain)[4]	32 D-antigen unit
Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 micrograms 20 - 40 micrograms

[1]adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$) 0.5 milligrams Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisiae*) by recombinant DNA technology
[3]adsorbed on aluminium phosphate ($AlPO_4$) 0.32 milligrams Al^{3+}
[4]propagated in VERO cells

The DTPa-HBV-IPV component is presented as a turbid white suspension. Upon storage, a white deposit and clear supernatant can be observed.

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The Hib component is presented as a white powder.

Excipients

It is mandatory for country product information to include both the complete list of excipients for all locally marketed presentations, and any locally imposed excipient warning statements.

Lactose

Sodium chloride (NaCl)

Medium 199 (as stabilizer including amino acids, mineral salts and vitamins)

Water for injections

Residues

Potassium chloride

Disodium phosphate

Monopotassium phosphate

Polysorbate 20 and 80

Glycine

Formaldehyde

Neomycin sulphate

Polymyxin B sulphate

CLINICAL INFORMATION

Indications

Infanrix hexa is indicated for primary and booster vaccination of infants against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and *Haemophilus influenza* type b.

Dosage and Administration

Posology

- **Primary vaccination**

The primary vaccination schedule consists of three doses of 0.5 ml (e.g. 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months) or two doses (e.g. 3, 5 months). There should be an interval

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of at least 1 month between doses. The Expanded Program on Immunisation schedule (at 6, 10, 14 weeks of age) may only be used if a dose of hepatitis B vaccine has been given at birth.

Locally established immunoprophylactic measures against hepatitis B should be maintained. Where a dose of hepatitis B vaccine is given at birth, Infanrix hexa can be used as a replacement for supplementary doses of hepatitis B vaccine from the age of 6 weeks. If a second dose of hepatitis B vaccine is required before this age, monovalent hepatitis B vaccine should be used.

- **Booster vaccination**

After a vaccination with 2 doses (e.g. 3, 5 months) of Infanrix hexa a booster dose must be given at least 6 months after the last priming dose, preferably between 11 and 13 months of age.

After vaccination with 3 doses (e.g. 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months) of Infanrix hexa a booster dose may be given at least 6 months after the last priming dose and preferably before 18 months of age.

Booster doses should be given in accordance with the official recommendations.

Infanrix hexa can be considered for the booster if the composition is in accordance with the official recommendations.

Other combinations of antigens have been studied in clinical trials following primary vaccination with Infanrix hexa and may be used for a booster dose: diphtheria, tetanus, acellular pertussis (DTPa), diphtheria, tetanus, acellular pertussis, *Haemophilus influenzae* type b (DTPa+Hib), diphtheria, tetanus, acellular pertussis, inactivated poliomyelitis, *Haemophilus influenzae* type b (DTPa-IPV+Hib) and diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliomyelitis, *Haemophilus influenzae* type b (DTPa-HBV-IPV+Hib).

Method of administration

Infanrix hexa is for deep intramuscular injection.

Contraindications

Hypersensitivity to the active substances or to any of the excipients or residues (see *Formulation and Strength*, *Excipients* and *Residues*).

Hypersensitivity after previous administration of diphtheria, tetanus, pertussis, hepatitis B, polio or Hib vaccines.

Infanrix hexa is contraindicated if the child has experienced an encephalopathy of unknown aetiology, occurring within 7 days following previous vaccination with

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pertussis containing vaccine. In these circumstances pertussis vaccination should be discontinued and the vaccination course should be continued with diphtheria-tetanus, hepatitis B, inactivated polio and Hib vaccines.

Warnings and Precautions

As with other vaccines, administration of Infanrix hexa should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor infection is not a contra-indication.

Vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable events) and a clinical examination.

If any of the following events are known to have occurred in temporal relation to receipt of pertussis-containing vaccine, the decision to give further doses of pertussis-containing vaccines should be carefully considered:

- Temperature of ≥ 40.0°C within 48 hours, not due to another identifiable cause.
- Collapse or shock-like state (hypotonic-hyporesponsiveness episode) within 48 hours of vaccination.
- Persistent, inconsolable crying lasting ≥ 3 hours, occurring within 48 hours of vaccination.
- Convulsions with or without fever, occurring within 3 days of vaccination.

There may be circumstances, such as a high incidence of pertussis, when the potential benefits outweigh possible risks.

In children with progressive neurological disorders, including infantile spasms, uncontrolled epilepsy or progressive encephalopathy, it is better to defer pertussis (Pa or Pw) immunization until the condition is corrected or stable. However, the decision to give pertussis vaccine must be made on an individual basis after careful consideration of the risks and benefits.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

Infanrix hexa should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects.

Infanrix hexa should under no circumstances be administered intravascularly or intradermally.

Infanrix hexa contains traces of neomycin and polymyxin. The vaccine should be used with caution in patients with known hypersensitivity to one of these antibiotics.

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Infanrix hexa will not prevent disease caused by pathogens other than *Corynebacterium diphtheriae*, *Clostridium tetani*, *Bordetella pertussis*, hepatitis B virus, poliovirus or *Haemophilus influenzae* type b. However, it can be expected that hepatitis D will be prevented by immunisation as hepatitis D (caused by the delta agent) does not occur in the absence of hepatitis B infection.

A protective immune response may not be elicited in all vaccinees (see *Pharmacodynamic Effects*).

A history of febrile convulsions, a family history of convulsions or Sudden Infant Death Syndrome (SIDS) do not constitute contraindications for the use of Infanrix hexa. Vaccinees with a history of febrile convulsions should be closely followed up as such adverse events may occur within 2 to 3 days post vaccination.

Human Immunodeficiency Virus (HIV) infection is not considered as a contra-indication. The expected immunological response may not be obtained after vaccination of immunosuppressed patients.

Since the Hib capsular polysaccharide antigen is excreted in the urine a positive urine test can be observed within 1-2 weeks following vaccination. Other tests should be performed in order to confirm Hib infection during this period.

Limited data in 169 premature infants indicate that Infanrix hexa can be given to premature children. However, a lower immune response may be observed and the level of clinical protection remains unknown.

The potential risk of apnoea and the need for respiratory monitoring for 48-72h should be considered when administering the primary immunization series to very premature infants (born ≤ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.

Interactions

There are insufficient data with regard to the efficacy and safety of simultaneous administration of Infanrix hexa and Measles-Mumps-Rubella vaccine to allow any recommendation to be made.

Data on concomitant administration of Infanrix hexa with Prevenar (pneumococcal saccharide conjugated vaccine, adsorbed) have shown no clinically relevant interference in the antibody response to each of the individual antigens when given as a 3 dose primary vaccination.

However, high incidence of fever (> 39.5°C) was reported in infants receiving Infanrix hexa and Prevenar compared to infants receiving the hexavalent vaccine alone.

Antipyretic treatment should be initiated according to local treatment guidelines.

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As with other vaccines, it may be expected that in patients receiving immunosuppressive therapy, an adequate response may not be achieved.

Pregnancy and Lactation

Pregnancy

As Infanrix hexa is not intended for use in adults, information on the safety of the vaccine when used during pregnancy is not available.

Lactation

As Infanrix hexa is not intended for use in adults, information on the safety of the vaccine when used during lactation is not available.

Ability to perform tasks that require judgement, motor or cognitive skills

Not relevant.

Adverse Reactions

Clinical Trial Data

The safety profile presented below is based on data from more than 16,000 subjects.

As has been observed for DTPa and DTPa-containing combinations, an increase in local reactogenicity and fever was reported after booster vaccination with Infanrix hexa with respect to the primary course.

Adverse reactions reported are listed according to the following frequency:

Very common: ≥ 1/10
Common: ≥ 1/100 to < 1/10
Uncommon: ≥ 1/1000 to < 1/100
Rare: ≥ 1/10000 to < 1/1000
Very rare: < 1/10000

Infections and infestations

Uncommon: upper respiratory tract infection

Metabolism and nutrition disorders

Very common: appetite lost

Psychiatric disorders

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Very common: irritability, crying abnormal, restlessness
Common: nervousness

Nervous system disorders

Uncommon: somnolence
Very rare: convulsions (with or without fever)

Respiratory, thoracic and mediastinal disorders

Uncommon: cough*
Rare: bronchitis

Gastrointestinal disorders

Common: vomiting, diarrhoea

Skin and subcutaneous tissue disorders

Common: pruritus*
Rare: rash
Very rare: dermatitis, urticaria*

General disorders and administration site conditions

Very common: pain, redness, local swelling at the injection site (≤ 50 mm), fever ≥ 38°C, fatigue
Common: local swelling at the injection site (> 50 mm)**, fever >39.5°C, injection site reactions, including induration
Uncommon: diffuse swelling of the injected limb, sometimes involving the adjacent joint**

Post Marketing Data

Blood and lymphatic system disorders

Lymphadenopathy, thrombocytopenia

Immune system disorders

Allergic reactions (including anaphylactic and anaphylactoid reactions)

Nervous system disorders

Collapse or shock-like state (hypotonic-hyporesponsiveness episode)

Respiratory, thoracic and mediastinal disorders

Apnoea* *[see Warnings and Precautions for apnoea in very premature infants (≤ 28 weeks of gestation)]*

Skin and subcutaneous tissue disorders

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Angioneurotic oedema*

General disorders and administration site conditions

Extensive swelling reactions, swelling of the entire injected limb**, vesicles at the injection site

* observed with other GSK DTPa-containing vaccines

** Children primed with acellular pertussis vaccines are more likely to experience swelling reactions after booster administration in comparison with children primed with whole cell vaccines. These reactions resolve over an average of 4 days.

Experience with hepatitis B vaccine:

Meningitis, mimicking serum sickness, paralysis, encephalitis, encephalopathy, neuropathy, neuritis, hypotension, vasculitis, lichen planus, erythema multiforme, arthritis, muscular weakness have been reported during post-marketing surveillance following GlaxoSmithKline Biologicals' hepatitis B vaccine in infants < 2 years old. The causal relationship to the vaccine has not been established.

Overdosage

Insufficient data are available.

Clinical Pharmacology

Pharmacodynamics

ATC Code

Pharmaco-therapeutic group: Bacterial and viral vaccines combined, ATC code J07CA09

Pharmacodynamic Effects

Result obtained in the clinical studies for each of the components are summarised in the tables below:

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Active Name: Combined diphtheria, tetanus, pertussis (acellular), hepatitis B, poliomyelitis (inactivated) and *Haemophilus influenzae* type b vaccine
Version Number: 010
Version Date: 21 Oct 2010

Percentage of subjects with antibody titres ≥ assay cut-off one month after primary vaccination with Infanrix hexa

Antibody (cut-off)	**Two doses**	**Three doses**			
	3-5 months N= 530 (4 studies)	**2-3-4 months N= 196 (2 studies)**	**2-4-6 months N= 1693 (6 studies)**	**3-4-5 months N= 1055 (6 studies)**	**6-10-14 weeks N= 265 (1 study)**
	%	**%**	**%**	**%**	**%**
Anti-diphtheria (0.1 IU/ml) †	98.0	100.0	99.8	99.7	99.2
Anti-tetanus (0.1 IU/ml) †	100.0	100.0	100.0	100.0	99.6
Anti-PT (5 EL.U/ml)	99.5	100.0	100.0	99.8	99.6
Anti-FHA (5 EL.U/ml)	99.7	100.0	100.0	100.0	100.0
Anti-PRN (5 EL.U/ml)	99.0	100.0	100.0	99.7	98.9
Anti-HBs (10 mIU/ml) †	96.8	99.5	98.9	98.0	98.5*
Anti-Polio type 1 (1/8 dilution) †	99.4	100.0	99.9	99.7	99.6
Anti-Polio type 2 (1/8 dilution) †	96.3	97.8	99.3	98.9	95.7
Anti-Polio type 3 (1/8 dilution) †	98.8	100.0	99.7	99.7	99.6
Anti-PRP (0.15 μg/ml) †	91.7	96.4	96.6	96.8	97.4

N=number of subjects
* in a subgroup of infants not administered hepatitis B vaccine at birth, 77.7% of subjects had anti-HBs titres ≥ 10 mIU/ml
† cut-off accepted as indicative of protection

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Percentage of subjects with antibody titres ≥ assay cut-off one month after booster vaccination with Infanrix hexa

Antibody (cut-off)	**Booster vaccination at 11 months of age following a 3-5 month primary course N=532 (3 studies)**	**Booster vaccination during the second year of life following a three dose primary course N= 2009 (12 studies)**
	%	**%**
Anti-diphtheria (0.1 IU/ml) †	100.0	99.9
Anti-tetanus (0.1 IU/ml) †	100.0	99.9
Anti-PT (5 EL.U/ml)	100.0	99.9
Anti-FHA (5 EL.U/ml)	100.0	99.9
Anti-PRN (5 EL.U/ml)	99.2	99.5
Anti-HBs (10 mIU/ml) †	98.9	98.4
Anti-Polio type 1 (1/8 dilution) †	99.8	99.9
Anti-Polio type 2 (1/8 dilution) †	99.4	99.9
Anti-Polio type 3 (1/8 dilution) †	99.2	99.9
Anti-PRP (0.15 μg/ml) †	99.6	99.7

N= Number of subjects
† cut-off accepted as indicative of protection

As the immune response to pertussis antigens following Infanrix hexa administration is equivalent to that of Infanrix, the protective efficacy of the two vaccines is expected to be equivalent.

The protective efficacy of the pertussis component of Infanrix against WHO-defined typical pertussis (≥ 21 days of paroxysmal cough) was demonstrated in:

- a prospective blinded household contact study performed in Germany (3, 4, 5 months schedule). Based on data collected from secondary contacts in households where there was an index case with typical pertussis, the protective efficacy of the vaccine was 88.7%.

- a NIH sponsored efficacy study performed in Italy (2, 4, 6 months schedule). The vaccine efficacy was found to be 84%. In a follow-up of the same cohort, the efficacy

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was confirmed up to 60 months after completion of primary vaccination without administration of a booster dose of pertussis.

Results of long term follow-up in Sweden demonstrate that acellular pertussis vaccines are highly efficacious in infants when administered according to the 3 and 5 months primary vaccination schedule, with a booster dose administered at approximately 12 months. However, data indicate that protection against pertussis may be waning at 7-8 years of age. This suggests that a second booster dose of pertussis vaccine is warranted in children aged 5-7 years who have previously been vaccinated following this schedule.

Protective immunity against hepatitis B has been shown to persist for at least 3.5 years in more than 90% of children administered four doses of Infanrix hexa. Antibody levels were not different from what was observed in a parallel cohort administered monovalent hepatitis B vaccine.

The effectiveness of the Hib component of Infanrix hexa was investigated via an extensive post-marketing surveillance study conducted in Germany. Over a seven year follow-up period, the effectiveness of the Hib components of two hexavalent vaccines, of which one was Infanrix hexa, was 89.6% for a full primary series and 100% for a full primary series plus booster dose (irrespective of the Hib vaccine used for priming).

Pharmacokinetics

Evaluation of pharmacokinetic properties is not required for vaccines.

Clinical Studies

See *Pharmacodynamic Effects*.

NON-CLINICAL INFORMATION

Preclinical data reveal no special hazard for humans based on conventional studies of safety, specific toxicity, repeated dose toxicity and compatibility of ingredients.

PHARMACEUTICAL INFORMATION

Shelf-Life

The expiry date of the vaccine is indicated on the label and packaging. The expiry date refers to the last day of the month mentioned.

The shelf-life is 3 years.

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Storage

Infanrix hexa should be stored at +2°C to +8°C. Protect from light.

During transport, recommended conditions of storage must be respected.

The DTPa-HBV-IPV suspension and the reconstituted vaccine must not be frozen. Discard if it has been frozen.

Nature and Contents of Container

The DTPa-HBV-IPV component is presented in a pre-filled syringe or vial.

The Hib component is presented as a white pellet in a glass vial.

The vials and pre-filled syringes are made of neutral glass type I, which conforms to European Pharmacopoeia Requirements.

Vial and pre-filled syringe presentations (with or without needles) are available in packs of 1, 10, 20 and 50.
Vial and vial presentation is available in pack sizes of 1 and 50.

Incompatibilities

Infanrix hexa should not be mixed with other vaccines in the same syringe.

Use and Handling

1. Wording for vial and pre-filled syringe presentation

The DTPa-HBV-IPV suspension should be well shaken in order to obtain a homogeneous turbid white suspension. The DTPa-HBV-IPV suspension and the Hib powder should be inspected visually for any foreign particulate matter and/or variation of physical aspect. In the event of either being observed, discard the vaccine.

Infanrix hexa must be reconstituted by adding the entire content of the pre-filled syringe to the vial containing the Hib powder.

It is good clinical practice to only inject a vaccine when it has reached room temperature. In addition, a vial at room temperature ensures sufficient elasticity of the rubber closure to minimise any coring of rubber particles. To achieve this, the vial should be kept at room temperature (25 ± 3 °C) for at least five minutes before connecting the pre-filled syringe and reconstituting the vaccine.

The reconstituted vaccine presents as a slightly more cloudy suspension than the liquid component alone. This is normal and does not impair the performance of the vaccine. In the event of other variation being observed, discard the vaccine.

After reconstitution, the vaccine should be injected immediately. However the vaccine may be kept for up to 8 hours at room temperature (21°C).

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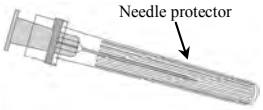
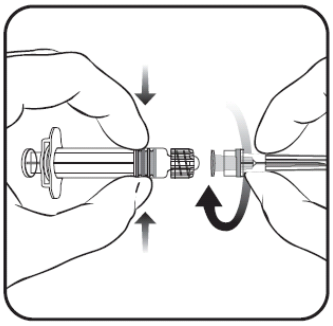
Withdraw the entire contents of the vial.

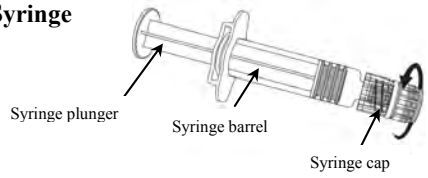
- ***Specific instructions for the pre-filled syringe with a luer lock adaptor (PRTC)***

Needle





Syringe



1. Holding the syringe **barrel** in one hand (avoid holding the syringe plunger), unscrew the syringe cap by twisting it anticlockwise.
2. To attach the needle to the syringe, twist the needle clockwise into the syringe until you feel it lock (see picture).
3. Remove the needle protector, which on occasion can be a little stiff.
4. Administer the vaccine.

2. Wording for vial and vial presentation

Upon storage, a white deposit and clear supernatant may be observed in the vial containing the DTPa-HBV-IPV suspension. This does not constitute a sign of deterioration.

Infanrix hexa must be reconstituted by adding the entire content of the vial containing the DTPa-HBV-IPV suspension to the vial containing the Hib powder. To do so, draw up the suspension with a syringe and add the suspension to the powder. The mixture should be well shaken until the powder is completely dissolved in the suspension.

The reconstituted vaccine presents as a slightly more cloudy suspension than the liquid component alone. This is normal and does not impair the performance of the vaccine.

The reconstituted vaccine should be inspected visually for any foreign particulate matter and/or abnormal physical appearance. In the event of either being observed, discard the vaccine.

A new needle should be used to administer the vaccine.

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After reconstitution, the vaccine should be used immediately.

Withdraw the entire contents of the vial.

Any unused product or waste material should be disposed of in accordance with local requirements.

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Active Name: Combined diphtheria, tetanus, pertussis (acellular), hepatitis B, poliomyelitis (inactivated) and *Haemophilus influenzae* type b vaccine
Version Number: 010
Version Date: 21 Oct 2010

GLOBAL PATIENT LEAFLET

Title

Infanrix hexa, powder and suspension for suspension for injection

Diphtheria (D), tetanus (T), pertussis (acellular, component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and *Haemophilus influenzae* type b vaccine (adsorbed)

Read all of this leaflet carefully before your child receives this vaccine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This vaccine has been prescribed for your child. Do not pass it on to others.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, tell your doctor or pharmacist.

In this leaflet

1. **What Infanrix hexa is and what it is used for**
2. **Before your child receives Infanrix hexa**
3. **How Infanrix hexa is given**
4. **Possible side effects**
5. **How to store Infanrix hexa**
6. **Further information**

1. What Infanrix hexa is and what it is used for

Infanrix hexa is a vaccine used to protect your child against six diseases:

- **Diphtheria:** a serious bacterial infection that mainly affects the airways and sometimes the skin. The airways become swollen causing serious breathing problems and sometimes suffocation. The bacteria also release a poison. This can cause nerve damage, heart problems, and even death.
- **Tetanus (Lockjaw):** tetanus bacteria enter the body through cuts, scratches or wounds in the skin. Wounds that are more likely to get tetanus infection are burns, fractures, deep wounds or wounds that have soil, dust, horse manure or wood splinters in them. The bacteria release a poison. This can cause muscle stiffness, painful

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muscle spasms, fits and even death. The muscle spasms can be strong enough to cause bone fractures of the spine.

- **Pertussis (Whooping cough):** a highly infectious illness that affects the airways. It causes severe coughing that may lead to problems with breathing. The coughing often has a "whooping" sound. The cough may last for one to two months or longer. Whooping cough can also cause ear infections, chest infections (bronchitis) which may last a long time, lung infections (pneumonia), fits, brain damage and even death.
- **Hepatitis B:** is caused by the hepatitis B virus and damages the liver. The virus is found in body fluids such as in the vagina, blood, semen or spit (saliva) of infected people.
- **Poliomyelitis (Polio):** a viral infection. Polio is often only a mild illness. However, sometimes it can be very serious and cause permanent damage or even death. Polio can make the muscles unable to move (paralysis). This includes the muscles needed for breathing and walking. The arms or legs affected by the disease may be painfully twisted (deformed).
- ***Haemophilus influenzae* type b (Hib):** can cause brain swelling (inflammation). This can lead to serious problems such as mental slowness (retardation), cerebral palsy, deafness, epilepsy or partial blindness. It can also cause swelling of the throat. This can cause death by suffocation. Less commonly, the bacteria can also infect the blood, heart, lungs, bones, joints, and tissues of the eyes and mouth.

How the vaccine works

- Infanrix hexa helps your child's body make its own protection (antibodies). This will protect your child against these diseases.
- As with all vaccines, Infanrix hexa may not fully protect all children who are vaccinated.
- The vaccine cannot cause the diseases that it protects against.

2. Before your child receives Infanrix hexa

Infanrix hexa should not be given:

- if your child is allergic (hypersensitive) to Infanrix hexa or any ingredients contained in Infanrix hexa. The active substances and other ingredients in Infanrix hexa are listed in section 6 of the leaflet. Signs of an allergic reaction may include itchy skin rash, shortness of breath and swelling of the face or tongue.
- if your child has previously had an allergic reaction to any vaccine against diphtheria, tetanus, pertussis (whooping cough), hepatitis B, poliomyelitis (polio) or *Haemophilus influenzae* type b diseases.
- if your child experienced problems of the nervous system within 7 days after previous vaccination with a vaccine against pertussis (whooping cough) disease.

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Check with your doctor if you think any of these apply to your child.

Take special care with Infanrix hexa:

- if your child has a severe infection with a high temperature. In these cases, the vaccination will be postponed until recovery. A minor infection such as a cold should not be a problem, but talk to your doctor first.
- if after previously having Infanrix hexa or another vaccine against pertussis (whooping cough) disease, your child had any problems, especially:
  - A high temperature (over 40°C) within 48 hours of vaccination
  - A collapse or shock-like state within 48 hours of vaccination
  - Persistent crying lasting 3 hours or more within 48 hours of vaccination
  - Seizures/fits with or without a high temperature within 3 days of vaccination
- if your child is suffering from neurological disorders, including infantile spasms, uncontrolled epilepsy or progressive encephalopathy (a disease of the brain)
- if your child has a bleeding problem or bruises easily
- if your child has a tendency to seizures/fits due to a fever, or if there is a history in the family of this
- if your child has breathing difficulties, please contact your doctor. This may be more common in the first three days following vaccination if your child was born prematurely (before or at 28 weeks of pregnancy).
- Children with a weakened immune system, for example due to HIV infection or due to medicines that suppress the immune system, may not get the full benefit from Infanrix hexa.
- Fainting can occur following, or even before, any needle injection, therefore tell the doctor or nurse if your child fainted with a previous injection.

Using other medicines or vaccines

Tell your doctor if your child is taking or has recently taken any other medicines, including medicines obtained without a prescription or has recently received any other vaccine.

Important information about some of the ingredients of Infanrix hexa

This vaccine contains neomycin and polymyxin (antibiotics). Tell your doctor if your child has had an allergic reaction to these ingredients.

3. How Infanrix hexa is given

- The doctor or nurse will give the recommended dose of Infanrix hexa to your child.

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- Usually, your child will receive a total of three or two injections with an interval of at least one month between each one. Each injection is given on a separate visit.
- Infanrix hexa is given as an injection of 0.5 ml into a muscle.
- You will be informed when your child should come back for the next injection.
- If additional injections ("boosters") are necessary, the doctor or nurse will tell you.

If your child misses a dose of Infanrix hexa

If your child misses a scheduled injection, it is important that you make another appointment.

Make sure your child finishes the complete vaccination course. If not, your child may not be fully protected against the diseases.

4. Possible side effects

Like all medicines, Infanrix hexa can cause side effects, although not everybody gets them.

The following side effects may happen with this vaccine:

Allergic reactions

As with all injectable vaccines, severe allergic reactions (anaphylactic and anaphylactoid reactions) may very rarely occur (up to 1 in 10,000 doses of vaccine). These can be recognised by:

- itchy rash of the hands and feet
- swelling of the eyes and face
- difficulty in breathing or swallowing
- sudden drop in blood pressure and loss of consciousness

These reactions will usually occur before leaving the doctor's surgery. However, if your child gets any of these symptoms you should contact a doctor urgently.

See your doctor straight away if your child has any of the following serious side effects:

- collapse
- times when they lose consciousness or have a lack of awareness
- fits – this may be when they have a fever

These side effects have happened very rarely with other vaccines against whooping cough. They usually happen within 2 to 3 days after vaccination.

Other side effects include:

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Very common (these may occur with more than 1 in 10 doses of the vaccine):

- loss of appetite
- unusual crying
- feeling irritable or restless
- pain, redness and swelling where the injection was given
- fever of 38°C or higher
- feeling tired

Common (these may occur with up to 1 in 10 doses of the vaccine):

- feeling nervous
- being sick (vomiting)
- diarrhoea
- fever higher than 39.5°C
- swelling larger than 5 cm where the injection was given
- hard lump where the injection was given
- itching

Uncommon (these may occur with up to 1 in 100 doses of the vaccine):

- upper respiratory tract infection
- feeling sleepy
- cough
- large swelling of the vaccinated limb

Rare (these may occur with up to 1 in 1,000 doses of the vaccine):

- bronchitis
- rash

Very Rare (these may occur with up to 1 in 10,000 doses of the vaccine):

- swollen glands in the neck, armpit or groin (*lymphadenopathy*)
- Bleeding or bruising more easily than normal (*thrombocytopenia*)
- temporarily stopping breathing (*apnoea*)
- in babies born very prematurely (at or before 28 weeks of gestation) longer gaps than normal between breaths may occur for 2-3 days after vaccination
- swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing (*angioneurotic oedema*)
- swelling of the whole injected limb
- blister where the injection was given
- hives (*urticaria*)
- skin rash (*dermatitis*)

If your child gets side effects

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If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, tell your doctor or pharmacist.

5. How to store Infanrix hexa

- Store in a refrigerator (2°C – 8°C).
- Store in the original package in order to protect from light.
- Do not freeze. Freezing destroys the vaccine.
- Keep out of the reach and sight of children.
- Do not use Infanrix hexa after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Further information

What Infanrix hexa contains

1 dose (0.5 ml) contains:

The active substances are:

Diphtheria toxoid[1]	not less than 30 International Units
Tetanus toxoid[1]	not less than 40 International Units
Bordetella pertussis antigens	
Pertussis toxoid[1]	25 micrograms
Filamentous Haemagglutinin[1]	25 micrograms
Pertactin[1]	8 micrograms
Hepatitis B surface antigen[2,3]	10 micrograms
Poliovirus (inactivated)	
type 1 (Mahoney strain)[4]	40 D-antigen unit
type 2 (MEF-1 strain)[4]	8 D-antigen unit
type 3 (Saukett strain)[4]	32 D-antigen unit
Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate)[3]	10 micrograms
conjugated to tetanus toxoid as carrier protein	20-40 micrograms

[1]adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$) 0.5 milligrams Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisiae*) by recombinant DNA technology
[3]adsorbed on aluminium phosphate ($AlPO_4$) 0.32 milligrams Al^{3+}
[4]propagated in VERO cells

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The other ingredients in Infanrix hexa are:

Hib powder: lactose

DTPa-HBV-IPV suspension: sodium chloride (NaCl), Medium 199 (as stabilizer including amino acids, mineral salt and vitamins) and water for injections.

Potassium chloride, disodium phosphate, monopotassium phosphate, polysorbate 20 and 80, glycine, formaldehyde, neomycin sulphate and polymyxin B sulphate are present as residues.

What Infanrix hexa looks like and contents of the pack

The diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliomyelitis (DTPa-HBV-IPV) component is a turbid white suspension presented in a pre-filled syringe (0.5 ml) or vial (0.5 ml).

The Hib component is a white powder presented in a vial.

Infanrix hexa is available in packs of 1, 10, 20 and 50 with or without needles (pre-filled syringe and vial presentation) or in packs of 1 and 50 (vial and vial presentation).

Not all pack sizes may be marketed.

Instructions for use

The following information is intended for medical or healthcare professionals only:

- Administration of the vial and pre-filled syringe presentation

The DTPa-HBV-IPV suspension should be well shaken in order to obtain a homogeneous turbid white suspension. The DTPa-HBV-IPV suspension and the Hib powder should be inspected visually for any foreign particulate matter and/or variation of physical aspect. In the event of either being observed, discard the vaccine.

Infanrix hexa must be reconstituted by adding the entire content of the pre-filled syringe to the vial containing the Hib powder.

It is good clinical practice to only inject a vaccine when it has reached room temperature. In addition, a vial at room temperature ensures sufficient elasticity of the rubber closure to minimise any coring of rubber particles. To achieve this, the vial should be kept at room temperature (25 ± 3 °C) for at least five minutes before connecting the pre-filled syringe and reconstituting the vaccine.

The reconstituted vaccine presents as a slightly more cloudy suspension than the liquid component alone. This is normal and does not impair the performance of the vaccine. In the event of other variation being observed, discard the vaccine.

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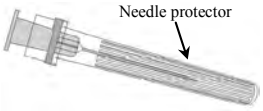
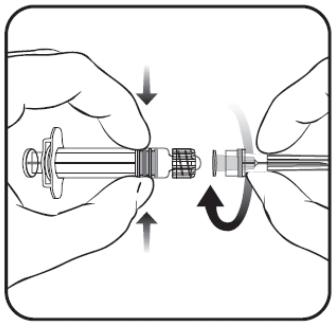
After reconstitution, the vaccine should be injected immediately. However the vaccine may be kept for up to 8 hours at room temperature (21°C).

Withdraw the entire contents of the vial.

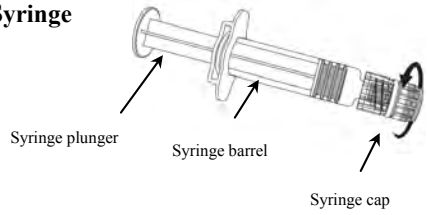
- *Specific instructions for the pre-filled syringe with a luer lock adaptor (PRTC)*

Needle





Syringe



1. Holding the syringe **barrel** in one hand (avoid holding the syringe plunger), unscrew the syringe cap by twisting it anticlockwise.
2. To attach the needle to the syringe, twist the needle clockwise into the syringe until you feel it lock (see picture).
3. Remove the needle protector, which on occasion can be a little stiff.
4. Administer the vaccine.

Any unused product or waste material should be disposed of in accordance with local requirements.

- Administration of the vial and vial presentation

Upon storage, a white deposit and clear supernatant may be observed in the vial containing the DTPa-HBV-IPV suspension. This does not constitute a sign of deterioration.

Infanrix hexa must be reconstituted by adding the entire content of the vial containing the DTPa-HBV-IPV suspension to vial containing the Hib powder. To do so, draw up the suspension with a syringe and add the suspension to the powder. The mixture should be well shaken until the powder is completely dissolved in the solvent.

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The reconstituted vaccine presents as a slightly more cloudy suspension than the liquid component alone. This is normal and does not impair the performance of the vaccine.

The reconstituted vaccine should be inspected visually for any foreign particulate matter and/or abnormal physical appearance. In the event of either being observed, discard the vaccine.

A new needle should be used to administer the vaccine.

After reconstitution, the vaccine should be used immediately.

Withdraw the entire contents of the vial.

Any unused product or waste material should be disposed of in accordance with local requirements.

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APPENDIX 3A : All serious spontaneous cases (excluding consumer reports), all serious attributable clinical trial cases and all non-serious unlisted cases (excluding consumer and regulatory reports)

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APPENDIX 3 INDIVIDUAL CASE HISTORIES RECEIVED IN TIME PERIOD OF PSUR

KEY

U, UN Unknown

Report Source

CN	Contact
CO	Consumer
DE	Dentist
HP	Other Health Professional
IN	Internet
LI	Literature
LW	Lawyer
MD	Physician
MR	Medic via Representative
NP	Newspaper
OM	Other Manufacturer
OT	Other
PH	Pharmacist
RA	Regulatory Authority
RG	Registry
RP	Representative
C	Clinical Trial
P	Post-Marketing Surveillance Study

TDD (Total Daily Dose)

VA	Variable dose
z	See comment

TTO/SLD (Time to Onset Since Last Dose)

I	Immediate
S	Seconds
N	Minutes
D	Days
A	Same day
H	Hours
W	Weeks
M	Months
Y	Years

Formulation (Form'n)

Outcome

F	Fatal
I	Improved
N	Unresolved
R	Resolved
S	Resolved with sequelae
W	Worse
X	Not applicable

Age

E	Elderly
F	Foetus
I	Infant
N	Neonate
T	Teenager

Events

*and** Post-treatment and dose reduction events

† If treatment start date unknown, treatment duration is entered in this column if available.

Serious case (not all cases will meet criteria for expedited reporting).

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Appendix 3A: Individual Case Histories Received in Time Period of PSUR for:

Infanrix hexa

Case No.	Country	Report Source	Age/Sex	Form'n or Route	TDD	Treatment Dates†	Event Onset	TTO / TTOSLD	Events	Outcome	Comments
Blood and lymphatic system disorders											
#B0636708A	Italy	RA	3 Months/F	INJ	U	03Jul2009-03Jul2009	03Jul2009	U/0 Days	Anaemia*, Apnoea*, Metabolic acidosis*, Retinal haemorrhage*, Child maltreatment syndrome*	R	
#D0066256A	Germany	RA	2 Months/M	INJ	.5ML	30Sep2009-30Sep2009	30Sep2009	U/0 Days	Anaemia*, C-reactive protein increased*, Pyrexia*, Insomnia*, Crying*, Crying*, Ill-defined disorder*	R	
#D0068631A	Germany	RA	9 Weeks/M	INJ	.5ML	28Jun2010-28Jun2010	01Jul2010	U/3 Days	Granulocytopenia*, Neutropenia*, C-reactive protein increased*, Oxygen saturation decreased*	R	
#D0066805A	Germany	MD,RA,RP	12 Months/F	INJ	U	27Nov2009-27Nov2009	16Dec2009	U/19 Days	Idiopathic thrombocytopenic purpura*, Haematoma*, Petechiae*, Mouth haemorrhage*	N	

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#B0619820A	France	MD	3 Months/M	INJ	U	04Dec2009-04Dec2009	04Dec2009	U/0 Days	Idiopathic thrombocytopenic purpura*, Haematoma*, Rectal haemorrhage, Purpura*	R
#B0656703A	France	RA	2 Months/M	INJ	U	19Mar2010-19Mar2010	27Mar2010	U/8 Days	Idiopathic thrombocytopenic purpura*, Petechiae*, Abnormal behaviour*, Purpura*	R
#D0068471A	Germany	MD,RA	8 Months/M	INJ, INJ	U, U	28Aug2008-28Aug2008, 03Jul2008-03Jul2008	05Dec2008	U/99 Days, U/5 Months	Idiopathic thrombocytopenic purpura, Petechiae, Haematoma, Hypochromic anaemia*, Upper respiratory tract infection, Rhinitis, Pyrexia, Constipation*	N
#D0067175A	Germany	RA	4 Months/F	INJ	U	28Jul2009-28Jul2009	28Aug2009	U/31 Days	Idiopathic thrombocytopenic purpura*, Thrombocytopenia*	R
#B0639439A	Poland	RA	1 Months/M	INJ	U	10Oct2009-10Oct2009	10Oct2009	U/4 Hours	Leukocytosis*, Cyanosis*, Injection site reaction*, Restlessness*, Crying*	R

#B0648028A	Poland	RA	3 Months/F	INJ	U	05Jan2010-05Jan2010	20Feb2010	U/46 Days	Leukocytosis*, Lymphadenopathy*, Pain in extremity*, Petechiae*, Condition aggravated*	U
B0665220A	Poland	MD,RA	23 Months/U	INJ	U	31Mar2010-31Mar2010	01Apr2010	U/1 Days	Lymph node pain, Injection site reaction	R
#B0675418A	Italy	MD,RA	4 Months/M	INJ	U	10Aug2010-10Aug2010	11Aug2010	U/1 Days	Microcytosis, Convulsion, Escherichia urinary tract infection, Pyrexia	U
#B0647986A	Italy	RA	5 Months/M	INJ	U	22Mar2010-22Mar2010	23Mar2010	U/1 Days	Neutropenia*, Decreased appetite*, Somnolence*	U
#B0615557A	Italy	RA	5 Months/M	INJ	U	14Oct2009-14Oct2009	05Nov2009	U/22 Days	Thrombocytopenia*	U
#B0665357A	Italy	RA	U/M	INJ	U	U	01Jul2010	U/Unknown	Thrombocytopenia*	U

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#D0067177A	Germany	RA	15 Months/F	INJ	U	25Feb2010-25Feb2010	25Feb2010	U/0 Days	Thrombocytopenia*, Idiopathic thrombocytopenic purpura*, Gastroenteritis*, Petechiae*, Haematoma*, Vomiting*, Diarrhoea*, Injection site inflammation*, Injection site induration*, Incorrect route of drug administration	N
#B0630988A	Italy	RA	12 Months/F	INJ	U	12Jun2007-12Jun2007	30Jun2007	U/15 Days	Thrombocytopenic purpura*, Viral infection*, Pyrexia*, Rash*, Petechiae*, Ecchymosis*	R
#D0069059A	Germany	CO,MD,RA	4 Months/M	INJ	U	05Aug2010-05Aug2010	10Aug2010	U/5 Days	Warm type haemolytic anaemia, Thrombocytopenia, Jugular vein thrombosis, Jaundice acholuric, Incorrect route of drug administration	N
Cardiac disorders										
#D0067784A	Germany	RA	4 Months/M	INJ	.5ML	11May2010-11May2010, 13Apr2010-13Apr2010	11May2010	U/5 Minutes, U/U	Bradycardia*, Pallor*	R

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#B0605003A	Italy	RA	2 Months/F	INJ	U	10Aug2009-10Aug2009	10Aug2009	U/0 Days	Cardiac arrest*, Convulsion*, Hypokinesia*	F
#D0064259A	Germany	RA	3 Months/M	INJ	.5ML	29Sep2009-29Sep2009	02Oct2009	U/3 Days	Cardiac arrest, Sudden infant death syndrome*, Sepsis*, Viral infection*, Resuscitation*, Pyrexia*, Loss of consciousness*, Cyanosis*	F
#B0632575A	Switzerland	RA	10 Weeks/F	INJ	U	05Jan2010-05Jan2010	05Jan2010	U/5 Hours	Cyanosis*, Apnoea*, Apparent life threatening event*, Somnolence*, Hypotonic-hyporesponsive episode*, Hypothermia*, Vomiting*, Skin discolouration*, Hypotonia*	R
#B0657507A	Ireland	RA	2 Months/F	INJ	U	07Apr2010-07Apr2010	07Apr2010	U/0 Days	Cyanosis*, Bradycardia*, Hypotonia*, Oxygen saturation decreased*, Pallor*, Vomiting*, Dyspnoea*	R
#B0604826A	Czech Republic	RA	8 Months/F	INJ	U	03Jul2009-03Jul2009, U	03Jul2009	U/Hours, U/U	Cyanosis*, Convulsion*, Loss of consciousness*, Somnolence*	R

#B0677866A	France	RA	4 Months/M	INJ	U	29Jul2010-29Jul2010	29Jul2010	U/Hours	Cyanosis*, Crying*, Crying*, Tachycardia*, Livedo reticularis*	R
#B0642862A	Italy	RA	2 Months/F	INJ	U	16Mar2010-16Mar2010	16Mar2010	U/0 Days	Cyanosis*, Crying*, Cyanosis*	R
#B0656982A	Italy	LW,MD,RA	2 Months/F	INJ	U	20May2010-20May2010	20May2010	U/0 Days	Cyanosis*, Depressed level of consciousness, Body temperature decreased, Presyncope, Lip swelling, Skin discolouration*, Rash macular*, Ill-defined disorder*, Auricular swelling*, Asthenia*, Pallor*, Weight decreased*, Swelling face*, Local swelling*, Erythema*, Lip oedema*, Erythema*, Hyperaemia*, Pain in extremity*, Feeling cold*, Pallor*, Pulse pressure increased, Injection site swelling*, Somnolence*, Decreased appetite*, Vomiting*, Urticaria*, Irritability*, Crying*, Injection site erythema*	R

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#B0643302A	Italy	RA	2 Months/M	INJ	U	11Mar2010-11Mar2010	11Mar2010	U/0 Days	Cyanosis*, Depressed level of consciousness*, Pallor*, Hypotonia*, Rotavirus infection*	R
#B0675235A	Ireland	MD,RA	2 Months/F	INJ	U	30Aug2010-30Aug2010	30Aug2010	U/0 Days	Cyanosis*, Discomfort*, Emotional distress*, Erythema*, Screaming*	R
#B0651949A	Latvia	RA	2 Months/F	INJ	.5ML	12Apr2010-12Apr2010	12Apr2010	U/4 Hours	Cyanosis*, Dyspnoea*, Pyrexia*	R
#B0604992A	Italy	RA	2 Months/M	INJ	U	12Nov2009-12Nov2009	12Nov2009	U/0 Days	Cyanosis*, Hypotonia*, Poor sucking reflex*, Crying*	R
#B0677571A	Italy	MD,RA	2 Months/M	INJ	U	23Sep2010-23Sep2010	23Sep2010	U/0 Days	Cyanosis, Hypotonic-hyporesponsive episode	R
#B0645116A	Belgium	RA	8 Weeks/M	INJ	U	1 Days	24Feb2010	U/Unknown	Cyanosis*, Loss of consciousness*, Hypotonia*, Pallor*	R

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#B0647347A	Italy	RA	5 Months/F	INJ	U	07Sep2009-07Sep2009	07Sep2009	U/0 Days	Cyanosis*, Pallor*, Hypotonia*	R
#B0629247A	Italy	RA	4 Months/M	INJ	U	16Dec2009-16Dec2009	16Dec2009	U/0 Days	Cyanosis*, Pallor*, Hypotonia*, Diarrhoea*, Vomiting*, Injection site reaction*	R
#B0651924A	Italy	RA	3 Months/M	INJ	U	08Feb2010-08Feb2010	09Feb2010	U/1 Days	Cyanosis*, Pyrexia*	R
#B0614414A	Brazil	MD	2 Months/F	INJ	U	04Dec2009-04Dec2009	04Dec2009	U/2 Hours	Cyanosis*, Vomiting*, Hypotonia*	R
Congenital, familial and genetic disorders										
#D0065891A	Germany	RA	2 Months/M	INJ	U	28Apr2008-28Apr2008, 26May2008-26May2008, 25Jun2008-25Jun2008	16May2008	U/18 Days, U/U, U/U	Cerebral palsy*, Hypotonia*, Dystonia*, Choreoathetosis*, Muscular weakness*, Psychomotor skills impaired*, Mental retardation*, Vaccination complication*	U

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#B0639175A	Italy	HP	Child/M	INJ	U	1 Days		U/Unknown	Haemophilia*	U
Eye disorders										
#B0619494A	Italy	RA	5 Months/F	INJ	U	03Nov2009-03Nov2009	18Nov2009	U/15 Days	Eye disorder*, Crying*	R
#B0654132A	Poland	RA	U/M	INJ	U	23Feb2010-23Feb2010	24Feb2010	U/1 Days	Eyelid oedema*, Local swelling*	R
#B0643810A	Italy	RA	1 Months/F	INJ	U	25Jul2008-25Jul2008	25Jul2008	U/0 Days	Eye movement disorder*	U
#B0668856A	Netherlands	RA	2 Months/M	INJ	U	13Apr2010-13Apr2010	01Apr2010	U/4 Hours	Gaze palsy*, Crying*, Pyrexia*, Myoclonus*	R

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#B0647634A	Netherlands	RA	2 Months/F	INJ	U	31Aug2009-31Aug2009	31Aug2009	U/0 Days	Gaze palsy*, Pyrexia*, Mental impairment*, Crying*	R
#D0068913A	Germany	PH	U/M	INJ	.5ML	1 Days		U/0 Years	Ophthalmoplegia*	I
#D0068913B	Germany	PH	1 Years/M	INJ	.5ML	01Jan2010-01Jan2010	01Jan2010	U/6 Weeks	Ophthalmoplegia*	I
Gastrointestinal disorders										
B0625276A	France	PH	2 Months/M	INJ, INJ	U, U	19Dec2009-19Dec2009, 13Jan2010-13Jan2010	19Dec2009	U/8 Hours, U/0 Months	Diarrhoea*, Decreased appetite*, Pyrexia*, Diarrhoea*, Pyrexia*, Incorrect route of drug administration, Inappropriate schedule of drug administration	R
D0065699A	Germany	MD	3 Months/M	INJ	U	09Dec2009-09Dec2009	09Dec2009	U/0 Days	Diarrhoea*, Poor weight gain neonatal*	N

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#B0605655A	Poland	RA	3 Months/U	INJ	U	08Oct2009-08Oct2009	08Oct2009	U/0 Days	Diarrhoea*, Pyrexia*, Crying*	R
#D0065923A	Germany	RA	3 Months/M	INJ	U	16Dec2009-16Dec2009	16Dec2009	U/0 Days	Enteritis*, Pyrexia*, Vomiting*	R
#D0068909A	Germany	MD	4 Months/F	INJ	U	17Sep2010-17Sep2010	17Sep2010	U/0 Days	Haematochezia, Crying, Mucous stools, Restlessness	R
B0615474A	France	MD	3 Months/M	INJ	U	13Nov2009-13Nov2009	13Nov2009	U/0 Days	Haematochezia*, Diarrhoea*, Pyrexia*	R
B0605572A	Greece	MD,RP	2 Months/M	INJ, INJ	U, U	01Aug2009-01Aug2009, 01Oct2009-01Oct2009		U/2 Days, U/2 Days	Haematochezia*, Haematochezia*	R
#D0068600A	Germany	RA	3 Months/M	INJ	.5ML	01Sep2009-01Sep2009	01Sep2009	U/0 Days	Haematochezia*, Mucous stools*, Faeces discoloured*, Crying*	R

#D0065893A	Germany	RA	3 Months/M	INJ	.5ML	19May2009-19May2009	20May2009	U/1 Days	Ileus paralytic*, Peritonitis*, Ileostomy*, Microcephaly*, Inguinal hernia*, Acute abdomen*, General physical health deterioration*, Ascites*, Sepsis*, Vomiting*, Leukocytosis*, Hyponatraemia*, Muscle disorder*	U	
#B0643201A	Poland	RA	9 Weeks/U	INJ	U	06Jan2010-06Jan2010	11Jan2010	U/5 Days	Intussusception*, Haematochezia*, Peritoneal disorder*, Gastrointestinal inflammation*, Gastrointestinal hypomotility*, Intestinal dilatation*, Abdominal rigidity*, Body temperature decreased*, Hypotonic-hyporesponsive episode*, Rash maculo-papular*, Sepsis*	U	BCWG level 0
#B0651961A	Belgium	MD	6 Months/M	INJ	U	12Mar2010-12Mar2010, 12Jan2010-12Jan2010	01May2010	U/50 Days, U/U	Intussusception*, Rectal haemorrhage*, Diarrhoea haemorrhagic*, Lymphadenopathy*, Pyrexia*, Vomiting*, Dyspepsia, Scar, Wound infection, Diarrhoea*	S	BCWG level 1
#B0656738A	South Africa	HP	10 Months/F	INJ	U	20Aug2009-20Aug2009, 21Sep2009-21Sep2009, 22Oct2009-22Oct2009	12May2010	U/7 Months, U/U, U/U	Intussusception*, Small intestinal resection*, Vomiting*, Colectomy*, Abdominal pain*	R	BCWG level 1

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#B0624719A	Italy	RA	2 Months/M	INJ	U	08Oct2007-08Oct2007	08Oct2007	U/0 Days	Melaena*, Oesophagitis*, Pyrexia*, Vomiting*, Irritability*	R
#B0671786A	United Arab Emirates	MD	2 Months/F	INJ	U	U		U/2 Days	Rectal haemorrhage*, Abdominal pain*, Haematochezia*	R
#B0679722A	Italy	MD,RA	3 Months/M	INJ	U	30Oct2009-30Oct2009	30Oct2009	U/0 Days	Vomiting	R
General disorders and administration site conditions										
D0067180A	Germany	MD	14 Months/M	INJ	U	27Nov2009-27Nov2009	27Nov2009	U/0 Days	Abasia*	R
#D0063315A	Germany	MD	4 Months/M	INJ	U	11Aug2008-11Aug2008, 14Jul2008-14Jul2008		U/Unknown, U/U	Abscess sterile*	S

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#D0063315B	Germany	MD	6 Months/M	INJ	U	15Oct2008-15Oct2008		U/Unknown	Abscess sterile*	U
#D0063315C	Germany	MD	16 Months/M	INJ	U	12Aug2009-12Aug2009	01Jan2009	U/Unknown	Abscess sterile*	U
#D0068941A	Germany	MD,RA	2 Years/M	INJ, INJ	.5ML, .5ML	1 Days, 30Jul2010-30Jul2010	01Aug2010	U/4 Weeks, U/Unknown	Abscess sterile*, Injection site reaction*, Injection site nodule*, Injection site swelling*, Injection site reaction*	N
#D0067243A	Germany	MD,RP	4 Months/M	INJ	.5ML	12Mar2010-12Mar2010	12Mar2010	U/0 Days	Application site discolouration*, Injection site reaction*, Skin depigmentation*, Rash*	N
#D0069211A	Germany	MD	U/U	INJ	U	U		U/U	Death	U
#D0063296A	Germany	RA	12 Weeks/M	INJ	.5ML	09Jan2006-09Jan2006	20Jan2006	U/11 Days	Death*	F

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#B0608494A	Netherlands	HP	14 Weeks/U	INJ	U	12Nov2009-12Nov2009	16Nov2009	U/4 Days	Death*	F
#B0599802A	Netherlands	HP,RA	4 Months/F	INJ	U	05Oct2009-05Oct2009	16Oct2009	U/11 Days	Death*, Adverse drug reaction*	F
B0617991A	Kenya	MD	Child/U	INJ	U	U		U/Unknown	Discomfort, Pain*, Irritability*, Pyrexia*	R
B0672556A	Greece	PH	2 Months/F	INJ	.5ML	10Aug2010-10Aug2010	10Aug2010	U/Hours	Discomfort, Vomiting	R
B0650707A	France	HP	17 Months/F	INJ	U	28Apr2010-28Apr2010	29Apr2010	U/1 Days	Extensive swelling of vaccinated limb*, Injection site erythema*, Injection site warmth*	N
B0665283A	Poland	MD,RA	17 Months/U	INJ	U	10May2010-10May2010	10May2010	U/0 Days	Extensive swelling of vaccinated limb, Injection site warmth, Injection site oedema, Injection site erythema, Injection site pain, Injection site pain*	R

#B0665361A	Austria	RA	1 Years/M	INJ	U	1 Days	22Jun2010	U/Unknown	Extensive swelling of vaccinated limb*, Pyrexia*	R
D0067605A	Germany	MD,RP	7 Months/U	INJ	.5ML	29Apr2010-29Apr2010	06May2010	U/7 Days	Fatigue*, Fatigue*	U
B0626686A	Netherlands	RA	398 Days/M	IM	U	25May2009-U		U/1 Weeks	Fibrosis*	R
D0069022A	Germany	MD,RA	22 Months/M	INJ	U	24Aug2010-24Aug2010	30Aug2010	U/6 Days	Gait deviation, Arthritis	R
B0608567A	France	MD,RP	16 Months/M	INJ	U	13Oct2009-13Oct2009	15Oct2009	U/2 Days	Gait disturbance*, Injected limb mobility decreased*, Injection site inflammation*, Injection site haemorrhage*, Injection site pain*, Injection site nodule*	I

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B0651926A	France	MD	22 Months/F	INJ, INJ	U, U	05May2010-05May2010, 05May2010-05May2010	05May2010	U/Same day, U/4 Hours	Gait disturbance*, Joint stiffness*, Pyrexia*, Injection site reaction*, Accidental overdose, Wrong technique in drug usage process	R
D0066847A	Germany	MD	4 Months/M	INJ, INJ, INJ	U, U, U	1 Days, 07Jan2010-07Jan2010, 19Nov2009-19Nov2009	01Jan2009	U/10 Days, U/10 Days, U/Unknown	Granuloma*, Granuloma*, Granuloma*, Granuloma*	N
D0066606A	Germany	MD	7 Months/M	INJ	U	13Aug2009-13Aug2009	20Sep2009	U/1 Months	Granuloma*, Induration*	U
B0676368A	France	MD	18 Months/M	INJ	U	01Sep2010-01Sep2010	01Sep2009	U/0 Months	Hyperthermia	R
#B0669511A	Latvia	HP,RA	10 Months/F	INJ	.5ML	13Jul2010-13Jul2010	13Jul2010	U/6 Hours	Hyperthermia	U
#B0667522A	Latvia	HP,RA	9 Months/F	INJ	U	21Apr2010-21Apr2010	21Apr2010	U/5 Hours	Hyperthermia, Erythema, Dermatitis atopic	R

B0669113A	Belgium	MD	Child/U	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/See text	Incorrect product storage	X
B0645785A	France	MD	2 Months/F	INJ	U	27Feb2010-27Feb2010	27Feb2010	U/See text	Incorrect product storage	X
B0657352A	France	PH	17 Months/M	INJ	U	23May2010-23May2010	23May2010	U/See text	Incorrect product storage	X
B0659551A	France	PH	3 Months/M	INJ	U	08Jun2010-08Jun2010	08Jun2010	U/See text	Incorrect product storage	X
B0660531A	France	MD	2 Months/F	INJ	U	25May2010-25May2010	25May2010	U/See text	Incorrect product storage	X
B0669707A	France	MD	12 Weeks/F	INJ	U	12Aug2010-12Aug2010	12Aug2010	U/See text	Incorrect product storage	X

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B0670473A	France	MD	3 Months/F	INJ	U	18Aug2010-18Aug2010	18Aug2010	U/See text	Incorrect product storage	X
B0673448A	France	PH	2 Months/M	INJ	U	06Sep2010-06Sep2010	06Sep2010	U/See text	Incorrect product storage	X
B0679075A	France	PH	2 Months/F	INJ	U	12Oct2010-12Oct2010	12Oct2010	U/See text	Incorrect product storage	X
B0679798A	France	PH	2 Months/M	INJ	U	15Oct2010-15Oct2010	15Oct2010	U/See text	Incorrect product storage	X
B0675786A	Tunisia	MD	2 Months/F	INJ	U	01Aug2010-01Aug2010	01Aug2010	U/See text	Incorrect product storage	X
B0603011A	France	PH	2 Months/M	INJ	U	09Nov2009-09Nov2009		U/See text	Incorrect product storage*	X

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B0608554A	France	MD	3 Months/F	INJ	U	1 Days		U/See text	Incorrect product storage*	X
B0659658A	France	MD	2 Months/F	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/See text	Incorrect product storage*	X
B0670338A	France	PH	1 Months/M	INJ	U	16Jun2010-16Jun2010	16Jun2010	U/See text	Incorrect product storage, Inappropriate schedule of drug administration	X
B0674209A	France	PH	12 Months/F	INJ	U	10Sep2010-10Sep2010	10Sep2010	U/See text	Incorrect product storage, Inappropriate schedule of drug administration	X
#B0622875A	Austria	RA	1 Years/F	INJ	U	25Nov2009-25Nov2009	27Nov2009	U/2 Days	Induration*	N
B0659537A	Lebanon	MD	4 Months/F	INJ	U	05Apr2010-05Apr2010	05Apr2010	U/0 Days	Inflammation*	R

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B0664449A	Netherlands	HP,RA	14 Months/F	INJ	.5ML	19Jan2010-19Jan2010	19Jan2010	U/Hours	Inflammation, Pruritus, Rash, Injection site inflammation	I
#D0067836A	Germany	RA	18 Months/F	INJ, INJ	.5ML, .5ML	06Jan2010-06Jan2010, 1 Days	01Aug2009	U/34 Days, U/Unknown	Injection site abscess sterile*, Injection site swelling*, Injection site abscess sterile*	R
B0677978A	France	MD	Infant/F	INJ	U	03Feb2009-03Feb2009	01Jan2009	U/0 Months	Injection site discolouration	N
B0618576A	France	MD	2 Months/M	INJ	U	01Nov2009-01Nov2009	01Nov2009	U/0 Days	Injection site eczema*, Eczema*, Injection site erythema*	R
#B0628875A	France	MD	16 Months/U	INJ	U	13Jan2010-13Jan2010	13Jan2010	U/0 Days	Injection site erythema*, Injection site haematoma*, Injection site warmth*, Injection site pruritus*, Injection site haemorrhage*, Injection site oedema*	N

D0067481A	Germany	MD	6 Months/F	INJ	U	22Apr2010-22Apr2010	01Apr2010	U/0 Weeks	Injection site erythema*, Injection site induration*, Injection site pain*, Hypokinesia*, Nonspecific reaction*	N
B0664827A	France	MD,RP	24 Months/M	INJ	U	01Jul2010-01Jul2010	01Jul2010	U/1 Days	Injection site erythema*, Injection site inflammation*, Injection site pain*	N
#B0652864A	France	RA	23 Months/F	INJ	U	24Mar2010-24Mar2010	26Mar2010	U/2 Days	Injection site erythema*, Injection site oedema*	R
B0636954A	France	MD,RP	2 Months/F	INJ	U	08Jan2010-08Jan2010	08Jan2010	U/Same day	Injection site erythema*, Injection site oedema*, Crying*, Skin discolouration*, Erythema*, Crying*	R
D0063921A	Germany	PH	10 Years/F	INJ	U	11Nov2009-11Nov2009	11Nov2009	U/0 Days	Injection site erythema*, Injection site pain*, Off label use	R
B0670363A	France	MD	2 Months/F	INJ	U	16Aug2010-16Aug2010	16Aug2010	U/Same day	Injection site erythema, Injection site swelling, Crying, Wrong technique in drug usage process	R

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D0069011A	Germany	MD,RP	2 Years/F	INJ	U	29Sep2010-29Sep2010	01Jan2010	U/0 Days	Injection site erythema, Injection site swelling, Lethargy, Pain, Pyrexia*	I
D0065352A	Germany	PH,MD,RA	15 Months/M	INJ	U	22Oct2009-22Oct2009	22Oct2009	U/0 Days	Injection site erythema*, Injection site warmth*, Injection site induration*, Injection site swelling*	R
B0643344A	Ukraine	MD	20 Months/M	INJ	U	31Oct2009-31Oct2009	07Nov2009	U/7 Days	Injection site extravasation*	I
#B0662514A	Poland	RA	19 Months/U	INJ	U	17May2010-17May2010	18May2010	U/1 Days	Injection site extravasation*, Injection site warmth*, Injection site erythema*, Injection site oedema*, Urticaria*	R
B0672349A	Netherlands	HP,RA	3 Months/M	INJ	U	15Apr2010-15Apr2010	16Apr2010	U/1 Days	Injection site haematoma, Injection site pain, Pyrexia, Crying, Injection site inflammation	R
#D0066638A	Germany	RA	2 Years/F	INJ	.5ML	07Jan2010-07Jan2010, 22Oct2007-22Oct2007, 12Nov2007-12Nov2007, 03Jan2008-03Jan2008	08Jan2010	U/1 Days, U/U, U/U, U/U	Injection site hypersensitivity*, Injection site erythema*, Injection site swelling*, Pyrexia*	R

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D0069145A	Germany	MD,RP	Child/U	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/0 Years	Injection site induration	U
D0066901A	Germany	MD,RP	Infant/U	INJ	U	1 Days		U/4 Days	Injection site induration*	U
D0067541A	Germany	PH	4 Months/M	INJ, INJ	U, U	01Apr2010-01Apr2010, 29Apr2010-29Apr2010	01Jan2010	U/4 Weeks, U/0 Months	Injection site induration*	R
D0068163A	Germany	MD,RP	4 Months/M	INJ	U	01Jun2010-01Jun2010		0 Months/U	Injection site induration*	U
B0673668A	Greece	MD	6 Months/M	INJ	U	01Dec2009-01Dec2009, 01Feb2010-01Feb2010	01Feb2010	U/0 Months, U/U	Injection site induration*	N
#B0646579A	Ireland	RA	6 Months/F	INJ	U	10Mar2010-10Mar2010	01Jan2010	U/Unknown	Injection site induration*	N

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B0663658A	France	PH	17 Months/M	INJ	U	29Jun2010-29Jun2010	30Jun2010	U/1 Days	Injection site induration*, Injection site erythema*	U
#B0609838A	Ireland	RA	6 Months/F	INJ	.5ML	27Apr2009-27Apr2009	27Apr2009	U/0 Days	Injection site induration*, Injection site erythema*, Injection site pain*, Injection site swelling*	R
#B0646683A	Ireland	RA	4 Months/F	INJ	U	10Mar2009-10Mar2009	10Mar2009	U/0 Days	Injection site induration*, Injection site erythema*, Injection site pain*, Injection site swelling*, Pyrexia*	R
#B0646683B	Ireland	RA	6 Months/F	INJ	U	15May2009-15May2009, 10Mar2009-10Mar2009	15May2009	U/0 Days, U/0 Days	Injection site induration*, Injection site erythema*, Injection site pain*, Injection site swelling*, Pyrexia*	R
B0659808A	Belgium	MD,RP	21 Months/F	INJ	U	26Feb2010-26Feb2010	26Feb2010	U/0 Days	Injection site induration*, Injection site erythema*, Injection site swelling*	R
B0646258A	France	CO,MD	2 Months/F	INJ, INJ	U, U	06Jan2010-06Jan2010, 08Mar2010-08Mar2010	07Jan2010	U/1 Days, U/1 Days	Injection site induration*, Injection site induration*	R

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D0066460A	Germany	PH	3 Months/M	INJ, INJ	U, U	19Nov2009-19Nov2009, 07Jan2010-07Jan2010		U/0 Years, U/0 Years	Injection site induration*, Injection site induration*	N
B0676979A	Poland	MD,RA	18 Months/U	INJ	U	18Jun2010-18Jun2010	19Jun2010	U/1 Days	Injection site induration*, Injection site pallor*, Injection site oedema*, Body temperature increased*, Injection site erythema*	R
D0068902A	Germany	HP,MD	7 Months/M	INJ, INJ	U, U	09Mar2010-09Mar2010, 22Apr2010-22Apr2010	13Apr2010	U/35 Days, U/Unknown	Injection site induration, Injection site swelling, Injection site erythema, Injection site induration, Injection site swelling, Injection site erythema	R
B0647972A	France	PH	16 Months/M	INJ	U	12Apr2010-12Apr2010	12Apr2010	U/Same day	Injection site induration*, Injection site swelling*, Injection site erythema*, Injection site warmth*	N
B0639778A	France	PH	18 Months/M	INJ	U	09Mar2010-09Mar2010	09Mar2010	U/0 Days	Injection site induration*, Injection site swelling*, Injection site erythema*, Injection site warmth*, Injection site pain*	I
B0672365A	Belgium	MD	Child/U	INJ	U	1 Days		U/Unknown	Injection site induration, Injection site swelling, Injection site pain, Crying	U

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B0676833A	Italy	MD	Child/F	INJ	U	13Sep2010-13Sep2010	13Sep2010	U/0 Days	Injection site induration*, Pyrexia, Wrong technique in drug usage process*	R
B0663986A	France	PH,MD	Child/U	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/Unknown	Injection site inflammation*, Injection site erythema*	R
B0661515A	France	MD	6 Years/F	INJ	U	16Jun2010-16Jun2010	16Jun2010	U/2 Days	Injection site inflammation*, Injection site induration*, Injection site pruritus*, Injection site erythema*, Inappropriate schedule of drug administration	N
B0659171A	France	MD	3 Years/M	INJ	U	02Jun2010-02Jun2010	02Jun2010	U/0 Days	Injection site inflammation*, Injection site oedema*, Injection site erythema*, Injection site warmth*	N
B0666855A	Netherlands	HP,RA	2 Months/F	INJ	U	23Nov2009-23Nov2009	23Nov2009	U/Hours	Injection site inflammation*, Oligodipsia*, Injection site induration*, Pyrexia*, Somnolence*	R

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#B0614454A	Italy	RA	10 Months/M	INJ	U	12Nov2009-12Nov2009	12Nov2009	U/0 Days	Injection site inflammation*, Pyrexia*	R
D0066040A	Germany	MD	2 Months/F	INJ, INJ	U, U	01Dec2009-01Dec2009, 15Oct2009-15Oct2009	15Oct2009	U/4 Hours, U/4 Hours	Injection site inflammation*, Pyrexia*, Pain*, Crying*, Injection site inflammation*, Pyrexia*, Pain*, Crying*	R
#B0667079A	South Africa	HP,PH	4 Months/F	INJ	U	04Jun2010-04Jun2010	04Jun2010	U/0 Days	Injection site mass, Thrombosis, Swelling, Crying, Injection site swelling	N
#D0069186A	Germany	MD	Infant/U	INJ	.5ML	1 Days		U/0 Weeks	Injection site necrosis*, Injection site vesicles*	U
D0066316A	Germany	MD	2 Months/M	INJ	U	01Nov2009-01Nov2009		U/Unknown	Injection site nodule*	R
D0066318A	Germany	MD	1 Months/F	INJ	U	01Nov2009-01Nov2009		U/Unknown	Injection site nodule*	R

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D0066319A	Germany	MD	3 Months/F	INJ	U	01Nov2009-01Nov2009	U/Unknown	Injection site nodule*	R
D0066320A	Germany	MD	2 Months/F	INJ	U	01Nov2009-01Nov2009	U/Unknown	Injection site nodule*	R
D0066321A	Germany	MD	3 Months/F	INJ	U	01Nov2009-01Nov2009	U/Unknown	Injection site nodule*	R
D0066322A	Germany	MD	1 Months/F	INJ	U	01Nov2009-01Nov2009	U/Unknown	Injection site nodule*	R
D0066323A	Germany	MD	3 Months/M	INJ	U	01Nov2009-01Nov2009	U/Unknown	Injection site nodule*	R
D0066324A	Germany	MD	2 Months/M	INJ	U	01Oct2009-01Oct2009	U/Unknown	Injection site nodule*	R

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D0066325A	Germany	MD	2 Months/F	INJ	U	01Dec2009-01Dec2009		U/Unknown	Injection site nodule*	R
D0066326A	Germany	MD	3 Months/M	INJ	U	01Dec2009-01Dec2009		U/Unknown	Injection site nodule*	R
D0067489A	Germany	MD	3 Years/F	INJ	U	1 Days		U/Unknown	Injection site nodule*	U
B0668555A	France	MD	Infant/F	INJ	U	02Apr2010-02Apr2010	01Jan2010	U/See text	Injection site nodule*, Injection site erythema*	N
B0606863A	France	MD	20 Months/M	INJ	U	27Jul2009-27Jul2009	01Jan2009	U/0 Weeks	Injection site nodule*, Injection site erythema*, Injection site induration*	R
B0653484A	France	MD,RP	2 Months/M	INJ, INJ, INJ	U, U, U	28Oct2008-28Oct2008, 05Jan2009-05Jan2009, 28Oct2009-28Oct2009	01Jan2009	U/Unknown, U/Unknown, U/Unknown	Injection site nodule*, Injection site nodule*, Injection site swelling*, Lymphadenopathy*, Eczema*, Injection site inflammation	N

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B0672492A	France	MD	12 Months/M	INJ	U	1 Days		U/Months	Injection site nodule, Injection site pruritus, Injection site reaction	N
B0680091A	France	MD	Infant/M	INJ, INJ, INJ	U, U, U	1 Days, 01Jan2008-01Jan2008, 01Jan2008-01Jan2008	01Jan2008	U/Immediate, U/Immediate, U/Immediate	Injection site nodule, Injection site pruritus, Injection site reaction	N
B0652412A	France	MD	Infant/F	INJ, INJ	U, U	30Jun2009-30Jun2009, 22Apr2009-22Apr2009	01Jan2009	U/0 Years, U/0 Years	Injection site nodule*, Injection site pruritus*, Injection site reaction*, Injection site erythema*	N
D0068654A	Germany	MD,RP	4 Months/M	INJ, INJ	U, U	29Oct2009-29Oct2009, 22Sep2009-22Sep2009	01Jan2009	U/Unknown, U/Unknown	Injection site nodule, Purulent discharge, Injection site abscess, Erythema, Injection site nodule	S
B0641359A	France	MD	17 Months/M	INJ	U	15Mar2010-15Mar2010	17Mar2010	U/2 Days	Injection site oedema*, Injection site erythema*, Injection site inflammation*, Injection site pain*	R
#B0658540A	Poland	RA	20 Months/M	INJ	U	02Apr2010-02Apr2010	02Apr2010	U/0 Days	Injection site oedema*, Injection site erythema*, Injection site pain*	R

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#B0658155A	Poland	RA	5 Years/U	INJ	U	06Apr2010-06Apr2010	07Apr2010	U/1 Days	Injection site oedema*, Injection site erythema*, Pain in extremity*	R
#B0673578A	Poland	MD,RA	2 Years/U	INJ	U	11Aug2010-11Aug2010	11Aug2010	U/6 Hours	Injection site oedema, Injection site erythema, Pyrexia	R
#B0678020A	Poland	MD,RA	16 Months/U	INJ	U	25Aug2010-25Aug2010	26Aug2010	U/1 Days	Injection site oedema*, Injection site pain*, Crying*, Pyrexia*	R
#B0652110A	France	RA	18 Months/M	INJ	U	19Apr2010-19Apr2010	20Apr2010	U/1 Days	Injection site oedema*, Injection site pain*, Injection site rash*	I
#B0649921A	Poland	RA	U/U	INJ	U	04Mar2010-04Mar2010	01Jan2010	U/0 Days	Injection site oedema*, Injection site pain*, Rash*, Pallor*, Somnolence*, Injection site reaction*	R
#B0613569A	Poland	RA	1 Years/M	INJ	U	20Aug2009-20Aug2009	21Aug2009	U/1 Days	Injection site oedema*, Pyrexia*, Restlessness*, Poor quality sleep*	R

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#B0655708A	Poland	RA	19 Months/U	INJ	U	25Mar2010-25Mar2010	26Mar2010	U/1 Days	Injection site pain*, Injection site oedema*, Injection site erythema*, Pyrexia*	R
D0068221A	Germany	MD	4 Months/M	INJ	U	06Jul2010-06Jul2010	07Jul2010	U/1 Days	Injection site reaction*	U
B0602844A	Brazil	HP	6 Months/F	INJ	U	05Nov2009-05Nov2009	05Nov2009	U/0 Days	Injection site reaction*, Injection site haematoma*, Injection site oedema*	R
B0622056A	France	HP	18 Months/U	INJ	U	01Jan2009-01Jan2009	01Jan2009	U/Unknown	Injection site reaction*, Injection site induration*, Injection site erythema*	U
#B0670247A	Poland	MD,RA	5 Months/U	INJ	U	21Jul2010-21Jul2010	21Jul2010	U/0 Days	Injection site reaction*, Injection site oedema*, Crying*, Tearfulness*, Irritability*	R
B0671464A	Austria	PH	7 Years/U	INJ	U	1 Days		U/Unknown	Injection site reaction*, Injection site pain*	N

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#B0657538A	Poland	RA	18 Months/U	INJ	U	23Mar2010-23Mar2010	24Mar2010	U/1 Days	Injection site reaction*, Injection site reaction*, Injection site pain*, Injection site erythema*	R
B0669195A	Italy	CO,RA	11 Months/F	INJ	U	15Jul2010-15Jul2010	15Jul2010	U/0 Days	Injection site reaction, Injection site swelling, Pyrexia	U
D0063385A	Germany	MD,RP	0-9 Years/F	INJ	U	1 Days		U/Unknown	Injection site reaction*, Injection site swelling*, Pyrexia*	U
#B0670408A	Austria	RA	1 Years/M	INJ	U	20Jul2010-20Jul2010	21Jul2010	U/1 Days	Injection site reaction*, Injection site warmth*, Injection site swelling*	U
#B0669693A	Poland	MD,RA	2 Years/F	INJ	U	09Jul2010-09Jul2010	10Jul2010	U/1 Days	Injection site reaction*, Pyrexia*	U
D0066405A	Germany	MD,RP	20 Months/M	INJ	U	03Feb2010-03Feb2010	03Feb2010	U/0 Days	Injection site reaction*, Swelling*, Erythema*, Feeling hot*, Induration*	R

D0067441A	Germany	MD,RA	3 Months/M	INJ	U	12Apr2010-12Apr2010	12Apr2010	U/0 Days	Injection site swelling*, Fluid intake reduced*, Injection site erythema*, Injection site warmth*, Screaming*, Restlessness*, Pyrexia*	N
D0068256A	Germany	MD	3 Months/F	INJ	U	08Jul2010-08Jul2010	08Jul2010	U/0 Days	Injection site swelling, Inappropriate schedule of drug administration	U
#D0067565A	Germany	RA	4 Months/F	INJ	.5ML	26Feb2010-26Feb2010	26Feb2010	U/0 Days	Injection site swelling*, Injection site discolouration*, Injection site pallor*, Erythema*, Crying*	R
#D0066395A	Germany	MD	4 Months/F	INJ	U	17Nov2009-17Nov2009	17Nov2009	U/0 Days	Injection site swelling*, Injection site erythema*	R
D0066163A	Germany	MD	23 Months/M	INJ	U	20Jan2010-20Jan2010	21Jan2010	U/1 Days	Injection site swelling*, Injection site erythema*, Erythema*, Local swelling*, Lymphadenopathy*	R
D0068015A	Germany	MD	22 Months/M	INJ	U	16Jun2010-16Jun2010	01Jun2010	U/0 Weeks	Injection site swelling*, Injection site erythema*, Injection site warmth*, Injection site pallor*	N

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B0632199A	France	HP,MD	17 Months/F	INJ	U	01Feb2010-01Feb2010	01Feb2010	U/Same day	Injection site swelling*, Injection site erythema*, Pyrexia*, Injection site inflammation*	R
D0066446A	Germany	MD	3 Months/M	INJ	U	08Feb2010-08Feb2010	09Feb2010	U/1 Days	Injection site swelling*, Injection site induration*	R
D0067093A	Germany	MD	Infant/M	INJ	U	26Jan2010-26Jan2010	01Jan2010	U/Unknown	Injection site swelling*, Injection site reaction*, Crying*	R
D0068815A	Germany	MD	17 Months/M	INJ, INJ, INJ	U, U, U	11Jan2010-11Jan2010, 1 Days, 23Feb2010-23Feb2010		U/0 Years, U/0 Years, U/Unknown	Injection site swelling*, Injection site swelling*, Malaise*	N
D0063347A	Germany	MD	14 Months/M	INJ	U	26Oct2009-26Oct2009	26Oct2009	U/0 Days	Injection site swelling*, Injection site warmth*, Injection site pain*, Product quality issue*	R
D0066178A	Germany	MD	3 Years/M	INJ	U	19Jan2010-19Jan2010	22Jan2010	U/3 Days	Injection site swelling*, Myositis*	N

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D0068025A	Germany	PH,RA	22 Months/M	INJ	U	04Jun2010-04Jun2010	05Jun2010	U/1 Days	Injection site swelling, Pain, Injection site warmth, Hyperaesthesia, Hypokinesia	I
B0604609A	South Africa	HP	20 Months/F	INJ	U	11Nov2009-11Nov2009	11Nov2009	U/0 Days	Injection site swelling*, Pyrexia*, Oedema peripheral*, Injection site swelling*, Swelling*	U
D0063452A	Germany	MD	7 Months/F	INJ	U	26Oct2009-26Oct2009	26Oct2009	U/0 Days	Injection site swelling*, Restlessness*, Pain*, Product quality issue*	R
#B0662522A	South Africa	HP	2 Years/U	INJ	U	24Jun2010-24Jun2010	24Jun2010	U/0 Days	Injection site vesicles*	R
#B0640116A	Latvia	MD	18 Months/F	INJ	.5ML	09Mar2010-09Mar2010	09Mar2010	U/0 Days	Injection site warmth*, Injection site erythema*, Injection site swelling*	I
B0663785A	Poland	MD,RA	22 Months/U	INJ	U	15Apr2010-15Apr2010	15Apr2010	U/0 Days	Injection site warmth, Injection site inflammation, Injection site extravasation, Injection site oedema, Body temperature increased	R

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#B0661562A	Ireland	RA	6 Months/F	INJ	U	06May2010-06May2010	06May2010	U/Hours	Irritability*, Injection site erythema*, Crying*, Pyrexia*	R
B0623343A	Kenya	MD	U/U	INJ	U	01Jan2009-01Jan2009		U/Unknown	Irritability*, Insomnia*, Pyrexia*, Pain*	R
B0649576A	Belgium	MD	2 Months/F	INJ	U	23Apr2010-23Apr2010, 23Apr2010-23Apr2010	23Apr2010	U/0 Days, U/U	Irritability, Overdose*	R
B0677762A	Belgium	MD	3 Months/F	INJ, INJ	U, U	21Sep2010-21Sep2010, 21Sep2010-21Sep2010	21Sep2010	U/0 Days, U/0 Days	Irritability, Wrong technique in drug usage process, Overdose	U
B0635715A	Austria	MD,RA	3 Months/F	INJ	U	22Feb2010-22Feb2010	23Feb2010	U/1 Days	Local reaction*, Muscle rigidity*, Erythema*, Pyrexia*, Product quality issue*	I
#B0643785A	Italy	RA	13 Months/M	INJ	U	U	26Jan2010	U/Unknown	Local reaction*, Pyrexia*	R

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D0067704A	Germany	MD,RP	6 Months/M	INJ, INJ	U, U	19Apr2010-19Apr2010, 1 Days	09May2010	U/20 Days, U/1 Days	Local swelling*, Erythema*, Vaccination complication*	U
B0601826A	Austria	MD	4 Years/F	INJ	U	15Sep2009-15Sep2009	15Sep2009	U/0 Days	Local swelling*, Injection site erythema*	R
B0673424A	Netherlands	HP,RA	4 Months/M	INJ	.5ML	26Apr2010-26Apr2010	27Apr2010	U/1 Days	Malaise*, Crying*, Pyrexia*	R
#B0650653A	Belgium	MD	5 Months/F	INJ	U	1 Days		U/0 Days	Malaise*, Hypotonia*, Pallor*, Pyrexia*	U
#B0677473A	Switzerland	RA	78 Days/M	INJ	U	04Aug2010-04Aug2010, 03Jul2010-03Jul2010	04Aug2010	U/10 Minutes, U/U	Malaise, Pallor, Hypotonia	R
B0668099A	Netherlands	HP,RA	2 Months/F	INJ	U	18Feb2010-18Feb2010	01Feb2010	U/1 Days	Malaise, Rash, Cough, Nasopharyngitis, Crying	R

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B0647305A	France	LI	8 Months/F	INJ	U	1 Days		U/2 Months	Nodule*, Hypersensitivity*, Pruritus*	N	Firgeron A. et al. Hypersensibility rétardée à l'aluminium des Vaccines: à propos de 3 cas. French magasin of allergology 2010: 50;327-338
B0601837A	Austria	MD	25 Months/M	INJ	U	16Sep2009-16Sep2009	16Sep2009	U/0 Days	Oedema peripheral*	R	
B0673190A	South Africa	HP	18 Months/U	INJ	U	26Aug2010-26Aug2010	26Aug2010	U/0 Days	Oedema peripheral*	R	
B0603715A	France	MD	2 Months/U	INJ	U	01Oct2009-01Oct2009	01Oct2009	U/2 Hours	Oedema peripheral*, Erythema*, Inflammation*	R	
#D0065702A	Germany	MD	2 Years/F	INJ	U	17Dec2009-17Dec2009	18Dec2009	U/1 Days	Oedema peripheral*, Erythema*, Inflammation*, Pain*, Pyrexia*, Abnormal faeces*, Movement disorder*, C-reactive protein increased*, Soft tissue infection*	I	

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#B0635257A	Austria	RA	1 Years/M	INJ	U	18Dec2009-18Dec2009	18Dec2009	U/14 Hours	Oedema peripheral*, Erythema*, Pyrexia*	R
B0602616A	France	MD	2 Months/M	INJ	U	01Jan2009-01Jan2009	01Jan2009	U/Hours	Oedema peripheral*, Induration*, Erythema*, Inflammation*, Skin warm*, Skin discolouration*, Crying*, Erythema*	R
#B0667863A	Poland	MD,RA	17 Months/F	INJ	U	13May2010-13May2010	13May2010	U/0 Days	Oedema peripheral, Oedema peripheral, Injection site oedema	R
#B0639601A	Kenya	HP,RP	Child/U	INJ	U	U		U/0 Days	Oedema peripheral*, Pain in extremity*, Pyrexia*, Restlessness*	U
B0649489A	South Africa	HP	21 Months/M	INJ	.5ML	19Apr2010-19Apr2010	19Apr2010	U/0 Days	Pain*, Erythema*, Injection site nodule*, Induration*, Injection site scab*, Skin warm*, Mobility decreased*, Pain in extremity*, Pyrexia*, Extensive swelling of vaccinated limb*	U

B0664450A	Netherlands	HP,RA	2 Months/F	INJ	.5ML	29Dec2009-29Dec2009	29Dec2009	U/0 Days	Pain, Malaise, Respiration abnormal, Hypotonia, Pyrexia, Somnolence	R
#B0671571A	Latvia	MD,RA	9 Months/M	INJ	U	03Aug2010-03Aug2010	03Aug2010	U/12 Hours	Pyrexia	R
#B0671815A	Poland	MD,RA	24 Months/M	INJ	U	12Aug2010-12Aug2010	13Aug2010	U/24 Hours	Pyrexia	R
#B0679882A	Poland	MD,RA	17 Months/M	INJ	U	30Sep2010-30Sep2010	01Oct2010	U/1 Days	Pyrexia	R
B0615472A	France	MD	3 Months/F	INJ	U	07Dec2009-07Dec2009	11Dec2009	U/4 Days	Pyrexia*	R
#D0066117A	Germany	PH,MD,RA	12 Months/F	INJ	U	12Jan2010-12Jan2010	12Jan2010	U/0 Days	Pyrexia*	R

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#D0067514A	Germany	RA	5 Months/F	INJ	.5ML	04Mar2010-04Mar2010	04Mar2010	U/0 Days	Pyrexia*	R
#B0651488A	Ireland	RA	2 Months/F	INJ	U	14Jan2010-14Jan2010	14Jan2010	U/0 Days	Pyrexia*	R
#B0600330A	Italy	RA	11 Months/F	INJ	U	23Jul2009-23Jul2009	23Jul2009	U/0 Days	Pyrexia*	R
#B0611380A	Italy	RA	3 Months/M	INJ	U	15Sep2009-15Sep2009	15Sep2009	U/0 Days	Pyrexia*	R
#B0630232A	Italy	RA	5 Months/F	INJ	U	03Jun2009-03Jun2009	03Jun2009	U/0 Days	Pyrexia*	R
#B0648936A	Italy	RA	4 Months/F	INJ	U	15Mar2010-15Mar2010	15Mar2010	U/0 Days	Pyrexia*	R

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#B0620045A	Poland	RA	17 Months/U	INJ	U	15Oct2009-15Oct2009	15Oct2009	U/0 Days	Pyrexia*	R
#B0651968A	Poland	RA	3 Months/U	INJ	U	10Mar2010-10Mar2010	11Mar2010	U/1 Days	Pyrexia*	R
#B0656943A	Poland	RA	19 Months/U	INJ	U	17Mar2010-17Mar2010	17Mar2010	U/4 Hours	Pyrexia*	R
#B0659491A	Poland	RA	6 Months/U	INJ	U	24Mar2010-24Mar2010	24Mar2010	U/0 Days	Pyrexia*	R
#B0662668A	Poland	MD,RA	5 Months/U	INJ	U	12May2010-12May2010	12May2010	U/0 Days	Pyrexia*	R
#B0673013A	Spain	RA	6 Years/F	INJ	U	26Aug2010-26Aug2010	27Aug2010	U/1 Days	Pyrexia*	R

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#B0662191A	Sweden	RA	5 Months/M	INJ	U	01Mar2010-01Mar2010	01Mar2010	U/Hours	Pyrexia*	R
D0067375A	Germany	CO,MD,RP	29 Days/M	INJ	U	21Apr2010-21Apr2010	21Apr2010	U/0 Days	Pyrexia*, Agitation*, Fatigue*, Drug administration error	R
#D0068261A	Germany	MD	11 Weeks/M	INJ	.5ML	23Jun2010-23Jun2010	23Jun2010	U/0 Days	Pyrexia*, Apathy*, Crying*, Skin discolouration*, Asthenia*, Fluid intake reduced*	R
D0066791A	Germany	MD,RP	2 Months/M	INJ, INJ	U, U	23Feb2010-23Feb2010, 15Jan2010-15Jan2010	16Jan2010	U/1 Days, U/7 Days	Pyrexia*, Crying*, Restlessness*, Flatulence*, Immune system disorder*, Selective IgA immunodeficiency*, Blood immunoglobulin M decreased*, Diarrhoea*, Ill-defined disorder*	N
#D0066915A	Germany	PH	U/M	INJ	U	17Mar2010-17Mar2010	17Mar2010	U/0 Days	Pyrexia*, Infection*	U

D0069153A	Germany	MD	6 Months/F	INJ	U	17Sep2010-17Sep2010, 24Sep2010-24Sep2010	24Sep2010	U/0 Days, U/U	Pyrexia, Infection, Inappropriate schedule of drug administration	U
B0673318A	France	MD	2 Months/F	INJ	U	02Sep2010-02Sep2010	02Sep2010	U/Same day	Pyrexia, Injection site erythema, Injection site induration, Incorrect storage of drug	R
#B0668396A	Poland	MD,RA	17 Months/F	INJ	U	22Jun2010-22Jun2010	22Jun2010	U/0 Days	Pyrexia*, Injection site oedema*, Injection site erythema*, Injection site swelling*, Injection site induration*, Injection site warmth*, Injection site haematoma*	U
D0065182A	Germany	MD	14 Months/M	INJ	U	30Nov2009-30Nov2009	01Dec2009	U/1 Days	Pyrexia*, Injection site swelling*, Injection site warmth*, Erythema*, Lymphadenopathy*	R
B0663536A	Italy	MD	7 Months/M	INJ	U	1 Days		U/Unknown	Pyrexia, Overdose	U

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#D0068811A	Germany	RA	16 Months/M	INJ	U	1 Days		U/Unknown	Pyrexia, Pain, Gait disturbance, Myositis, Pyrexia, Somnolence	R
D0066362A	Germany	MD	7 Months/U	INJ, INJ, INJ	U, U, U	1 Days, 1 Days, 1 Days		U/Unknown, U/Unknown, U/Unknown	Pyrexia*, Pyrexia*, Pyrexia*, Swelling*	U
D0068423A	Germany	MD,RP	Child/U	INJ	U	1 Days		U/Unknown	Pyrexia, Rash macular	U
D0063314A	Germany	MD,RP	Infant/M	INJ	U	16Oct2009-16Oct2009	16Oct2009	U/0 Days	Pyrexia*, Rash*, Pruritus*	U
D0066173A	Germany	MD	6 Months/M	INJ, INJ	U, U	19Jan2010-19Jan2010, 05Mar2009-05Mar2009	01Jan2009	U/0 Days, U/0 Years	Pyrexia*, Restlessness*, Decreased appetite*, Fluid intake reduced*, Injection site swelling*, Induration*, Pyrexia*	R
#B0646588A	Ireland	RA	6 Months/M	INJ	U	25Mar2010-25Mar2010	25Mar2010	U/0 Days	Pyrexia*, Vomiting*	R

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B0673893A	Sweden	HP	6 Months/F	INJ	U	08Sep2010-08Sep2010	08Sep2010	U/0 Months	Pyrexia, Wrong technique in drug usage process*	U
B0676832A	Italy	MD	Child/M	INJ	U	13Sep2010-13Sep2010	13Sep2010	U/0 Days	Pyrexia*, Wrong technique in drug usage process*	R
#D0064689A	Germany	RA	3 Months/M	INJ	.5ML	04Nov2009-04Nov2009	13Nov2009	U/9 Days	Sudden infant death syndrome*	F
#D0065445A	Germany	MD	3 Months/F	INJ	.5ML	09Dec2009-09Dec2009	10Dec2009	U/1 Days	Sudden infant death syndrome*	F
#D0066068A	Germany	MD,RA,RP	3 Months/M	INJ	.5ML	29Dec2009-29Dec2009	29Dec2009	U/0 Days	Sudden infant death syndrome*	F
#B0601431A	Netherlands	HP,RA	3 Months/F	INJ	U	21Oct2009-21Oct2009	23Oct2009	U/2 Days	Sudden infant death syndrome*	F

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#B0657890A	Australia	HP,RP	2 Months/M	INJ	U	27Apr2010-27Apr2010	27Apr2010	U/12 Hours	Sudden infant death syndrome*, Apnoeic attack*, Pallor*, Oxygen saturation decreased*, Heart rate decreased*	F
#B0639243A	Singapore	MD	7 Weeks/F	INJ	U	01Mar2010-01Mar2010	05Mar2010	U/4 Days	Sudden infant death syndrome*, Asphyxia*	F
#D0067790A	Germany	RA	9 Weeks/M	INJ	.5ML	31Mar2010-31Mar2010	03Apr2010	U/3 Days	Sudden infant death syndrome*, Death*, Apnoea*, Cardiac arrest*, Cardiac arrest*, Loss of consciousness*, Resuscitation*	F
D0063392A	Germany	MD,RP	Infant/M	INJ	U	1 Days		U/Unknown	Swelling*	U
B0643582A	Pakistan	MD	2 Months/F	INJ	U	24Mar2010-24Mar2010	24Mar2010	U/0 Days	Swelling*, Screaming*	R
#D0069205A	Germany	RA	U/M	U	U	U		U/U	Vaccination site abscess sterile	U

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D0068567A	Germany	MD,RP	U/U	INJ	U	1 Days		U/Unknown	Vaccination site granuloma	U
B0635714A	Austria	MD,RA	21 Months/M	INJ	U	19Feb2010-19Feb2010	19Feb2010	U/0 Days	Vaccination site induration*, Muscle rigidity*, Vaccination site swelling*, Vaccination site pain*, Vaccination site erythema*, Product quality issue*	I
B0606002A	France	MD,RP	Infant/U	INJ	U	03Nov2009-03Nov2009	01Nov2009	U/0 Months	Vaccination site oedema*, Injection site induration*	R
B0606006A	France	MD,RP	Infant/U	INJ	U	06Nov2009-06Nov2009	01Nov2009	U/0 Months	Vaccination site oedema*, Injection site induration*	R
B0606007A	France	MD,RP	Infant/U	INJ	U	06Nov2009-06Nov2009	01Nov2009	U/0 Months	Vaccination site oedema*, Injection site induration*	R

B0635705A	Austria	MD,RA	20 Months/M	INJ	U	19Feb2010-19Feb2010	19Feb2010	U/0 Days	Vaccination site reaction*, Muscle rigidity*, Erythema*, Injection site pain*, Product quality issue*	I	
Hepatobiliary disorders											
#B0636132A	Greece	LI	70 Days/M	INJ	U	1 Days		U/1 Days	Jaundice*, Hepatitis B surface antigen positive*	R	Elpis M et al. Transient hepatitis B surface antigen circulation after Infanrix hexa: a case report and view of the literature.EU J Pediatr Springer 2010; published on line.
Immune system disorders											
#B0664784A	Italy	MD,RA	4 Months/M	INJ	U	02Jul2010-02Jul2010	02Jul2010	U/1 Hours	Anaphylactic reaction*, Agitation, Heart rate increased, Conjunctival hyperaemia, Urticaria, Crying	R	
#B0663295A	Thailand	MD	6 Months/M	INJ	.5ML	26Jun2010-26Jun2010	26Jun2010	U/20 Minutes	Anaphylactic reaction*, Haematochezia*, Intestinal obstruction*, Intussusception*, Somnolence*, Pallor*, Vomiting*, Pulse abnormal*, Capillary disorder*, Vomiting*	R	BCWG level 1

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#D0068761A	Germany	MD,RA,RP	30 Months/F	INJ	U	24Aug2010-24Aug2010	24Aug2010	U/30 Minutes	Anaphylactic reaction, Hypersensitivity, Dyspnoea, Urticaria, Angioedema, Bronchospasm, Stridor	R
#B0652232A	Spain	RA	2 Years/F	INJ	U	16Feb2009-16Feb2009	16Feb2009	U/0 Days	Anaphylactic shock*	R
#D0066052A	Germany	MD,RA	3 Months/M	INJ	U	28Dec2009-28Dec2009	28Dec2009	U/0 Hours	Hypersensitivity*, Injection site erythema*, Injection site swelling*, Agitation*, Tachycardia*, Inflammation*, Rash*	R
D0067601A	Germany	CO,MD	2 Months/F	INJ	U	06May2010-06May2010	06May2010	U/0 Days	Hypersensitivity*, Pain*, Crying*, Injection site erythema*	R
#D0068074A	Germany	HP,RA	14 Months/M	INJ	U	17Jun2010-17Jun2010	18Jun2010	U/1 Days	Hypersensitivity*, Rash*	R
B0626593A	Philippines	MD	0 Years/M	INJ	U	01Nov2009-01Nov2009	01Nov2009	U/12 Hours	Hypersensitivity*, Rash maculo-papular*	R

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#B0643014A	Austria	RA	1 Years/F	INJ, INJ	U, U	01Feb2010-01Feb2010, 01Jan2009-01Jan2009		U/18 Hours, U/Unknown	Type III immune complex mediated reaction*, Oedema peripheral*, Feeling hot*, Local reaction*, Swelling*	R
B0601843A	France	MD	18 Months/M	INJ	U	1 Days		U/2 Days	Type III immune complex mediated reaction*, Urticaria*, Rash macular*, Prurigo*	R
Infections and infestations										
#D0066818A	Germany	MD,RP	4 Months/F	INJ	U	26Jan2010-26Jan2010	23Feb2010	U/28 Days	Abscess*, Incision site abscess*	U
B0622903A	Netherlands	RA	14 Months/M	IM	.5ML	25Feb2009-25Feb2009		U/5 Weeks	Abscess*, Inflammation*, Vomiting*, Pyrexia*	R
#B0647618A	Italy	RA	12 Months/F	INJ	U	15Mar2010-15Mar2010	18Mar2010	U/3 Days	Acute tonsillitis*, Pyrexia*	R

#B0599577A	Romania	MD,RP	10 Weeks/F	INJ	U	07Oct2009-07Oct2009	09Oct2009	U/2 Days	Bronchiolitis*, Productive cough*, Cough*, General physical health deterioration*, Infection*	R
#B0677146A	Taiwan, ROC	MD	18 Months/F	INJ	U	14Sep2010-14Sep2010, 26May2009-26May2009, 25Aug2009-25Aug2009	16Sep2010	U/2 Days, U/U, U/U	Cellulitis	R
#D0067880A	Germany	RA	22 Months/M	INJ	.5ML	20May2010-20May2010, 28Aug2008-28Aug2008, 25Sep2008-25Sep2008, 23Oct2008-23Oct2008	22May2010	U/2 Days, U/U, U/U, U/U	Cellulitis*	R
#B0661015A	Austria	MD,RA	2 Years/M	INJ	U	10Jun2010-10Jun2010	10Jun2010	U/0 Days	Cellulitis*, Erythema, Swelling	N
#D0069118A	Germany	HP,RA	3 Years/F	INJ	U	28Sep2010-28Sep2010	30Sep2010	U/2 Days	Cellulitis, Injection site erythema, Injection site swelling, Injection site warmth, Injection site induration	N
#B0661012A	Austria	MD,RA	2 Years/F	INJ	U	09Jun2010-09Jun2010	11Jun2010	U/2 Days	Cellulitis*, Injection site erythema, Pyrexia, Injection site swelling	N

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#B0661014A	Austria	MD,RA	23 Months/F	INJ	U	10Jun2010-10Jun2010	11Jun2010	U/1 Days	Cellulitis*, Oedema peripheral, Erythema	N
D0068185A	Germany	MD,RP	Child/U	INJ	U	1 Days		U/Unknown	Croup infectious*, Rash*	U
D0068538A	Germany	MD,RP	Child/U	INJ	U	1 Days		U/Unknown	Croup infectious*, Rash*	U
#B0669436A	France	RA	19 Weeks/M	INJ	U	20Jul2010-20Jul2010	24Jul2010	U/4 Days	Eczema herpeticum*, Disease recurrence*, Eosinophilia*, C-reactive protein increased*, Blood immunoglobulin E increased*, Allergy test positive*	I
#B0675363A	Australia	CO,HP	3 Years/M	INJ, INJ, INJ	U, U, U	14Aug2007-14Aug2007, 15Oct2007-15Oct2007, 27Dec2007-27Dec2007	12Sep2010	U/3 Years, U/3 Years, U/3 Years	Epiglottitis, Haemophilus infection, Vaccination failure	R

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#D0064684A	Germany	RA	3 Years/F	INJ	U	05Jan2007-05Jan2007, 03Nov2009-03Nov2009	03Nov2009	U/0 Days, U/U	Erysipelas*, Vaccination site infection*, Injection site swelling*, Injection site erythema*, Pyrexia*, Injection site warmth*	R
#D0067444A	Germany	MD	3 Months/M	INJ, INJ, INJ, INJ	U, U, U, U	23Apr2009-23Apr2009, 08Jun2009-08Jun2009, 13Jul2009-13Jul2009, 12Mar2010-12Mar2010	23Apr2009	U/0 Days, U/0 Days, U/0 Days, U/0 Years	Gastroenteritis*, Pyrexia*, Pyrexia*, Pyrexia*, Pyrexia*	R
#D0068392A	Germany	RA	3 Months/M	INJ	.5ML	19Apr2010-19Apr2010	27Apr2010	U/8 Days	Gastroenteritis rotavirus*, Gastroenteritis viral*, Enteritis infectious*, Rotavirus test positive*, Circadian rhythm sleep disorder*, Vomiting*, Apathy*, Crying*, Decreased appetite*	R
#D0067065A	Germany	MD	3 Months/F	INJ	U	24Mar2010-24Mar2010	27Mar2010	U/3 Days	Gastroenteritis rotavirus*, Vomiting*, Pyrexia*, Dehydration*, Diarrhoea*	I
#B0680271A	Italy	RA	10 Months/F	INJ	U	13Oct2010-13Oct2010	13Oct2010	U/0 Days	Gastroenteritis, Vomiting	R

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B0671539A	France	MD	5 Months/F	INJ	U	01Jun2010-01Jun2010	15Jul2010	U/1 Months	Gianotti-Crosti syndrome*, Rash*	N
#D0068853A	Germany	MD	14 Months/M	INJ	U	19Jul2010-19Jul2010	10Aug2010	U/22 Days	Gianotti-Crosti syndrome*, Skin lesion excision*	S
#B0653461A	Australia	HP	3 Years/U	INJ, INJ, INJ	U, U, U	03Mar2007-03Mar2007, 29May2007-29May2007, 02Oct2007-02Oct2007		U/Unknown, U/Unknown, U/Unknown	Haemophilus infection*, Vaccination failure*	R
#B0653464A	Australia	HP	7 Months/F	INJ, INJ, INJ	U, U, U	24Nov2009-24Nov2009, 01Feb2010-01Feb2010, 30Mar2010-30Mar2010	05May2010	U/5 Months, U/93 Days, U/36 Days	Haemophilus infection*, Vaccination failure*	R
#B0679172A	Peru	MD	14 Years/F	INJ, INJ	U, U	02Oct2006-02Oct2006, 02May2008-02May2008	20Aug2010	U/4 Years, U/2 Years	Hepatitis viral, Transaminases increased, Vaccination failure	I
#B0661002A	France	RA	7 Months/M	INJ	U	04Jan2010-04Jan2010	18Feb2010	U/45 Days	Injection site abscess*	R

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B0607303A	South Africa	PH	6 Weeks/F	INJ	U	23Sep2009-23Sep2009		U/Unknown	Injection site abscess*	U
#D0068798C	Germany	MD	20 Months/M	INJ	U	01Aug2010-01Aug2010	01Jan2010	U/0 Years	Injection site abscess*, Incision site abscess*	S
#D0068798B	Germany	MD	4 Months/M	INJ	U	01Apr2009-01Apr2009	01Jan2009	U/Unknown	Injection site abscess*, Incision site abscess*, Injection site induration*, Injection site erythema*, Injection site swelling*, Injection site nodule*	U
#D0068798A	Germany	MD	3 Months/M	INJ	U	01Mar2009-01Mar2009	01Jan2009	U/Unknown	Injection site abscess*, Incision site abscess*, Injection site reaction*, Injection site induration*, Injection site erythema*, Injection site swelling*, Injection site nodule*	U
D0067672A	Germany	MD	2 Years/U	INJ, INJ	U, U	23Apr2010-23Apr2010, 01Jan2008-01Jan2008	01Nov2008	U/23 Days, U/U	Injection site abscess*, Injection site abscess*	U

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#B0680202A	Czech Republic	MD	6 Months/M	INJ	U	03Jun2010-03Jun2010	01Jun2010	U/Days	Injection site abscess*, Injection site haematoma*	I
B0648147A	Kenya	MD	6 Weeks/M	INJ	U	05Jun2009-05Jun2009	05Jun2009	U/0 Days	Injection site abscess*, Insomnia, Pyrexia*, Crying*, Insomnia*	R
#B0600650A	South Africa	HP	19 Months/M	INJ	U	20Aug2009-20Aug2009	01Jan2009	U/1 Months	Injection site abscess*, Pain in extremity*	R
#B0675146A	France	RA	17 Months/M	INJ	U	01Jul2010-01Jul2010	01Jul2010	U/Same day	Injection site cellulitis*, Injection site oedema*, Blister*, Injection site erythema*, Injection site pain*, Injection site induration*, Injection site vesicles*, Lymphadenopathy*, Ecchymosis*, C-reactive protein increased*, Leukocytosis*, Skin chapped*	R
#B0651993A	Spain	RA	18 Months/M	INJ	U	02Dec2008-02Dec2008	03Dec2008	U/1 Days	Meningitis aseptic*	R

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#B0677923A	Belgium	MD	2 Years/M	INJ	U	U	01Jan2010	U/Unknown	Meningitis haemophilus, Osteomyelitis, Vaccination failure	U
B0650143A	Austria	PH	Infant/U	INJ	U	1 Days, 1 Days, 1 Days		U/Unknown, U/U, U/U	Pertussis*	W
D0067933A	Germany	MD	4 Months/F	INJ	U	21Apr2010-21Apr2010	17May2010	U/26 Days	Pertussis*	R
#B0668296A	Italy	MD,RA	2 Months/F	INJ	U	24Jun2010-24Jun2010	30Jun2010	U/6 Days	Pertussis, Apnoeic attack*, Cough*, Gastrooesophageal reflux disease, Inflammation	I
D0068073A	Germany	MD,RP	8 Months/F	INJ, INJ	U, U	23Sep2009-23Sep2009, 29Oct2009-29Oct2009	01Apr2010	U/6 Months, U/5 Months	Pertussis*, Cough*	U
D0067293A	Germany	MD,RP	8 Months/M	INJ, INJ	U, U	20Oct2009-20Oct2009, 19Nov2009-19Nov2009	25Mar2010	U/5 Months, U/4 Months	Pertussis*, Cough*, Bronchitis*	N

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#B0603739A	France	OT,HP,MD	17 Months/M	INJ	U	26Aug2009-26Aug2009	20Sep2009	U/25 Days	Pertussis*, Cough*, Hypochromasia*, Leukocytosis*, Regurgitation*, Vaccination failure*	R
#B0675234A	France	MD,RP	12 Months/M	INJ, INJ	U, U	01Jan2009-01Jan2009, 01Jan2009-01Jan2009	01Jul2010	U/10 Months, U/8 Months	Pertussis*, Cough*, Salivary hypersecretion*, Pertussis*, Vaccination failure	R
#D0069119A	Germany	RA	7 Years/F	INJ, INJ, INJ, INJ	U, U, U, U	30Apr2003-30Apr2003, 30Apr2003-30Apr2003, 28May2003-28May2003, 09Jul2003-09Jul2003	01Jan2010	U/7 Years, U/7 Years, U/7 Years, U/7 Years	Pertussis, Cough, Sneezing, Vaccination failure	U
#D0065887A	Germany	RA	5 Years/F	INJ, INJ, INJ, INJ	U, U, U, U	01Sep2004-01Sep2004, 18Oct2004-18Oct2004, 07Dec2004-07Dec2004, 1 Days	26Oct2009	U/5 Years, U/5 Years, U/4 Years, U/Unknown	Pertussis*, Cough*, Vaccination failure*	R
#D0068650A	Germany	PH	Child/U	INJ	U	1 Days		U/Unknown	Pertussis, Vaccination failure	U
#D0068825A	Germany	RA	10 Years/M	INJ	U	10May2002-10May2002	16Aug2010	U/8 Years	Pertussis, Vaccination failure	U

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#D0066535A	Germany	MD,RP	5 Years/F	INJ, INJ, INJ, INJ	U, U, U, U	18Jan2006-18Jan2006, 16Feb2006-16Feb2006, 16Mar2006-16Mar2006, 25Sep2006-25Sep2006	04Feb2010	U/4 Years, U/3 Years, U/3 Years, U/3 Years	Pertussis*, Vaccination failure*	I	
#D0067934A	Germany	MD	14 Months/F	INJ	U	06May2010-06May2010	02Jun2010	U/27 Days	Pertussis*, Vaccination failure*	R	
#B0674120A	Ireland	LI	1 Years/U	INJ	U	1 Days	01Jan2010	U/Unknown	Pertussis*, Vaccination failure*	U	Barret S et al. Pertussis outbreak in northwest Ireland, January- June 2010. Rapid Communication Eurovigilance org: 1-5
#B0675100A	Ireland	LI	1 Years/U	INJ	U	1 Days	01Jan2010	U/Unknown	Pertussis*, Vaccination failure*	U	Barret S et al. Pertussis outbreak in northwest Ireland, January- June 2010. Rapid Communication Eurovigilance org: 1-5

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#B0675102A	Ireland	LI	1 Years/U	INJ	U	1 Days	01Jan2010	U/Unknown	Pertussis*, Vaccination failure*	U	Barret S et al. Pertussis outbreak in northwest Ireland, January- June 2010. Rapid Communication Eurovigilance org: 1-5
#B0675103A	Ireland	LI	2 Years/U	INJ	U	1 Days	01Jan2010	U/Unknown	Pertussis*, Vaccination failure*	U	Barret S et al. Pertussis outbreak in northwest Ireland, January- June 2010. Rapid Communication Eurovigilance org: 1-5
#B0675104A	Ireland	LI	2 Years/U	INJ	U	1 Days	01Jan2010	U/Unknown	Pertussis*, Vaccination failure*	U	Barret S et al. Pertussis outbreak in northwest Ireland, January- June 2010. Rapid Communication Eurovigilance org: 1-5
#D0063484A	Germany	MD,RP	Child/F	INJ, INJ, INJ, INJ	U, U, U, U	08Nov2006-08Nov2006, 14Dec2006-14Dec2006, 13Mar2007-13Mar2007, 14Nov2007-14Nov2007	13Mar2007	U/Unknown, U/Unknown, U/Unknown, U/Unknown	Pertussis*, Vaccination failure*, Inappropriate schedule of drug administration	R	

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#D0063511A	Germany	MD,RP	Child/M	INJ, INJ, INJ, INJ	U, U, U, U	13Jul2007-13Jul2007, 08Aug2007-08Aug2007, 26Sep2007-26Sep2007, 28May2008-28May2008		U/Unknown, U/Unknown, U/Unknown, U/Unknown	Pertussis*, Vaccination failure*, Inappropriate schedule of drug administration	R
#D0063525A	Germany	MD,RP	Child/F	INJ, INJ, INJ, INJ	U, U, U, U	28Sep2005-28Sep2005, 15Nov2005-15Nov2005, 23Feb2006-23Feb2006, 18Jul2006-18Jul2006	23Feb2006	U/Unknown, U/Unknown, U/Unknown, U/Unknown	Pertussis*, Vaccination failure*, Inappropriate schedule of drug administration	R
#B0605675A	Poland	RA	5 Months/U	INJ	U	07Oct2009-07Oct2009	07Oct2009	U/0 Hours	Pneumonia*, Dyspnoea*, Urticaria papular*, Rash macular*, Hypersensitivity*	U
#B0660020A	Netherlands	RA	11 Months/F	INJ	U	03Feb2010-03Feb2010	03Feb2010	U/2 Hours	Pneumonia*, Loss of consciousness*, Gaze palsy*, Convulsion*, Nasopharyngitis*, Drooling*, Pallor*, Pyrexia*	R
D0067406A	Germany	CO,MD	4 Months/F	INJ	U	14Apr2010-14Apr2010	15Apr2010	U/1 Days	Rash pustular*, Feeling hot*, Rash macular*, Generalised erythema*	R
#B0624563A	Philippines	MD	2 Months/M	INJ	.5ML	08Dec2009-08Dec2009	10Dec2009	U/48 Hours	Urinary tract infection*, Pyrexia*, White blood cell count increased*	R

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#D0066615A	Germany	MD	Infant/M	INJ	U	08Sep2009-08Sep2009	01Jan2010	U/Unknown	Vaccination site abscess*	R
#D0068928A	Germany	RA	4 Months/F	INJ	U	03Jun2010-03Jun2010	01Jun2010	U/Unknown	Vaccination site abscess, Incision site abscess, Staphylococcus test positive	S
#B0671537A	Italy	MD,RA	13 Months/M	INJ	U	26May2010-26May2010	26May2010	U/0 Days	Viral infection, Urticaria, Urticaria, Oedema peripheral, Pyrexia*	R
Injury, poisoning and procedural complications										
B0636577A	France	PH	3 Months/U	INJ	U	25Feb2010-25Feb2010	25Feb2010	U/See text	Accidental overdose	X
D0066019A	Germany	CO,MD	5 Months/F	INJ	U	13Jan2010-13Jan2010	13Jan2010	U/0 Days	Accidental overdose	X

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B0653007A	Australia	MD	6 Months/U	INJ	U	12May2010-12May2010	12May2010	U/During	Accidental overdose*	X
B0647962A	France	MD,RP	Infant/U	INJ	U	1 Days		U/See text	Drug administered at inappropriate site	X
B0673344A	Czech Republic	MD	17 Months/M	INJ	.5ML	01Jul2009-01Jul2009, 03Aug2009-03Aug2009, 19Oct2009-19Oct2009, 24Jun2010-24Jun2010, 02Sep2010-02Sep2010	02Sep2010	U/See text, U/U, U/U, U/U, U/U	Drug administration error	X
B0677348A	France	PH	6 Weeks/U	INJ	U	14Aug2008-14Aug2008	14Aug2008	U/U	Drug administration error	X
B0677522A	France	MD	4 Weeks/F	INJ	U	09Aug2010-09Aug2010	09Aug2010	U/See text	Drug administration error	X
D0066397A	Germany	MD,RP	10 Months/M	INJ	U	04Feb2010-04Feb2010	04Feb2009	U/0 Days	Drug administration error	X

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D0066616A	Germany	PH	4 Weeks/F	INJ	U	26Feb2010-26Feb2010	26Feb2010	U/0 Days	Drug administration error	X
D0068584A	Germany	MD	2 Years/M	INJ	U	29Oct2009-29Oct2009, 06Feb2008-06Feb2008, 07Mar2008-07Mar2008, 07May2008-07May2008, 25Jun2009-25Jun2009	29Oct2009	U/0 Days, U/U, U/U, U/U, U/U	Drug administration error	X
D0068632A	Germany	MD,RP	14 Years/F	INJ	U	1 Days		U/0 Days	Drug administration error	X
D0068803A	Germany	MD	6 Weeks/M	INJ	U	07Sep2010-07Sep2010	07Sep2010	U/0 Days	Drug administration error	X
B0657241A	Poland	MD	5 Years/U	INJ	U	1 Days		U/During	Drug administration error*	X
B0647495A	South Africa	HP	4 Months/F	INJ	U	12Apr2010-12Apr2010, 1 Days, 1 Days, 1 Days	12Apr2010	U/See text, U/U, U/U, U/U	Drug administration error*	X

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B0680034A	France	PH	7 Years/M	INJ	U	15Oct2010-15Oct2010	15Oct2010	U/See text	Drug dispensing error, Wrong drug administered	X
B0680035A	France	PH	7 Years/F	INJ	U	15Oct2010-15Oct2010	15Oct2010	U/See text	Drug dispensing error, Wrong drug administered	X
B0606306A	France	MD	28 Years/F	INJ	U	13Nov2009-13Nov2009	13Nov2009	U/See text	Drug exposure during pregnancy, Live birth, Inappropriate schedule of drug administration	X
B0621683A	Brazil	MD	6 Months/M	INJ	.5ML	01Nov2009-01Nov2009	01Nov2009	U/During	Expired drug administered*	R
B0659529A	Ireland	MD	2 Months/U	INJ	U	02Jun2010-02Jun2010	02Jun2010	U/During	Expired drug administered*	X
B0673657A	Ireland	HP	Infant/U	INJ	U	06May2010-06May2010	06May2010	U/During	Expired drug administered*	X

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B0649146A	Malta	MD	2 Months/M	INJ	.5ML	21Apr2010-21Apr2010	21Apr2010	U/During	Expired drug administered*	X
B0661316A	Tanzania, United Republic of	MD	3 Months/M	INJ	U	01Jun2010-01Jun2010, 01May2010-01May2010	01Jun2010	U/During, U/U	Expired drug administered*	X
B0662215A	Turkey	MD	2 Months/M	INJ	U	21May2010-21May2010	21May2010	U/During	Expired drug administered*	X
B0669502A	Czech Republic	HP	6 Months/F	INJ	U	10Aug2010-10Aug2010	10Aug2010	U/During	Inappropriate schedule of drug administration	X
B0625323A	France	MD	3 Months/M	INJ	U	07Jan2010-07Jan2010	07Jan2010	U/See text	Inappropriate schedule of drug administration	X
B0629503A	France	MD	5 Months/F	INJ	U	23Jan2010-23Jan2010	23Jan2010	U/See text	Inappropriate schedule of drug administration	X

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B0629550A	France	MD	7 Weeks/M	IM	U	26Jan2010-26Jan2010	26Jan2010	U/See text	Inappropriate schedule of drug administration	X
B0629551A	France	MD	6 Years/F	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/See text	Inappropriate schedule of drug administration	X
B0629553A	France	OT,MD	3 Months/F	INJ	U	17Mar2009-17Mar2009, 18Feb2009-18Feb2009	17Mar2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0630830A	France	OT,MD	1 Months/M	INJ	U	06Dec2008-06Dec2008	06Dec2008	U/See text	Inappropriate schedule of drug administration	X
B0630832A	France	OT,MD	1 Months/F	INJ	U	24Oct2008-24Oct2008	24Sep2008	U/See text	Inappropriate schedule of drug administration	X
B0630833A	France	OT,MD	1 Months/F	INJ	U	27Jan2009-27Jan2009	27Jan2009	U/See text	Inappropriate schedule of drug administration	X

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B0630890A	France	OT,MD	5 Months/M	INJ	U	13May2008-13May2008	13May2008	U/See text	Inappropriate schedule of drug administration	X
B0630895A	France	OT,MD	1 Months/M	INJ	U	04Dec2008-04Dec2008	04Dec2008	U/See text	Inappropriate schedule of drug administration	X
B0630900A	France	OT,MD	1 Months/F	INJ	U	02Feb2009-02Feb2009	02Feb2009	U/See text	Inappropriate schedule of drug administration	X
B0630903A	France	OT,MD	7 Weeks/M	INJ	U	20Oct2008-20Oct2008	20Oct2008	U/See text	Inappropriate schedule of drug administration	X
B0630911A	France	OT,MD	7 Weeks/F	INJ	U	01Dec2008-01Dec2008	01Dec2008	U/See text	Inappropriate schedule of drug administration	X
B0630974A	France	OT,MD	7 Weeks/F	INJ	U	09Jan2009-09Jan2009	09Jan2009	U/See text	Inappropriate schedule of drug administration	X

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B0631421A	France	OT,MD	4 Months/M	INJ	U	13Mar2009-13Mar2009, 15Jan2009-15Jan2009	13Mar2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0631424A	France	OT,MD	4 Months/F	INJ	U	21Apr2009-21Apr2009, 09Feb2009-09Feb2009	21Apr2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0631426A	France	OT,MD	3 Months/F	INJ	U	17Dec2008-17Dec2008, 21Oct2008-21Oct2008	17Dec2008	U/See text, U/U	Inappropriate schedule of drug administration	X
B0631428A	France	OT,MD	7 Weeks/F	INJ	U	23Sep2008-23Sep2008	23Sep2008	U/See text	Inappropriate schedule of drug administration	X
B0632116A	France	OT,MD	3 Months/M	INJ	U	22Dec2008-22Dec2008, 26Nov2008-26Nov2008	22Dec2008	U/See text, U/U	Inappropriate schedule of drug administration	X
B0632441A	France	OT,MD	3 Months/M	INJ	U	28Jan2009-28Jan2009	28Jan2009	U/See text	Inappropriate schedule of drug administration	X

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B0632598A	France	OT,MD	4 Months/M	INJ	U	13Jan2008-13Jan2008	13Jan2008	U/See text	Inappropriate schedule of drug administration	X
B0632930A	France	OT,MD	5 Months/M	INJ	U	13Feb2009-13Feb2009, 19Apr2009-19Apr2009	19Apr2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0633060A	France	OT,MD	3 Months/F	INJ	U	14Apr2009-14Apr2009, 17Feb2009-17Feb2009	14Apr2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0633276A	France	OT,MD	4 Months/M	INJ	U	03Mar2009-03Mar2009, 05Jan2009-05Jan2009	03Mar2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0635080A	France	MD	4 Weeks/M	INJ	U	19Jan2010-19Jan2010	19Jan2010	U/See text	Inappropriate schedule of drug administration	X
B0635357A	France	OT,MD	7 Weeks/F	INJ	U	27Jan2009-27Jan2009	27Jan2009	U/See text	Inappropriate schedule of drug administration	X

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B0635394A	France	OT,MD	5 Months/M	INJ	U	01Apr2009-01Apr2009, 22Jan2009-22Jan2009	01Apr2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0635395A	France	OT,MD	4 Months/F	INJ	U	06Apr2009-06Apr2009, 06Feb2009-06Feb2009	06Apr2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0635397A	France	OT,MD	1 Years/M	INJ	U	13Feb2009-13Feb2009	13Feb2009	U/See text	Inappropriate schedule of drug administration	X
B0635399A	France	OT,MD	1 Years/M	INJ	U	13Feb2009-13Feb2009	13Feb2009	U/See text	Inappropriate schedule of drug administration	X
B0635410A	France	OT,MD	7 Weeks/M	INJ	U	16Oct2008-16Oct2008	16Oct2008	U/See text	Inappropriate schedule of drug administration	X
B0635440A	France	OT,MD	7 Weeks/F	INJ	U	03Feb2009-03Feb2009	03Feb2009	U/See text	Inappropriate schedule of drug administration	X

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B0635702A	France	OT,MD	3 Months/M	INJ	U	28Apr2009-28Apr2009, 03Mar2009-03Mar2009	28Apr2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0635746A	France	OT,MD	6 Days/M	INJ	U	15Dec2008-15Dec2008	15Dec2008	U/See text	Inappropriate schedule of drug administration	X
B0635963A	France	OT,MD	3 Months/M	INJ	U	09Mar2009-09Mar2009	09Mar2009	U/See text	Inappropriate schedule of drug administration	X
B0636324A	France	OT,MD	4 Months/F	INJ	U	09Apr2009-09Apr2009, 09Feb2009-09Feb2009	09Apr2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0636330A	France	OT,MD	4 Months/M	INJ	U	07Jan2009-07Jan2009, 08Nov2008-08Nov2008	07Jan2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0636412A	France	OT,MD	6 Weeks/M	INJ	U	17Jan2009-17Jan2009	17Jan2009	U/See text	Inappropriate schedule of drug administration	X

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B0636424A	France	OT,MD	6 Weeks/M	INJ	U	19Jan2009-19Jan2009	19Jan2009	U/See text	Inappropriate schedule of drug administration	X
B0638107A	France	OT,MD	16 Months/M	INJ	U	16Apr2009-16Apr2009	16Apr2009	U/See text	Inappropriate schedule of drug administration	X
B0638119A	France	OT,MD	17 Months/F	INJ	U	03Jun2009-03Jun2009	03Jun2009	U/See text	Inappropriate schedule of drug administration	X
B0638124A	France	OT,MD	3 Months/M	INJ	U	02Apr2009-02Apr2009	02Apr2009	U/See text	Inappropriate schedule of drug administration	X
B0638231A	France	OT,MD	2 Months/M	INJ	U	21Apr2009-21Apr2009, 26Feb2009-26Feb2009	25Mar2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0638232A	France	OT,MD	7 Weeks/F	INJ	U	13Jan2009-13Jan2009	13Jan2009	U/See text	Inappropriate schedule of drug administration	X

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B0640120A	France	OT,MD	7 Weeks/M	INJ	U	26Feb2009-26Feb2009	26Feb2009	U/See text	Inappropriate schedule of drug administration	X
B0640129A	France	OT,MD	7 Weeks/F	INJ	U	13Mar2009-13Mar2009	13Mar2009	U/See text	Inappropriate schedule of drug administration	X
B0640132A	France	OT,MD	7 Weeks/M	INJ	U	11Mar2009-11Mar2009	11Mar2009	U/See text	Inappropriate schedule of drug administration	X
B0640141A	France	OT,MD	7 Weeks/F	INJ	U	12Jan2009-12Jan2009	12Jan2009	U/See text	Inappropriate schedule of drug administration	X
B0640572A	France	OT,MD	7 Weeks/M	INJ	U	28Feb2009-28Feb2009	28Feb2009	U/See text	Inappropriate schedule of drug administration	X
B0640592A	France	OT,MD	1 Years/M	INJ	U	12Jan2009-12Jan2009	12Jan2009	U/See text	Inappropriate schedule of drug administration	X

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B0640598A	France	OT,MD	3 Months/M	INJ	U	23Apr2009-23Apr2009, 26Feb2009-26Feb2009	23Apr2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0640613A	France	OT,MD	7 Weeks/F	INJ	U	14Jan2009-14Jan2009	14Jan2009	U/See text	Inappropriate schedule of drug administration	X
B0640615A	France	OT,MD	4 Months/F	INJ	U	19May2009-19May2009, 19Mar2009-19Mar2009	19May2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0640647A	France	OT,MD	3 Months/F	INJ	U	04Mar2009-04Mar2009, 09Jan2009-09Jan2009	05Feb2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0640650A	France	OT,MD	1 Weeks/M	INJ	U	16Jan2009-16Jan2009	16Jan2009	U/See text	Inappropriate schedule of drug administration	X
B0640652A	France	OT,MD	4 Months/M	INJ	U	02Mar2009-02Mar2009, 05Jan2009-05Jan2009	02Mar2009	U/See text, U/U	Inappropriate schedule of drug administration	X

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B0641205A	France	OT,MD	4 Months/M	INJ	U	19Feb2009-19Feb2009, 19Dec2008-19Dec2008	19Feb2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0641206A	France	OT,MD	4 Weeks/F	INJ	U	22Jan2009-22Jan2009	22Jan2009	U/See text	Inappropriate schedule of drug administration	X
B0641773A	France	OT,MD	3 Months/F	INJ	U	09Sep2008-09Sep2008, 26Jul2008-26Jul2008	09Sep2008	U/See text, U/U	Inappropriate schedule of drug administration	X
B0641779A	France	OT,MD	4 Months/M	INJ	U	04May2009-04May2009, 09Mar2009-09Mar2009	04May2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0641803A	France	OT,MD	3 Months/F	INJ	U	03Mar2009-03Mar2009, 05Jan2009-05Jan2009	03Mar2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0642141A	France	OT,MD	6 Weeks/F	INJ	U	02Feb2009-02Feb2009	02Feb2009	U/See text	Inappropriate schedule of drug administration	X

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B0642168A	France	OT,MD	4 Months/F	INJ	U	12May2009-12May2009, 20Mar2009-20Mar2009	12May2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0642425A	France	OT,MD	4 Weeks/F	INJ	U	22Jan2009-22Jan2009	22Jan2009	U/See text	Inappropriate schedule of drug administration	X
B0642431A	France	OT,MD	7 Weeks/F	INJ	U	23Mar2009-23Mar2009	23Mar2009	U/See text	Inappropriate schedule of drug administration	X
B0642435A	France	OT,MD	3 Months/F	INJ	U	03Mar2009-03Mar2009, 08Jan2009-08Jan2009	03Mar2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0642436A	France	OT,MD	3 Months/F	INJ	U	06Apr2009-06Apr2009, 05Feb2009-05Feb2009	06Apr2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0642438A	France	OT,MD	7 Weeks/M	INJ	U	09Sep2008-09Sep2008	09Sep2008	U/See text	Inappropriate schedule of drug administration	X

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B0642444A	France	OT,MD	3 Months/F	INJ	U	21Apr2009-21Apr2009, 24Feb2009-24Feb2009	21Apr2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0642449A	France	OT,MD	4 Months/M	INJ	U	08Apr2009-08Apr2009, 06Feb2009-06Feb2009	08Apr2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0642456A	France	OT,MD	4 Months/F	INJ	U	14Apr2009-14Apr2009, 16Feb2009-16Feb2009	14Apr2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0642461A	France	OT,MD	7 Weeks/M	INJ	U	12Jan2009-12Jan2009	12Jan2009	U/See text	Inappropriate schedule of drug administration	X
B0642962A	France	OT,MD	18 Weeks/F	INJ	U	05May2009-05May2009, 05Mar2009-05Mar2009	05May2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0642967A	France	OT,MD	4 Months/F	INJ	U	06Mar2009-06Mar2009, 05Jan2009-05Jan2009	06Mar2009	U/See text, U/U	Inappropriate schedule of drug administration	X

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B0645392A	France	MD,RP	3 Months/F	INJ	U	18Feb2010-18Feb2010	18Feb2010	U/See text	Inappropriate schedule of drug administration	X
B0645539A	France	OT,MD	2 Months/M	INJ	U	06May2008-06May2008	06May2008	U/See text	Inappropriate schedule of drug administration	X
B0645542A	France	OT,MD	7 Weeks/M	INJ	U	16Dec2008-16Dec2008	16Dec2008	U/See text	Inappropriate schedule of drug administration	X
B0645571A	France	OT,MD	3 Months/M	INJ	U	02May2008-02May2008	02May2008	U/See text	Inappropriate schedule of drug administration	X
B0645576A	France	OT,MD	7 Weeks/M	INJ	U	17Jan2009-17Jan2009	17Jan2009	U/10 Days	Inappropriate schedule of drug administration	X
B0645581A	France	OT,MD	3 Months/M	INJ	U	02Mar2009-02Mar2009, 06Feb2009-06Feb2009	02Mar2009	U/U, U/U	Inappropriate schedule of drug administration	X

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B0645584A	France	OT,MD	4 Months/M	INJ	U	10Apr2009-10Apr2009, 06May2009-06May2009	06May2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0645587A	France	OT,MD	7 Weeks/M	INJ	U	19Dec2008-19Dec2008	19Dec2008	U/See text	Inappropriate schedule of drug administration	X
B0645589A	France	OT,MD	4 Months/M	INJ	U	16Apr2009-16Apr2009, 16Feb2009-16Feb2009	16Apr2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0645881A	France	OT,MD	4 Months/M	INJ	U	11Mar2009-11Mar2009, 13Jan2009-13Jan2009	11Mar2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0645918A	France	OT,MD	6 Weeks/F	INJ	U	10Mar2009-10Mar2009	10Mar2009	U/See text	Inappropriate schedule of drug administration	X
B0645922A	France	OT,MD	7 Weeks/M	INJ	U	27Feb2009-27Feb2009	27Feb2009	U/See text	Inappropriate schedule of drug administration	X

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B0645932A	France	OT,MD	4 Months/F	INJ	U	13May2009-13May2009, 17Mar2009-17Mar2009	13May2009	U/See text, U/U	Inappropriate schedule of drug administration	X
B0645938A	France	OT,MD	6 Weeks/F	INJ	U	17Mar2009-17Mar2009	17Mar2009	U/See text	Inappropriate schedule of drug administration	X
B0645939A	France	OT,MD	7 Weeks/F	INJ	U	10Mar2009-10Mar2009	10Mar2009	U/See text	Inappropriate schedule of drug administration	X
B0645943A	France	OT,MD	6 Weeks/F	INJ	U	16Feb2009-16Feb2009	16Feb2009	U/See text	Inappropriate schedule of drug administration	X
B0647691A	France	OT,MD	17 Weeks/M	INJ	U	U	14Apr2009	U/U	Inappropriate schedule of drug administration	U
B0647692A	France	OT,MD	6 Weeks/M	INJ	U	03Feb2009-03Feb2009	03Feb2009	U/See text	Inappropriate schedule of drug administration	X

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B0647697A	France	OT,MD	4 Months/F	INJ	U	U	18Apr2009	U/U	Inappropriate schedule of drug administration	U
B0647699A	France	OT,MD	18 Months/F	INJ	U	U	25May2009	U/U	Inappropriate schedule of drug administration	U
B0647909A	France	OT,MD	4 Months/F	INJ	U	U	26May2009	U/U	Inappropriate schedule of drug administration	U
B0647912A	France	OT,MD	4 Months/M	INJ	U	U	07Apr2009	U/U	Inappropriate schedule of drug administration	U
B0648489A	France	OT,MD	6 Weeks/F	INJ	U	U	01Feb2009	U/U	Inappropriate schedule of drug administration	U
B0648491A	France	OT,MD	5 Weeks/F	INJ	U	U	20Dec2008	U/U	Inappropriate schedule of drug administration	U

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B0648498A	France	OT,MD	5 Weeks/M	INJ	U	U	20Dec2008	U/U	Inappropriate schedule of drug administration	U
B0648499A	France	OT,MD	7 Weeks/M	INJ	U	U	01Dec2008	U/U	Inappropriate schedule of drug administration	U
B0648508A	France	OT,MD	7 Weeks/M	INJ	U	U	10Mar2009	U/U	Inappropriate schedule of drug administration	U
B0648591A	France	OT,MD	6 Weeks/M	INJ	U	U	04Mar2009	U/U	Inappropriate schedule of drug administration	U
B0648593A	France	OT,MD	5 Weeks/F	INJ	U	U	02Feb2008	U/U	Inappropriate schedule of drug administration	U
B0648641A	France	OT,MD	2 Months/F	INJ	U	U, U	30Apr2009	U/U, U/U	Inappropriate schedule of drug administration	U

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B0648645A	France	OT,MD	4 Months/F	INJ	U	U	26May2009	U/U	Inappropriate schedule of drug administration	U
B0648649A	France	OT,MD	7 Weeks/M	INJ	U	U	14Jan2009	U/U	Inappropriate schedule of drug administration	U
B0648660A	France	OT,MD	5 Months/F	INJ	U	U, U	17Jun2008	U/U, U/U	Inappropriate schedule of drug administration	U
B0648664A	France	OT,MD	16 Months/F	INJ	U	U	20Apr2009	U/U	Inappropriate schedule of drug administration	U
B0648865A	France	OT,MD	5 Months/M	INJ	U	U	20Mar2009	U/U	Inappropriate schedule of drug administration	U
B0648868A	France	OT,MD	18 Weeks/M	INJ	U	U	15May2009	U/U	Inappropriate schedule of drug administration	U

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B0648895A	France	OT,MD	5 Weeks/F	INJ	U	U	24Oct2008	U/U	Inappropriate schedule of drug administration	U
B0648906A	France	OT,MD	15 Weeks/M	INJ	U	U	10Jun2009	U/U	Inappropriate schedule of drug administration	U
B0648913A	France	OT,MD	7 Weeks/F	INJ	U	U	09Dec2008	U/U	Inappropriate schedule of drug administration	U
B0648919A	France	OT,MD	18 Weeks/F	INJ	U	U	29Jun2009	U/U	Inappropriate schedule of drug administration	U
B0648962A	France	OT,MD	16 Weeks/M	INJ	U	U	11Feb2009	U/U	Inappropriate schedule of drug administration	U
B0648963A	France	OT,MD	5 Months/M	INJ	U	U, U	02Mar2009	U/U, U/U	Inappropriate schedule of drug administration	U

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B0648967A	France	OT,MD	11 Months/M	INJ	U	U	16Dec2009	U/U	Inappropriate schedule of drug administration	U
B0648968A	France	OT,MD	24 Months/F	INJ	U	U, U	10Mar2009	U/U, U/U	Inappropriate schedule of drug administration	U
B0648971A	France	OT,MD	19 Weeks/M	INJ	U	U	11May2009	U/U	Inappropriate schedule of drug administration	U
B0649064A	France	OT,MD	7 Weeks/F	INJ	U	U	08Jan2009	U/U	Inappropriate schedule of drug administration	U
B0649083A	France	OT,MD	7 Weeks/M	INJ	U	U	17Oct2008	U/U	Inappropriate schedule of drug administration	U
B0649097A	France	OT,MD	7 Weeks/M	INJ	U	U	21Jan2009	U/U	Inappropriate schedule of drug administration	U

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B0649100A	France	OT,MD	15 Weeks/F	INJ	U	U	18Feb2009	U/U	Inappropriate schedule of drug administration	U
B0649102A	France	OT,MD	3 Months/F	INJ	U	U	04Feb2009	U/U	Inappropriate schedule of drug administration	U
B0649104A	France	OT,MD	19 Weeks/M	INJ	U	U	25May2009	U/U	Inappropriate schedule of drug administration	U
B0649105A	France	OT,MD	4 Months/F	INJ	U	U	21Mar2009	U/U	Inappropriate schedule of drug administration	U
B0649110A	France	OT,MD	19 Weeks/F	INJ	U	U	18Mar2009	U/U	Inappropriate schedule of drug administration	U
B0649130A	France	OT,MD	18 Weeks/M	INJ	U	U	17Mar2009	U/U	Inappropriate schedule of drug administration	U

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B0649132A	France	OT,MD	7 Weeks/F	INJ	U	U	20Mar2009	U/U	Inappropriate schedule of drug administration	U
B0649141A	France	OT,MD	17 Weeks/F	INJ	U	U	13May2009	U/U	Inappropriate schedule of drug administration	U
B0649954A	France	MD	5 Months/M	INJ	U	26Apr2010-26Apr2010, 14Jan2010-14Jan2010	26Apr2010	U/See text, U/U	Inappropriate schedule of drug administration	X
B0650141A	France	MD	5 Months/M	INJ	U	30Mar2010-30Mar2010, 02Feb2010-02Feb2010	30Mar2010	U/See text, U/U	Inappropriate schedule of drug administration	X
B0657348A	France	MD	7 Weeks/U	INJ	U	01May2010-01May2010	01May2010	U/See text	Inappropriate schedule of drug administration	X
B0657897A	France	MD	12 Months/U	INJ	U	01May2010-01May2010	01May2010	U/See text	Inappropriate schedule of drug administration	X

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B0659214A	France	MD	2 Months/M	INJ	U	03Jun2010-03Jun2010	03Jun2010	U/See text	Inappropriate schedule of drug administration	X
B0660806A	France	MD	7 Weeks/F	INJ	U	01May2010-01May2010	01May2010	U/See text	Inappropriate schedule of drug administration	X
B0666825A	France	MD	7 Weeks/U	INJ	U	22Jun2010-22Jun2010	22Jun2010	U/See text	Inappropriate schedule of drug administration	X
B0669562A	France	MD	6 Weeks/U	INJ	U	11Aug2010-11Aug2010	11Aug2010	U/See text	Inappropriate schedule of drug administration	X
B0672467A	France	PH	6 Weeks/M	INJ	U	01Aug2010-01Aug2010	01Aug2010	U/See text	Inappropriate schedule of drug administration	X
B0675128A	France	MD	5 Years/F	INJ	U	15Sep2010-15Sep2010	15Sep2010	U/See text	Inappropriate schedule of drug administration	X

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B0678718A	France	MD	Infant/U	INJ	U	07May2010-07May2010, 22Apr2010-22Apr2010	07May2010	U/See text, U/U	Inappropriate schedule of drug administration	X
D0066530A	Germany	MD	6 Months/F	INJ	U	22Dec2009-22Dec2009, 24Nov2009-24Nov2009, 16Feb2010-16Feb2010, 26Jan2010-26Jan2010	16Feb2010	U/U, U/U, U/U, U/U	Inappropriate schedule of drug administration	X
D0067540A	Germany	MD	3 Months/M	INJ	U	30Apr2010-30Apr2010, 23Apr2010-23Apr2010	30Apr2010	U/0 Days, U/U	Inappropriate schedule of drug administration	X
D0068192A	Germany	MD	8 Months/F	INJ	U	05Jul2010-05Jul2010	05Jul2010	U/0 Days	Inappropriate schedule of drug administration	X
D0068201A	Germany	MD	12 Months/M	INJ	U	02Jul2010-02Jul2010	02Jul2010	U/0 Days	Inappropriate schedule of drug administration	X
D0068801A	Germany	MD	3 Months/M	INJ	U	23Aug2010-23Aug2010, 09Aug2010-09Aug2010	23Aug2010	U/0 Days, U/U	Inappropriate schedule of drug administration	X

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D0068968A	Germany	MD	12 Months/M	INJ	U	06May2009-06May2009, 16Feb2009-16Feb2009	06May2009	U/0 Days, U/U	Inappropriate schedule of drug administration	X
B0676501A	Ireland	HP,MD	7 Months/M	INJ	U	13Sep2010-13Sep2010, 27Aug2010-27Aug2010, 17May2010-17May2010	13Sep2010	U/During, U/U, U/U	Inappropriate schedule of drug administration	X
B0609393A	France	MD	Infant/M	INJ	U	01Jan2008-01Jan2008	01Jan2008	U/See text	Inappropriate schedule of drug administration*	X
B0622328A	France	MD	1 Months/U	INJ	U	01Dec2009-01Dec2009	01Dec2009	U/See text	Inappropriate schedule of drug administration*	X
B0636416A	France	OT,MD	4 Months/M	INJ	U	20Jan2009-20Jan2009, 24Mar2009-24Mar2009	24Mar2009	U/See text, U/U	Inappropriate schedule of drug administration*	X
B0642980A	France	OT,MD	11 Weeks/F	INJ	U	09Mar2009-09Mar2009, 10Feb2009-10Feb2009	09Mar2009	U/See text, U/U	Inappropriate schedule of drug administration*	X

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D0065944A	Germany	MD	5 Months/M	INJ	U	08Jan2010-08Jan2010, 26Nov2009-26Nov2009	08Jan2009	U/0 Days, U/U	Inappropriate schedule of drug administration*	X
B0642351A	South Africa	HP	6 Weeks/F	INJ	U	17Feb2010-17Feb2010	17Feb2010	U/See text	Inappropriate schedule of drug administration*	X
B0630908A	France	OT,MD	7 Weeks/F	INJ, INJ	U, U	22Oct2008-22Oct2008, 19Dec2008-19Dec2008	22Oct2008	U/See text, U/See text	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	X
B0630931A	France	OT,MD	7 Weeks/M	INJ	U	29Oct2008-29Oct2008	29Oct2008	U/See text	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	X
B0632895A	France	OT,MD	6 Weeks/M	INJ, INJ	U, U	27Oct2008-27Oct2008, 19Jan2009-19Jan2009	27Oct2008	U/See text, U/See text	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	X
B0635710A	France	OT,MD	2 Months/M	INJ	U	17Dec2008-17Dec2008, 03Nov2008-03Nov2008	26Nov2008	U/See text, U/U	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	X

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B0638084A	France	OT,MD	3 Months/M	INJ	U	20Mar2009-20Mar2009, 26Feb2009-26Feb2009	20Mar2009	U/See text, U/U	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	X
B0638094A	France	OT,MD	5 Weeks/F	INJ	U	13Mar2009-13Mar2009	08Jan2009	U/See text	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	X
B0645574A	France	OT,MD	4 Months/F	INJ	U	16May2008-16May2008	16May2008	U/22 Days	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	X
B0645854A	France	OT,MD	7 Weeks/M	U	U	22May2009-22May2009	10Mar2008	U/See text	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	X
B0645911A	France	OT,MD	7 Weeks/F	U	U	20Feb2009-20Feb2009	20Feb2009	U/See text	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	X
B0645915A	France	OT,MD	7 Weeks/F	INJ, INJ	U, U	12Mar2009-12Mar2009, 14May2009-14May2009	12Mar2009	U/See text, U/See text	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	X

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B0645931A	France	OT,MD	7 Weeks/F	INJ	U	24Feb2009-24Feb2009	24Feb2009	U/See text	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	X
B0647698A	France	OT,MD	5 Weeks/M	INJ	U	U	14Nov2008	U/U	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	U
B0648974A	France	OT,MD	14 Weeks/M	INJ	U	U	02Apr2008	U/U	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	U
B0649060A	France	OT,MD	7 Weeks/F	INJ	U	U	12Mar2009	U/U	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	U
B0649061A	France	OT,MD	7 Weeks/M	INJ	U	U	11Mar2009	U/U	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	U
B0649071A	France	OT,MD	4 Weeks/M	INJ	U	U	12Dec2008	U/U	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	U

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B0649095A	France	OT,MD	7 Weeks/M	INJ	U	U	10Feb2009	U/U	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	U
B0649133A	France	OT,MD	10 Weeks/F	INJ	U	U	08Dec2008	U/U	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	U
B0649136A	France	OT,MD	3 Months/M	INJ	U	U	10Dec2008	U/U	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	U
B0642451A	France	OT,MD	4 Months/F	INJ	U	31Mar2009-31Mar2009	23Apr2008	U/12 Months	Inappropriate schedule of drug administration*, Inappropriate schedule of drug administration*	X
B0605689A	France	MD	5 Years/U	INJ, INJ	U, U	01Jun2009-01Jun2009, 01May2009-01May2009	01May2009	U/See text, U/See text	Inappropriate schedule of drug administration*, Inappropriate schedule of drug administration*, Inappropriate schedule of drug administration*	X
B0648977A	France	OT,MD	3 Years/M	INJ, INJ	U, U	U, U	17Dec2008	U/U, U/U	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration, Inappropriate schedule of drug administration,	U

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									Inappropriate schedule of drug administration	
B0603101A	South Africa	HP	3 Weeks/U	INJ, INJ	U, U	01Aug2009-01Aug2009, 1 Days	01Aug2009	U/During, U/During	Inappropriate schedule of drug administration*, Inappropriate schedule of drug administration*, Overdose*	X
B0630910A	France	OT,MD	3 Months/M	INJ, INJ	U, U	03Feb2009-03Feb2009, 17Mar2009-17Mar2009	03Feb2009	U/See text, U/See text	Inappropriate schedule of drug administration, Incorrect dose administered	X
B0637123A	France	OT,MD	2 Months/M	INJ, INJ	U, U	13Jan2009-13Jan2009, 18Mar2009-18Mar2009	13Jan2009	U/See text, U/See text	Inappropriate schedule of drug administration, Incorrect dose administered	X
B0605679A	France	MD	3 Years/U	INJ, INJ	U, U	01Nov2009-01Nov2009, 01Jun2009-01Jun2009	01Jun2009	U/See text, U/See text	Inappropriate schedule of drug administration*, Incorrect dose administered*, Inappropriate schedule of drug administration*	X
D0067600A	Germany	MD	27 Years/M	INJ	U	06May2010-06May2010	06May2010	U/0 Days	Inappropriate schedule of drug administration, Injection site erythema*	R

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B0632998A	France	OT,MD	7 Weeks/F	INJ, INJ	U, U	21Nov2008-21Nov2008, 19Dec2008-19Dec2008, 16Jan2009-16Jan2009	21Nov2008	U/See text, U/See text, U/U	Inappropriate schedule of drug administration, Wrong drug administered	X
B0638547A	France	OT,MD	12 Weeks/F	INJ	U	29Nov2007-29Nov2007, 20Dec2007-20Dec2007	20Dec2007	U/See text, U/U	Inappropriate schedule of drug administration, Wrong drug administered	X
B0653010A	France	MD	Infant/M	INJ	U	1 Days, 1 Days, 1 Days		U/See text, U/U, U/U	Inappropriate schedule of drug administration, Wrong drug administered	X
B0635390A	France	OT,MD	4 Months/M	INJ, INJ	U, U	23Dec2008-23Dec2008, 11Jan2009-11Jan2009, 26Nov2008-26Nov2008	23Dec2008	U/See text, U/See text, U/U	Inappropriate schedule of drug administration, Wrong drug administered, Inappropriate schedule of drug administration	X
B0643051A	France	OT,MD	4 Weeks/M	INJ, INJ, INJ	U, U, U	08Jan2009-08Jan2009, 09Feb2009-09Feb2009, 05Mar2009-05Mar2009	08Jan2009	U/See text, U/See text, U/See text	Inappropriate schedule of drug administration, Wrong drug administered, Inappropriate schedule of drug administration	X
B0624525A	France	MD	5 Months/M	INJ	U	06Nov2009-06Nov2009, 28Sep2009-28Sep2009, 07Jan2010-07Jan2010	07Jan2010	U/See text, U/U, U/U	Incorrect dose administered	X

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B0630187A	France	MD	7 Months/F	INJ	U	05Feb2009-05Feb2009, 08Jan2009-08Jan2009, 09Oct2008-09Oct2008	08Feb2009	U/3 Days, U/U, U/U	Incorrect dose administered	X
B0638218A	France	MD	9 Months/M	INJ	U	27Jan2009-27Jan2009, 15Jun2009-15Jun2009, 07Nov2008-07Nov2008	15Jun2009	U/See text, U/U, U/U	Incorrect dose administered	X
B0658662A	France	MD	18 Months/F	INJ	U	01Jun2010-01Jun2010	01Jun2010	U/See text	Incorrect dose administered	X
B0661906A	France	MD	6 Months/M	INJ	U	06May2010-06May2010, 10Jun2010-10Jun2010	10Jun2010	U/See text, U/U	Incorrect dose administered	X
B0666519A	France	MD	23 Months/U	INJ	U	01May2010-01May2010, 01Nov2008-01Nov2008, 01Feb2010-01Feb2010	01May2010	U/See text, U/U, U/U	Incorrect dose administered	X
B0599673A	France	MD	5 Months/M	INJ	U	23Oct2009-23Oct2009	23Oct2009	U/See text	Incorrect dose administered*	X

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D0068800A	Germany	MD	24 Months/M	INJ	U	07Sep2010-07Sep2010	07Sep2010	U/0 Days	Incorrect dose administered, Abnormal behaviour	R
B0676675A	France	MD,RP	2 Months/M	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/See text	Incorrect route of drug administration	X
B0669507A	Italy	MD	12 Months/M	INJ	U	10Aug2010-10Aug2010	10Aug2010	U/During	Incorrect route of drug administration	X
B0629454A	France	PH	2 Months/F	INJ	U	26Jan2010-26Jan2010	26Jan2010	U/See text	Incorrect storage of drug	X
B0630767A	France	PH	10 Weeks/M	INJ	U	28Jan2010-28Jan2010	28Jan2010	U/See text	Incorrect storage of drug	X
B0635116A	France	PH	18 Months/U	INJ	U	18Feb2010-18Feb2010	18Feb2010	U/See text	Incorrect storage of drug	X

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B0636321A	France	MD	Neonate/U	INJ	U	25Feb2010-25Feb2010	25Feb2010	U/See text	Incorrect storage of drug	X
B0639070A	France	MD	2 Months/F	INJ	U	09Mar2010-09Mar2010	09Mar2010	U/See text	Incorrect storage of drug	X
B0639265A	France	PH	2 Months/F	INJ	U	01Feb2010-01Feb2010	01Feb2010	U/See text	Incorrect storage of drug	X
B0639267A	France	PH	2 Months/M	INJ	U	01Feb2010-01Feb2010	01Feb2010	U/See text	Incorrect storage of drug	X
B0642235A	France	MD	2 Months/F	INJ	U	16Mar2010-16Mar2010	16Mar2010	U/See text	Incorrect storage of drug	X
B0647980A	France	MD	2 Months/F	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/See text	Incorrect storage of drug	X

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B0651889A	France	MD	20 Months/M	INJ	U	06May2010-06May2010	06May2010	U/See text	Incorrect storage of drug	X
B0651891A	France	MD	20 Months/M	INJ	U	06May2010-06May2010	06May2010	U/See text	Incorrect storage of drug	X
B0652679A	France	HP	24 Months/F	INJ	U	10Feb2010-10Feb2010	10Feb2010	U/See text	Incorrect storage of drug	X
B0668012A	France	PH	14 Months/F	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/See text	Incorrect storage of drug	X
B0668712A	France	PH	17 Months/U	INJ	U	1 Days		U/See text	Incorrect storage of drug	X
D0067580A	Germany	MD	U/U	INJ	U	1 Days		U/0 Days	Incorrect storage of drug	X

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B0667248A	Greece	MD	2 Months/F	INJ	U	17Jul2010-17Jul2010	17Jul2010	U/See text	Incorrect storage of drug	X	
B0676607A	Spain	MD	2 Months/U	INJ	U	01Jan2010-01Jan2010		U/See text	Incorrect storage of drug	X	5 subjects are concerned by this maladministration.
B0601361A	France	PH	4 Years/U	INJ	U	1 Days		U/See text	Incorrect storage of drug*	X	
B0605657A	France	MD	9 Weeks/F	INJ	U	01Jan2009-01Jan2009	01Jan2009	U/See text	Incorrect storage of drug*	X	
B0605715A	France	PH	3 Months/F	INJ	U	16Nov2009-16Nov2009	16Nov2009	U/See text	Incorrect storage of drug*	X	
B0612094A	France	PH	2 Months/F	INJ	U	03Nov2009-03Nov2009		U/See text	Incorrect storage of drug*	X	

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B0617418A	France	PH	2 Months/U	INJ	U	01Nov2009-01Nov2009	01Nov2009	U/See text	Incorrect storage of drug*	X
B0603597A	Greece	MD	2 Months/M	INJ	U	06Nov2009-06Nov2009	06Nov2009	U/During	Incorrect storage of drug*	X
B0642250A	France	MD	2 Months/F	INJ, INJ, INJ	U, U, U	11Jan2010-11Jan2010, 15Feb2010-15Feb2010, 13Mar2010-13Mar2010	11Jan2010	U/See text, U/See text, U/See text	Incorrect storage of drug, Inappropriate schedule of drug administration, Wrong drug administered	X
B0659288A	Australia	HP,RP	U/F	INJ	U	1 Days		U/See text	Laceration*, Accidental exposure*, Product quality issue*	U
B0632968A	Ireland	HP	1 Years/F	INJ	.5ML	18Jan2010-18Jan2010	18Jan2010	U/Unknown	Medication error*	U
B0660243A	France	MD	2 Months/M	INJ	U	10Jun2010-10Jun2010	10Jun2010	U/See text	Overdose	X

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D0063858A	Germany	MD	2 Years/M	INJ	U	11Nov2009-11Nov2009, 11Nov2009-11Nov2009	11Nov2009	U/0 Days, U/U	Overdose	X
B0621677A	Argentina	PH	2 Months/U	INJ	U	1 Days, U		U/During, U/U	Overdose*	X
B0660290A	France	MD	18 Months/M	INJ	U	10Jun2010-10Jun2010	10Jun2010	U/See text	Overdose, Incorrect route of drug administration	X
B0661905A	France	MD	4 Years/U	INJ, INJ, INJ	U, U, U	01Oct2008-01Oct2008, 01Nov2008-01Nov2008, 01Dec2008-01Dec2008	01Oct2008	U/See text, U/See text, U/U	Overdose, Overdose, Incorrect dose administered	X
B0675106A	France	CO,CN,PH	2 Months/F	INJ	U	16Sep2010-16Sep2010	16Sep2010	U/See text	Overdose, Pyrexia	R
B0664027A	Sweden	CO,HP	13 Months/U	INJ	U	02Jul2010-02Jul2010	02Jul2010	U/During	Overdose, Wrong drug administered	X

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B0673395A	Australia	HP	3 Months/M	INJ	U	U		U/During	Underdose	X
B0628882A	France	MD	22 Months/M	INJ	U	22Jan2010-22Jan2010	22Jan2010	U/See text	Underdose	X
B0643206A	France	MD	2 Months/M	INJ	U	24Mar2010-24Mar2010	24Mar2010	U/See text	Underdose	X
B0646087A	France	MD	2 Months/F	INJ	U	09Mar2010-09Mar2010	09Mar2010	U/See text	Underdose	X
B0664987A	France	MD	4 Months/M	INJ	U	09Jul2010-09Jul2010	09Jul2010	U/See text	Underdose	X
B0669551A	France	PH	2 Months/U	INJ	U	1 Days		U/See text	Underdose	X

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B0674375A	France	PH	4 Months/F	INJ	U	01Sep2010-01Sep2010	01Sep2010	U/See text	Underdose	X
B0675211A	France	MD	20 Months/F	U	U	01Sep2010-01Sep2010	01Sep2010	U/See text	Underdose	X
B0679812A	France	PH	16 Months/F	INJ	U	01Oct2010-01Oct2010	01Oct2010	U/See text	Underdose	X
B0627562A	Australia	MD	U/U	INJ	U	1 Days		U/During	Underdose*	X
B0609404A	France	MD	2 Months/F	INJ	U	23Nov2009-23Nov2009	23Nov2009	U/See text	Underdose*	X
B0612137A	France	MD	2 Months/F	INJ	U	03Dec2009-03Dec2009	03Dec2009	U/See text	Underdose*	X

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D0063308A	Germany	MD	10 Months/M	INJ	U	11Sep2009-11Sep2009	11Sep2009	U/0 Days	Underdose, Needle issue	X
B0626589A	France	MD,RP	Child/U	INJ	U	1 Days		U/See text	Underdose, Product quality issue	X
B0626856A	France	MD	Child/U	INJ	U	01Jan2009-01Jan2009	01Jan2009	U/See text	Underdose, Product quality issue	X
B0631505A	France	MD	Infant/M	INJ	U	01Feb2010-01Feb2010	01Feb2010	U/See text	Underdose, Product quality issue	X
B0645921A	France	PH	Infant/M	INJ	U	1 Days		U/See text	Underdose, Product quality issue	X
D0067952A	Germany	MD	U/U	INJ	U	1 Days		U/0 Days	Underdose, Product quality issue	X

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B0620732A	France	MD	2 Months/M	INJ	U	21Dec2009-21Dec2009	21Dec2009	U/See text	Underdose*, Product quality issue*	X
B0641963A	Ireland	MD	2 Months/F	INJ	U	19Mar2010-19Mar2010	19Mar2010	U/During	Underdose*, Product quality issue*	X
D0067231A	Germany	PH,MD,RP	Child/U	INJ	U	1 Days		U/Unknown	Vaccination complication*	U
D0067727A	Germany	CN,PH	3 Months/U	INJ	U	1 Days		U/Unknown	Vaccination complication*	U
D0068009A	Germany	PH,MD,RP	U/U	INJ	U	1 Days		U/Unknown	Vaccination complication*	U
D0068012A	Germany	PH,MD,RP	U/U	INJ	U	1 Days		U/Unknown	Vaccination complication*	U

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D0068013A	Germany	MD	U/U	INJ	U	1 Days		U/Unknown	Vaccination complication*	U
#B0666621A	Czech Republic	RA	4 Months/F	INJ	U	22Jun2010-22Jun2010	22Jun2010	U/3 Minutes	Vaccination complication*, Erythema*, Erythema*, Crying*	R
B0635538A	Austria	MD,RA	3 Years/M	INJ	U	15Feb2010-15Feb2010	16Feb2010	U/1 Days	Vaccination complication*, Oedema peripheral*, Swelling*, Pyrexia*, Product quality issue*	I
D0067276A	Germany	PH,MD,RP	Child/U	INJ	U	1 Days	01Apr2010	U/Unknown	Vaccination complication*, Product quality issue*	R
B0629555A	France	OT,MD	5 Months/F	INJ	U	23Mar2009-23Mar2009, 16Feb2009-16Feb2009, 26Dec2008-26Dec2008	23Mar2009	U/See text, U/U, U/See text	Wrong drug administered	X
B0630893A	France	OT,MD	16 Months/M	INJ	U	17Feb2009-17Feb2009	17Feb2009	U/See text	Wrong drug administered	X

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B0632731A	France	OT,MD	3 Months/M	INJ	U	26Mar2009-26Mar2009, 26Feb2009-26Feb2009, 26Jan2009-26Jan2009	26Feb2009	U/See text, U/U, U/See text	Wrong drug administered	X
B0632931A	France	OT,MD	10 Months/F	U	U	21Sep2009-21Sep2009, 19Mar2009-19Mar2009, 19Jan2009-19Jan2009	21Sep2009	U/See text, U/U, U/U	Wrong drug administered	X
B0632934A	France	OT,MD	3 Months/F	INJ	U	12Feb2009-12Feb2009, 14Jan2009-14Jan2009, 17Mar2009-17Mar2009	12Feb2009	U/See text, U/U, U/U	Wrong drug administered	X
B0632961A	France	HP,MD	3 Months/F	INJ	U	09Jan2009-09Jan2009, 12Mar2009-12Mar2009, 11Feb2009-11Feb2009	11Feb2009	U/See text, U/U, U/U	Wrong drug administered	X
B0632970A	France	OT,MD	3 Months/F	INJ	U	12Feb2009-12Feb2009, 08Jan2009-08Jan2009, 13Mar2009-13Mar2009	12Feb2009	U/See text, U/U, U/U	Wrong drug administered	X
B0632973A	France	OT,MD	3 Months/F	INJ	U	10Feb2009-10Feb2009, 06Jan2009-06Jan2009, 10Mar2009-10Mar2009	10Feb2009	U/See text, U/U, U/U	Wrong drug administered	X

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B0632977A	France	OT,MD	3 Months/M	INJ	U	09Feb2009-09Feb2009, 06Jan2009-06Jan2009, 10Mar2009-10Mar2009	09Feb2009	U/See text, U/U, U/U	Wrong drug administered	X
B0632992A	France	OT,MD	2 Months/F	INJ	U	20Jan2009-20Jan2009, 19Dec2008-19Dec2008, 23Feb2009-23Feb2009	20Jan2009	U/See text, U/U, U/U	Wrong drug administered	X
B0632994A	France	OT,MD	3 Months/M	INJ	U	12Feb2009-12Feb2009, 16Mar2009-16Mar2009, 13Jan2009-13Jan2009	12Feb2009	U/See text, U/U, U/U	Wrong drug administered	X
B0633002A	France	OT,MD	3 Months/M	INJ	U	13Feb2009-13Feb2009, 08Jan2009-08Jan2009, 13Mar2009-13Mar2009	13Feb2009	U/See text, U/U, U/U	Wrong drug administered	X
B0633005A	France	OT,MD	3 Months/F	INJ	U	06Mar2009-06Mar2009, 30Jan2009-30Jan2009, 03Apr2009-03Apr2009	06Mar2009	U/See text, U/U, U/U	Wrong drug administered	X
B0633273A	France	OT,MD	3 Months/M	INJ	U	12Jan2009-12Jan2009, 08Dec2008-08Dec2008, 09Feb2009-09Feb2009	12Jan2009	U/See text, U/U, U/U	Wrong drug administered	X

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B0633275A	France	OT,MD	3 Months/F	INJ	U	04Feb2009-04Feb2009, 07Jan2009-07Jan2009, 11Mar2009-11Mar2009	04Feb2009	U/See text, U/U, U/U	Wrong drug administered	X
B0635704A	France	OT,MD	4 Months/F	INJ	U	09Apr2008-09Apr2008, 29Feb2008-29Feb2008, 04Jun2008-04Jun2008	09Apr2008	U/See text, U/U, U/U	Wrong drug administered	X
B0640273A	France	OT,MD	4 Months/M	INJ	U	22Feb2008-22Feb2008, 20Jan2008-20Jan2008, 25Mar2008-25Mar2008	22Feb2008	U/See text, U/U, U/U	Wrong drug administered	X
B0640282A	France	OT,MD	3 Months/F	INJ	U	28Jan2009-28Jan2009, 27Dec2008-27Dec2008, 27Feb2009-27Feb2009	28Jan2009	U/See text, U/U, U/U	Wrong drug administered	X
B0640287A	France	OT,MD	3 Months/F	INJ	U	06Feb2009-06Feb2009, 05Jan2009-05Jan2009, 10Mar2009-10Mar2009	06Feb2009	U/See text, U/U, U/U	Wrong drug administered	X
B0642963A	France	OT,MD	3 Months/F	INJ	U	09Mar2008-09Mar2008, 08Feb2008-08Feb2008, 11Apr2008-11Apr2008	09Mar2008	U/See text, U/U, U/U	Wrong drug administered	X

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B0642989A	France	OT,MD	3 Months/F	INJ	U	12Feb2009-12Feb2009, 12Jan2009-12Jan2009, 12Mar2009-12Mar2009	12Feb2009	U/See text, U/U, U/U	Wrong drug administered	X
B0643007A	France	MD	5 Months/M	INJ	U	22Mar2010-22Mar2010, 08Jan2010-08Jan2010	22Mar2010	U/See text, U/U	Wrong drug administered	X
B0643021A	France	OT,MD	3 Months/F	INJ	U	16Jan2009-16Jan2009, 18Dec2008-18Dec2008, 19Feb2009-19Feb2009	16Jan2009	U/See text, U/U, U/U	Wrong drug administered	X
B0648565A	France	OT,MD	12 Weeks/M	INJ	U	U	16Apr2009	U/U	Wrong drug administered	U
B0664591A	France	PH	39 Years/M	INJ	U	05Jul2010-05Jul2010	05Jul2010	U/See text	Wrong drug administered	X
B0666822A	France	HP	3 Years/U	INJ, INJ	U, U	01Dec2009-01Dec2009, 01Feb2010-01Feb2010	01Dec2009	U/See text, U/See text	Wrong drug administered	X

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B0668947A	France	MD	9 Years/U	INJ	U	15Oct2009-15Oct2009	18Aug2010	U/10 Months	Wrong drug administered	X
B0672052A	France	MD	Infant/F	INJ, INJ	U, U	1 Days, 1 Days		U/See text, U/See text	Wrong drug administered	X
B0672497A	France	PH	39 Months/F	INJ	U	28Jul2010-28Jul2010	28Jul2010	U/See text	Wrong drug administered	X
B0676235A	France	MD	30 Years/F	INJ	U	01Jan2009-01Jan2009	01Jan2009	U/See text	Wrong drug administered	X
B0677658A	France	MD	12 Months/U	INJ	U	07Jul2010-07Jul2010, 16Sep2009-16Sep2009, 11Dec2009-11Dec2009	07Jul2010	U/See text, U/U, U/U	Wrong drug administered	X
B0630973A	France	OT,MD	4 Months/F	INJ	U	16Feb2009-16Feb2009, 17Dec2008-17Dec2008, 14Jan2009-14Jan2009	16Feb2009	U/See text, U/U, U/U	Wrong drug administered*	X

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B0638127A	France	OT,MD	15 Weeks/F	INJ	U	29Apr2009-29Apr2009, 26Feb2009-26Feb2009, 27Mar2009-27Mar2009	29Apr2009	U/See text, U/U, U/U	Wrong drug administered*	X
B0632744A	France	OT,MD	2 Months/M	INJ	U	08Jan2009-08Jan2009, 08Dec2008-08Dec2008, 07Nov2008-07Nov2008	08Dec2008	U/See text, U/U, U/U	Wrong drug administered, Inappropriate schedule of drug administration	X
B0632988A	France	OT,MD	3 Months/F	INJ, INJ	U, U	13Feb2009-13Feb2009, 09Jan2009-09Jan2009, 12Mar2009-12Mar2009	13Feb2009	U/See text, U/See text, U/U	Wrong drug administered, Inappropriate schedule of drug administration	X
B0640278A	France	OT,MD	3 Months/F	INJ, INJ	U, U	09Jan2009-09Jan2009, 11Feb2009-11Feb2009, 10Mar2009-10Mar2009	11Feb2009	U/See text, U/See text, U/U	Wrong drug administered, Inappropriate schedule of drug administration	X
B0640295A	France	OT,MD	3 Months/F	INJ	U	19Mar2009-19Mar2009, 23Feb2009-23Feb2009, 21Apr2009-21Apr2009	19Mar2009	U/See text, U/U, U/U	Wrong drug administered, Inappropriate schedule of drug administration	X
B0642985A	France	OT,MD	3 Months/F	INJ	U	16Mar2009-16Mar2009, 17Feb2009-17Feb2009, 17Apr2009-17Apr2009	16Mar2009	U/See text, U/U, U/U	Wrong drug administered, Inappropriate schedule of drug administration	X

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B0635102A	France	MD	Infant/F	INJ	U	01Jan2007-01Jan2007, 01Jan2007-01Jan2007, 01Jan2008-01Jan2008	01Jan2007	U/See text, U/U, U/U	Wrong drug administered, Incorrect dose administered	X
B0643059A	France	OT,MD	3 Months/F	INJ, INJ	U, U	25Feb2008-25Feb2008, 04Jan2008-04Jan2008, 06May2008-06May2008, 28Apr2008-28Apr2008	25Feb2008	U/See text, U/See text, U/U, U/U	Wrong drug administered, Incorrect dose administered	X
B0647478A	France	MD	2 Years/M	INJ, INJ	U, U	01Jun2009-01Jun2009, 01Nov2009-01Nov2009, 01May2009-01May2009	01Jun2009	U/See text, U/See text, U/U	Wrong drug administered, Incorrect dose administered	U
B0641223A	France	PH	8 Years/M	INJ	U	23May2003-23May2003, 29Apr2003-29Apr2003, 25Jun2003-25Jun2003	23May2003	U/See text, U/U, U/U	Wrong drug administered*, Incorrect dose administered*, Incorrect dose administered	X
B0643578A	Spain	MD	4 Months/F	INJ	U	22Mar2010-22Mar2010	22Mar2010	U/0 Days	Wrong drug administered*, Pyrexia*, Restlessness*	R
A0877059A	Canada	MD	9 Weeks/M	INJ	U	19Aug2010-19Aug2010	19Aug2010	U/See text	Wrong technique in drug usage process	X

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B0601970A	France	MD	2 Years/M	INJ	U	30Oct2009-30Oct2009	30Oct2009	U/See text	Wrong technique in drug usage process	X
B0624537A	France	MD	4 Months/U	INJ	U	06Jan2010-06Jan2010	06Jan2010	U/See text	Wrong technique in drug usage process	X
B0624867A	France	MD	4 Months/U	INJ	U	04Jan2010-04Jan2010	04Jan2010	U/See text	Wrong technique in drug usage process	X
B0635104A	France	MD	2 Months/U	INJ	U	19Feb2010-19Feb2010	19Feb2010	U/See text	Wrong technique in drug usage process	X
B0635359A	France	MD	16 Months/F	INJ	U	22Feb2010-22Feb2010	22Feb2010	U/See text	Wrong technique in drug usage process	X
B0638085A	France	MD	4 Months/F	INJ	U	05Mar2010-05Mar2010	05Mar2010	U/See text	Wrong technique in drug usage process	X

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B0641355A	France	MD	21 Months/M	INJ	U	17Mar2010-17Mar2010	17Mar2010	U/See text	Wrong technique in drug usage process	X
B0643838A	France	MD	6 Months/U	INJ	U	29Mar2010-29Mar2010	29Mar2010	U/See text	Wrong technique in drug usage process	X
B0651890A	France	MD	Infant/F	INJ	U	06May2010-06May2010	06May2010	U/See text	Wrong technique in drug usage process	X
B0653014A	France	MD	Infant/U	INJ	U	01May2010-01May2010	01May2010	U/See text	Wrong technique in drug usage process	X
B0658279A	France	MD	Infant/U	INJ	U	1 Days		U/See text	Wrong technique in drug usage process	X
B0659202A	France	MD	16 Months/U	INJ	U	04Jun2010-04Jun2010	04Jun2010	U/See text	Wrong technique in drug usage process	X

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B0659862A	France	MD	2 Months/M	INJ	U	08Jun2010-08Jun2010	08Jun2010	U/See text	Wrong technique in drug usage process	X
B0660545A	France	MD	Infant/U	INJ	U	14Jun2010-14Jun2010	14Jun2010	U/See text	Wrong technique in drug usage process	X
B0660800A	France	MD	4 Months/F	INJ	U	15Jun2010-15Jun2010	15Jun2010	U/See text	Wrong technique in drug usage process	X
B0664988A	France	MD	12 Months/U	INJ	U	12Jul2010-12Jul2010	12Jul2010	U/See text	Wrong technique in drug usage process	X
B0665664A	France	MD	2 Months/U	INJ	U	13Jul2010-13Jul2010	13Jul2010	U/See text	Wrong technique in drug usage process	X
B0666516A	France	MD	Infant/U	INJ	U	19Jul2010-19Jul2010	19Jul2010	U/See text	Wrong technique in drug usage process	X

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B0668487A	France	MD	Infant/U	INJ	U	02Aug2010-02Aug2010	02Aug2010	U/See text	Wrong technique in drug usage process	X
B0671133A	France	MD	5 Months/F	INJ	U	23Aug2010-23Aug2010	23Aug2010	U/See text	Wrong technique in drug usage process	X
B0671561A	France	MD	2 Months/F	INJ	U	24Aug2010-24Aug2010	24Aug2010	U/See text	Wrong technique in drug usage process	X
B0677257A	France	MD	Neonate/F	INJ	U	29Sep2010-29Sep2010	29Sep2010	U/See text	Wrong technique in drug usage process	X
B0677659A	France	PH	5 Months/F	INJ	U	30Sep2010-30Sep2010	30Sep2010	U/See text	Wrong technique in drug usage process	X
B0678737A	France	MD	2 Months/U	INJ	U	04Oct2010-04Oct2010	04Oct2010	U/See text	Wrong technique in drug usage process	X

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D0064868A	Germany	MD	U/U	INJ	U	1 Days		U/0 Days	Wrong technique in drug usage process	X
D0066115A	Germany	PH	U/U	INJ	U	1 Days		U/0 Days	Wrong technique in drug usage process	X
D0066304A	Germany	MD	4 Months/M	INJ	U	29Jan2010-29Jan2010	29Jan2010	U/0 Days	Wrong technique in drug usage process	X
D0066345A	Germany	MD	4 Months/M	INJ	U	01Feb2010-01Feb2010	01Feb2009	U/0 Days	Wrong technique in drug usage process	X
D0067005A	Germany	MD	6 Months/M	INJ	U	25Mar2010-25Mar2010	25Mar2010	U/0 Days	Wrong technique in drug usage process	X
D0067305A	Germany	MD,RP	1 Years/M	INJ	U	1 Days		U/0 Days	Wrong technique in drug usage process	X

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D0067367A	Germany	MD	4 Months/U	INJ	U	U		U/U	Wrong technique in drug usage process	X
D0068839A	Germany	MD	U/U	INJ	U	1 Days		U/During	Wrong technique in drug usage process	X
D0068896A	Germany	MD	2 Months/M	INJ	U	05Sep2010-05Sep2010	05Sep2010	U/0 Days	Wrong technique in drug usage process	X
D0069030A	Germany	MD	14 Months/M	INJ	U	1 Days		U/0 Days	Wrong technique in drug usage process	X
B0666071A	Greece	MD	U/F	INJ	U	15Jul2010-15Jul2010	15Jul2010	U/See text	Wrong technique in drug usage process	X
B0680693A	Ireland	MD	6 Months/M	IM	U	11Oct2010-11Oct2010	11Oct2010	U/U	Wrong technique in drug usage process	X

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B0668675A	Spain	MD	2 Months/M	INJ	U	04Aug2010-04Aug2010	04Aug2010	U/During	Wrong technique in drug usage process	X	
B0668740A	Sweden	HP	U/F	INJ	U	U		U/During	Wrong technique in drug usage process	X	
B0671450A	Sweden	MD	12 Months/M	INJ	U	19Aug2010-19Aug2010	19Aug2010	U/During	Wrong technique in drug usage process	X	
B0641967A	Australia	PH	Infant/U	INJ	U	1 Days		U/During	Wrong technique in drug usage process*	X	This case referred to seven infant subjects.
A0842383A	Canada	PH	Infant/F	INJ	U	31Jan2010-31Jan2010	31Jan2010	U/See text	Wrong technique in drug usage process*	X	
A0854304A	Canada	HP	6 Months/M	INJ	U	U		U/See text	Wrong technique in drug usage process*	X	

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A0868783A	Canada	MD	Child/U	INJ	U	U		U/See text	Wrong technique in drug usage process*	X
A0876193A	Canada	HP,RP	6 Months/U	INJ	U	U, U, U		U/See text, U/U, U/U	Wrong technique in drug usage process*	X
A0882525A	Canada	MD	6 Months/M	INJ	U	21Sep2010-21Sep2010, 21Sep2010-21Sep2010	21Sep2010	U/See text, U/U	Wrong technique in drug usage process*	X
B0601289A	France	MD	4 Months/F	INJ	U	U		U/See text	Wrong technique in drug usage process*	X
B0603718A	France	MD	17 Months/M	INJ	U	10Nov2009-10Nov2009	10Nov2009	U/See text	Wrong technique in drug usage process*	X
B0609123A	France	MD	3 Months/M	INJ	U	25Nov2009-25Nov2009	25Nov2009	U/See text	Wrong technique in drug usage process*	X

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B0616223A	France	MD	4 Months/F	INJ	U	14Dec2009-14Dec2009	14Dec2009	U/See text	Wrong technique in drug usage process*	X
B0606188A	Ireland	MD	7 Months/F	INJ	U	16Nov2009-16Nov2009	16Nov2009	U/During	Wrong technique in drug usage process*	X
B0623766A	Ireland	PH	U/M	INJ	U	U		U/Unknown	Wrong technique in drug usage process*	N
B0630866A	Ireland	MD	Child/U	INJ	U	U		U/See text	Wrong technique in drug usage process*	X
B0630869A	Ireland	MD	Child/U	INJ	.5ML	U		U/See text	Wrong technique in drug usage process*	X
B0638321A	Ireland	HP	4 Months/F	INJ	U	U		U/During	Wrong technique in drug usage process*	X

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B0676804A	Italy	MD	Child/U	INJ	U	13Sep2010-13Sep2010	13Sep2010	U/During	Wrong technique in drug usage process*	X	3 subjects are concerned by this maladministration.
B0676834A	Italy	MD	Child/U	INJ	U	13Sep2010-13Sep2010	13Sep2010	U/During	Wrong technique in drug usage process*	X	
B0676835A	Italy	MD	Child/U	INJ	U	13Sep2010-13Sep2010	13Sep2010	U/During	Wrong technique in drug usage process*	X	
B0631345A	New Zealand	PH	Child/U	INJ	U	U		U/See text	Wrong technique in drug usage process*	X	
B0641734A	Slovakia	MD	4 Months/M	INJ	U	11Feb2010-11Feb2010	11Feb2010	U/See text	Wrong technique in drug usage process*	X	
B0641739A	Slovakia	MD	5 Months/M	INJ	U	11Feb2010-11Feb2010	11Feb2010	U/See text	Wrong technique in drug usage process*	X	

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B0609269A	Spain	HP	2 Months/M	INJ	U	23Nov2009-23Nov2009	23Nov2009	U/During	Wrong technique in drug usage process*	U
B0676939A	Spain	PH	2 Months/M	INJ	U	14Sep2010-14Sep2010	14Sep2010	U/During	Wrong technique in drug usage process*	X
B0673690A	Sweden	HP	6 Months/M	INJ	U	02Sep2010-02Sep2010	02Sep2010	U/During	Wrong technique in drug usage process*	X
B0637597A	Switzerland	MD	6 Months/F	INJ	.5ML	U, 11Feb2010-11Feb2010, U	11Feb2010	U/See text, U/U, U/U	Wrong technique in drug usage process*	X
B0637749A	Switzerland	MD	6 Months/M	INJ	.5ML	U, U, 11Feb2010-11Feb2010	11Feb2010	U/See text, U/U, U/U	Wrong technique in drug usage process*	X
D0067715A	Germany	MD	9 Weeks/M	INJ, INJ	U, U	21May2010-21May2010, 21May2010-21May2010	21May2010	U/0 Days, U/0 Days	Wrong technique in drug usage process, Incorrect dose administered	X

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B0604894A	France	MD	6 Months/U	INJ	U	01Aug2009-01Aug2009	01Aug2009	U/See text	Wrong technique in drug usage process*, Incorrect dose administered*	X
B0618833A	Belgium	MD	3 Months/M	INJ	U	01Dec2009-01Dec2009, 11Dec2009-11Dec2009	11Dec2009	U/During, U/U	Wrong technique in drug usage process*, Incorrect route of drug administration*	X
B0671976A	Belgium	PH	2 Months/M	INJ	U	10Aug2010-10Aug2010	10Aug2010	U/During	Wrong technique in drug usage process*, Incorrect route of drug administration*	X
D0066271A	Germany	PH,MD	U/U	INJ	U	1 Days		U/0 Days	Wrong technique in drug usage process, Injection site reaction*, Injection site swelling*	U
D0068215A	Germany	MD	19 Months/M	INJ	U	06Jul2010-06Jul2010	06Jul2010	U/0 Days	Wrong technique in drug usage process, Wrong technique in drug usage process	X
D0068548A	Germany	MD	19 Months/M	INJ	U	06Jul2010-06Jul2010	06Jul2010	U/0 Days	Wrong technique in drug usage process, Wrong technique in drug usage process	X

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Investigations										
B0651809A	South Africa	HP	2 Years/M	INJ	U	03Sep2008-03Sep2008, 16Oct2009-16Oct2009, 09Jun2008-09Jun2008, 15Jul2008-15Jul2008		U/Unknown, U/U, U/U, U/U	Clostridium test negative*, Corynebacterium test negative*	X
D0069123A	Germany	MD	3 Years/M	INJ	U	01Sep2008-01Sep2008	01Oct2010	U/2 Years	Hepatitis B antibody negative	X
B0676375A	Hong Kong	MD	2 Years/U	INJ	U	U		U/U	Hepatitis B antigen positive*	U
#D0067371A	Germany	MD	6 Months/U	INJ	U	01Apr2010-01Apr2010	01Apr2010	U/0 Months	Transaminases increased*	U
#B0678705A	Italy	MD,RA	2 Months/M	INJ	U	26Aug2010-26Aug2010	27Aug2010	U/1 Days	Transaminases increased, Rash papular, Pyrexia, Urticaria, Irritability	R
Metabolism and nutrition disorders										

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#B0657744A	Italy	RA	2 Months/M	INJ	U	15Apr2010-15Apr2010	16Apr2010	U/1 Days	Acidosis*, Ammonia increased*, Yawning*, Sleep disorder*, Dizziness*, Eyelid disorder*, Hypotonia*, Food aversion*	R
#B0633695A	South Africa	HP	8 Weeks/M	INJ	U	27Jan2010-27Jan2010	27Jan2010	U/0 Days	Decreased appetite*, Dehydration*, Pyrexia*, Lactose intolerance*	R
#B0630342A	Poland	RA	4 Months/F	INJ	U	16Dec2009-16Dec2009	17Dec2009	U/1 Days	Decreased appetite*, Irritability*, Pyrexia*	R
B0666663A	Switzerland	PH,RA	4 Months/M	INJ	U	21Jun2010-21Jun2010, 21Apr2010-21Apr2010	21Jun2010	U/Hours, U/U	Ketoacidosis*, Pyrexia	N
#B0661542A	Spain	CO,MD	6 Months/M	INJ	U	01Mar2010-01Mar2010, 1 Days	25Mar2010	U/5 Days, U/U	Metabolic disorder*, Ataxia*, Balance disorder*, Diplopia*, Strabismus*, Nervous system disorder*	F
#B0636387A	Netherlands	RA	3 Months/F	INJ	U	27Jul2009-27Jul2009	27Jul2009	U/0 Days	Oligodipsia*, Crying*, Pyrexia*, Crying*	U

#D0064314A	Germany	HP	U/F	INJ	U	08May2008-08May2008, 04Jul2007-04Jul2007, 15Aug2007-15Aug2007, 19Sep2007-19Sep2007	13May2009	U/5 Days, U/U, U/U, U/U	Type 1 diabetes mellitus*, Polydipsia*, Enuresis*, Weight decreased*, Bronchitis*, Tracheitis*, Bronchitis bacterial*, Rhinitis*, Lichen striatus*	U
Musculoskeletal and connective tissue disorders										
D0066905A	Germany	MD	17 Months/F	INJ	U	15Mar2010-15Mar2010	01Mar2010	U/8 Hours	Arthritis*	R
D0067214A	Germany	MD,RA	20 Months/M	INJ	U	15Jan2010-15Jan2010	16Jan2010	U/24 Hours	Joint swelling*, Oedema peripheral*, Rash*, Rash erythematous*	R
#B0672473A	Italy	MD,RA	18 Months/M	INJ	U	02Aug2010-02Aug2010	02Aug2010	U/0 Days	Joint swelling*, Pyrexia*, Vomiting*, Gait disturbance*	R
B0630737A	Poland	CO,HP	5 Months/M	INJ	U	02Feb2010-02Feb2010	02Feb2010	U/0 Days	Muscle rigidity*, Pyrexia*, Hypertonia*	R

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#B0653182A	Poland	RA	17 Months/U	INJ	U	14Jan2010-14Jan2010	14Jan2010	U/0 Days	Myalgia*, Gait disturbance*, Malaise*, Hypokinesia*	U
#D0067162A	Germany	RA	5 Months/M	INJ	.5ML	12Jan2010-12Jan2010	13Jan2010	U/1 Days	Myofascitis*, Bacterial infection*, Skin warm*, Mobility decreased*, Skin oedema*, Inflammation*	R
#B0636580A	Poland	RA	33 Years/F	INJ	U	1 Days	25Nov2009	U/Unknown	Pain in extremity*, Oedema peripheral*, Injection site oedema*, Injection site erythema*, Injection site swelling*	U
B0666885A	Netherlands	HP,RA	20 Months/M	INJ	U	18Feb2010-18Feb2010	18Feb2010	U/3 Hours	Pain in extremity*, Rash*, Pyrexia*	R
Neoplasms benign, malignant and unspecified (incl cysts and polyps										
#D0068563A	Germany	CO,MD,RA	7 Months/M	INJ	U	22Jan2010-22Jan2010	01Jan2010	U/4 Days	B precursor type acute leukaemia, Anaemia, White blood cell disorder, Neutropenia, Decreased appetite, Body temperature increased, Asthenia, Fatigue, Infection, Weight decreased, Lymphadenopathy, Indifference, Cough,	U

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									Rhinitis, Pallor, Petechiae, Hepatosplenomegaly, Viral test positive, Bronchitis	
Nervous system disorders										
#B0642185A	Czech Republic	RA	15 Months/F	INJ	U	12Feb2010-12Feb2010	17Feb2010	U/5 Days	Altered state of consciousness*, Gaze palsy*, Tonic convulsion*, Convulsion*, Epilepsy*, Gastroenteritis*, Febrile convulsion*, Hypertonia*, Ear infection*, Gastritis*, Nasopharyngitis*, Hypotonia*, Body temperature increased*, Vomiting*, Diarrhoea*, Pyrexia*	U
#D0067138A	Germany	RA	3 Months/F	INJ	.5ML	27Jan2010-27Jan2010, 28Dec2009-28Dec2009	27Jan2010	U/0 Days, U/U	Altered state of consciousness*, Hypotonic-hyporesponsive episode*, Fatigue*, Hypotonia*, Eyelid disorder*, Pallor*, Unresponsive to stimuli*, Unresponsive to stimuli*, Tremor*, Vomiting*, Convulsion*, Cholinergic syndrome*, Presyncope*	R
#B0675304A	Netherlands	HP,RA	11 Months/F	INJ	U	26May2010-26May2010	01May2010	U/2 Days	Ataxia, Ill-defined disorder, Fall	R

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#D0068399A	Germany	HP,RA	5 Months/F	INJ, INJ, INJ	U, U, U	19Dec2000-19Dec2000, 16Jan2001-16Jan2001, 13Feb2001-13Feb2001	01Apr2001	U/3 Months, U/2 Months, U/1 Months	Autism, Epilepsy, Developmental delay	N
#D0068059A	Germany	MD	3 Months/M	INJ, INJ, INJ, INJ	U, U, U, U	07Mar2007-07Mar2007, 16May2007-16May2007, 20Jun2007-20Jun2007, 04Mar2008-04Mar2008		U/Unknown, U/Unknown, U/Unknown, U/Unknown	Autism*, Mutism*, Developmental delay*	N
#B0666511A	Latvia	MD	4 Months/F	INJ, INJ	U, U	15Jul2010-15Jul2010, 18May2010-18May2010		U/0 Months, U/1 Days	Cerebral haemorrhage*, Hemiparesis*, Lethargy*, Convulsion, Crying*, Nervousness*, Tension*	S
#D0068812A	Germany	HP,RA	13 Months/M	INJ	U	19Aug2010-19Aug2010		U/0 Months	Convulsion	R
#B0661402A	Ireland	RA	6 Months/F	INJ	U	14Apr2010-14Apr2010	14Apr2010	U/0 Days	Convulsion	R
#B0670232A	Italy	MD,RA	3 Years/M	INJ	U	12May2010-12May2010	13May2010	U/1 Days	Convulsion	R

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#B0676794A	Italy	MD,RA	4 Months/F	INJ	U	17Sep2010-17Sep2010	17Sep2010	U/0 Days	Convulsion	R
#B0678687A	Italy	MD,RA	5 Months/M	INJ	U	15Sep2010-15Sep2010	16Sep2010	U/1 Days	Convulsion	U
#D0065395A	Germany	RA	3 Months/F	INJ	.5ML	28Sep2009-28Sep2009	15Oct2009	U/17 Days	Convulsion*	N
#D0066554A	Germany	MD,RP	Infant/U	INJ	U	1 Days		U/Unknown	Convulsion*	U
#D0066774A	Germany	MD	3 Months/F	INJ	U	05Mar2010-05Mar2010	06Mar2010	U/24 Hours	Convulsion*	R
#B0665389A	South Africa	CO,HP	12 Weeks/M	INJ	U	11Jun2010-11Jun2010, 14May2010-14May2010	12Jun2010	U/23 Hours, U/U	Convulsion*	N

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#B0675951A	Sweden	RA	11 Months/F	INJ	U	04Jun2010-04Jun2010	01Jun2010	U/10 Hours	Convulsion*	R
#D0068401A	Germany	RA	4 Months/F	INJ	.5ML	23Jun2010-23Jun2010	23Jun2010	U/0 Days	Convulsion*, Apathy*, Unresponsive to stimuli*, Crying*, Vomiting*, Pallor*, Hyponatraemia*	R
#B0662600A	Switzerland	RA	75 Days/F	INJ	U	17Apr2010-17Apr2010	19Apr2010	U/40 Hours	Convulsion*, Apnoea*, Muscle rigidity*, Agitation*, Skin discolouration*, Crying*	U
#B0628086A	South Africa	HP	5 Months/F	INJ	U	26Oct2009-26Oct2009	01Jan2009	U/3 Weeks	Convulsion*, Convulsion*	R
#D0066414A	Germany	MD,RA	5 Months/F	INJ	.5ML	12Jan2010-12Jan2010, 29Oct2009-29Oct2009, 26Nov2009-26Nov2009	12Jan2010	U/0 Days, U/U, U/U	Convulsion*, Convulsion*, Febrile convulsion*, Atonic seizures*, Grand mal convulsion*, Pyrexia*, Diarrhoea*, Gaze palsy*, Cyanosis*, Disturbance in attention*, Staring*, Pharyngeal erythema*, Rhinitis*, Leukocytosis*, Gastroenteritis*, Gastroenteritis norovirus*	N

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#D0066491A	Germany	MD,RP	2 Months/F	INJ	.5ML	29Jan2010-29Jan2010	29Jan2010	U/6 Hours	Convulsion*, Convulsion*, Gaze palsy*, Muscle spasms*, Tremor*	R
#B0606100A	Austria	RA	4 Months/F	INJ	U	08Oct2009-08Oct2009	08Oct2009	U/12 Hours	Convulsion*, Convulsion*, Postictal paralysis*, Monoparesis*, Eye movement disorder*, Hypotonia*, Ill-defined disorder*, Muscle twitching*, Pallor*, General physical health deterioration*	R
#B0672543A	Netherlands	HP,RA	3 Months/M	INJ	U	14Apr2010-14Apr2010	14Apr2010	U/3 Minutes	Convulsion, Cyanosis central, Apnoea, Loss of consciousness, Staring, Oligodipsia, Pallor, Gastrooesophageal reflux disease, Milk allergy, Vomiting, Pyrexia, Crying	U
#D0068927A	Germany	RA	5 Months/M	INJ, INJ	.5ML, .5ML	09Jun2010-09Jun2010, 10May2010-10May2010	30May2010	U/1 Days, U/20 Days	Convulsion*, Cyanosis*, Convulsion*, Convulsion*	N
#B0676877A	Italy	MD,RA	3 Months/M	INJ	.5ML	20Sep2010-20Sep2010	20Sep2010	U/10 Minutes	Convulsion, Cyanosis, Grand mal convulsion, Sensory loss, Drooling, Hypotonia, Trismus, Tachypnoea, Tachycardia	I

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#B0677130A	Czech Republic	MD,RA	4 Months/M	INJ	U	03Sep2010-03Sep2010		U/13 Hours	Convulsion, Cyanosis, Musculoskeletal stiffness	R
#D0064824A	Germany	MD,RA,RP	3 Months/F	INJ	U	17Nov2009-17Nov2009	17Nov2009	U/4 Hours	Convulsion*, Dyskinesia*, Dyskinesia*, Dissociation*, Fatigue*, Epilepsy*, Dyskinesia*	I
#B0652090A	Netherlands	RA	12 Months/M	INJ	U	08Oct2009-08Oct2009	09Oct2009	U/1 Days	Convulsion*, Gaze palsy*, Loss of consciousness*, Pyrexia*, Otitis media*, Pallor*	R
#D0067732A	Germany	MD,RP	3 Months/M	INJ	.5ML	06May2010-06May2010	07May2010	U/1 Days	Convulsion*, Gaze palsy*, Musculoskeletal stiffness*, Cyanosis*	R
#B0672374A	Poland	MD,RA	2 Months/U	INJ	U	20Jul2010-20Jul2010	20Jul2010	U/1 Hours	Convulsion, Hypotonia, Pallor, Abnormal behaviour, Crying	R
#B0675842A	Italy	RA	12 Months/M	INJ	.5ML	02Sep2010-02Sep2010, 11Nov2009-11Nov2009, 19Jan2010-19Jan2010	02Sep2010	U/4 Hours, U/U, U/U	Convulsion, Leukocytosis, Pyrexia	U

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#D0066999A	Germany	HP,MD	1 Years/M	INJ	.5ML	25Feb2010-25Feb2010	26Feb2010	U/1 Days	Convulsion*, Loss of consciousness*, Disorientation*, Pyrexia*	R
#B0647090A	Italy	RA	12 Months/F	INJ	U	06Apr2010-06Apr2010	06Apr2010	U/0 Days	Convulsion*, Loss of consciousness*, Muscle spasms*, Eye disorder*	R
#D0065892A	Germany	RA	14 Months/M	INJ	U	05Oct2009-05Oct2009	07Oct2009	U/2 Days	Convulsion*, Microcytic anaemia*, Vomiting*, Hyponatraemia*, Upper respiratory tract infection*, Fatigue*, Erythema*, Eye rolling*, Muscle twitching*, Fall*, Acidosis*, Polyuria*, Polydipsia*	U
#B0646907A	Netherlands	RA	11 Months/M	INJ	U	23Sep2009-23Sep2009	23Sep2009	U/2 Hours	Convulsion*, Pallor*, Gaze palsy*, Loss of consciousness*, Hypotonia*, Pyrexia*, Pain*, Fatigue*	R
#D0067158A	Germany	RA	Infant/M	INJ, INJ, INJ, INJ	U, U, U, U	04Jul2008-04Jul2008, 12Aug2008-12Aug2008, 25Sep2008-25Sep2008, 24Apr2009-24Apr2009	01Aug2008	U/1 Months, U/0 Months, U/0 Years, U/86 Days	Convulsion*, Partial seizures*, Cerebral atrophy*, Demyelination*, Petechiae*, Developmental delay*, Schamberg's disease*, Rhinitis*	N

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#B0679302A	Italy	MD,RA	4 Months/M	INJ	U	14Jan2010-14Jan2010	16Jan2010	U/2 Days	Convulsion, Pyrexia	R
#B0667521A	Thailand	HP,RP	7 Months/M	INJ	U	28Jul2010-28Jul2010	28Jul2010	U/20 Hours	Convulsion, Pyrexia*	R
#D0065888A	Germany	RA	3 Years/M	INJ	U	1 Days		U/Unknown	Convulsion*, Pyrexia*	U
#B0659191A	Italy	RA	13 Months/M	INJ	U	31Mar2010-31Mar2010	31Mar2010	U/0 Days	Convulsion*, Pyrexia*	R
#B0604259A	Pakistan	MD	4 Months/M	IM	U	1 Days	21Oct2009	U/Unknown	Convulsion*, Pyrexia*	I
#D0067210A	Germany	RA	5 Months/F	INJ	.5ML	12Jan2010-12Jan2010	12Jan2010	U/0 Days	Convulsion*, Pyrexia*, Grand mal convulsion*, Febrile convulsion*, Tachycardia*	R

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#B0659953A	Belgium	CO,MD	17 Months/M	INJ	U	02Jun2010-02Jun2010	02Jun2010	U/0 Days	Convulsion*, Pyrexia*, Pyrexia*, Injection site swelling*, Injection site induration*, Livedo reticularis*, Injection site erythema*, Convulsion*, Hypertonia*, Staring*, Depressed level of consciousness*, Injection site warmth*, Periventricular leukomalacia*	S
#D0065885A	Germany	RA	3 Months/M	INJ	U	26Nov2009-26Nov2009	26Nov2009	U/0 Days	Convulsion*, Pyrexia*, Staring*, Eye rolling*, Muscle twitching*	R
#B0612916A	Spain	RA	2 Months/M	INJ	U	10Nov2009-10Nov2009	10Nov2009	U/0 Days	Convulsion*, Respiratory arrest*	U
#B0678409A	Poland	MD,RA	1 Months/U	INJ	U	09Sep2010-09Sep2010	09Sep2010	U/0 Days	Crying	R
B0609126A	France	MD	3 Months/M	INJ	U	20Oct2009-20Oct2009	20Oct2009	U/2 Hours	Crying*	R

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#B0624901A	France	RA	2 Months/M	INJ	U	27Nov2009-27Nov2009	27Nov2009	U/Same day	Crying*	R
B0630220A	France	MD	2 Months/U	INJ	U	1 Days		U/See text	Crying*	R
#B0624467A	Poland	RA	6 Weeks/M	INJ	U	27Apr2009-27Apr2009	27Apr2009	U/0 Days	Crying*	R
#B0630343A	Poland	RA	7 Weeks/F	INJ	U	22Sep2009-22Sep2009	22Sep2009	U/0 Days	Crying*	R
#B0664932A	Poland	RA	3 Months/U	INJ	U	21May2010-21May2010	21May2010	U/Hours	Crying*	R
#B0676318A	Poland	MD,RA	8 Months/U	INJ	U	27Aug2010-27Aug2010	27Aug2010	U/0 Days	Crying*	R

#B0661049A	Italy	RA	2 Months/F	INJ	U	18May2010-18May2010	18May2010	U/0 Days	Crying*, Hyperaemia, Decreased appetite*	R
B0622906A	Netherlands	RA	98 Days/F	IM	1ML	19May2009-U		U/1 Days	Crying*, Inflammation*, Chills*, Myoclonus*	R
#B0638559A	Poland	MD	6 Weeks/F	INJ	U	02Mar2010-02Mar2010	06Mar2010	U/4 Days	Crying*, Injection site reaction*, Inflammation*, Pyrexia*, Decreased appetite*, Diarrhoea*	R
#B0643730A	Ireland	RA	6 Months/M	INJ	U	09Mar2010-09Mar2010	10Mar2010	U/1 Days	Crying*, Irritability*	R
B0635730A	France	HP	2 Months/M	INJ	U	08Jan2010-08Jan2010	08Jan2010	U/Same day	Crying*, Irritability*, Agitation*	R
D0068630A	Germany	MD,RP	5 Months/F	INJ	U	27Apr2010-27Apr2010	28Apr2010	U/1 Days	Crying, Muscle spasms, Pyrexia	R

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#B0677163A	Italy	MD,RA	5 Months/M	INJ	U	19Nov2009-19Nov2009	19Nov2009	U/3 Hours	Crying, Oedema peripheral, Asthenia, Weight decreased, Hypotonia, Pyrexia, Injection site oedema, Decreased appetite	U
B0631136A	France	MD	8 Weeks/M	INJ	U	02Feb2010-02Feb2010	02Feb2010	U/4 Hours	Crying*, Pyrexia*	U
#B0607477A	Poland	RA	4 Months/M	INJ	U	06Oct2009-06Oct2009	10Oct2009	U/4 Days	Crying*, Pyrexia*	R
#B0639417A	Poland	RA	4 Months/U	INJ	U	12Jan2010-12Jan2010	12Jan2010	U/9 Hours	Crying*, Pyrexia*	R
B0620483A	Netherlands	RA	75 Days/M	IM	U	16Jun2009-U		U/3 Minutes	Crying*, Pyrexia*, Pain*, Rash*, Insomnia*	R
B0622905A	Netherlands	RA	89 Days/M	IM	1ML	25Jun2009-U		U/5 Hours	Crying*, Pyrexia*, Skin discolouration*, Petechiae*, Swelling*, Crying*	R

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#B0622098A	Poland	RA	16 Weeks/U	INJ	U	03Nov2009-03Nov2009	20Oct2009	U/5 Hours	Crying*, Restlessness*	R
#B0625403A	Poland	RA	2 Months/U	INJ	U	02Dec2009-02Dec2009	02Dec2009	U/0 Days	Crying*, Restlessness*	R
#D0068107A	Germany	MD,RP	4 Months/M	INJ	U	02Jun2010-02Jun2010	02Jun2010	U/4 Hours	Depressed level of consciousness*	R
#B0602021A	Italy	RA	3 Months/M	INJ	U	17Aug2009-17Aug2009	19Aug2009	U/2 Days	Depressed level of consciousness*	R
#B0675506A	Italy	RA	4 Months/M	INJ	U	10Aug2010-10Aug2010	10Aug2010	U/0 Days	Depressed level of consciousness, Asthenia, Hypotonia	R
#B0599801A	Netherlands	RA	2 Months/M	INJ	U	26May2009-26May2009	26May2009	U/3 Seconds	Depressed level of consciousness*, Crying*, Hyperhidrosis*, Vasodilatation*, Gaze palsy*, Depressed level of consciousness*, Pyrexia*,	R

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									Inflammation*	
#B0602787A	Netherlands	RA	11 Months/M	INJ	U	27May2009-27May2009	27May2009	U/2 Hours	Depressed level of consciousness*, Crying*, Pyrexia*	R
#B0672324A	Netherlands	HP,RA	1 Years/F	INJ	U	27Apr2010-27Apr2010	27Apr2010	U/3 Seconds	Depressed level of consciousness, Crying, Pyrexia, Decreased appetite, Inflammation, Oligodipsia, Abnormal behaviour, Rash	R
#B0672304A	Netherlands	HP,RA	4 Months/M	INJ	U	06Apr2010-06Apr2010	01Apr2010	U/Hours	Depressed level of consciousness, Crying, Pyrexia, Oligodipsia, Malaise, Pallor	R
#B0657949A	Italy	MD,RA	6 Months/M	INJ	U	26Feb2010-26Feb2010, 21May2010-21May2010	27Feb2010	U/1 Days, U/U	Depressed level of consciousness*, Cyanosis*, Hypotonia*, Skin ulcer*, Crying*	R
#B0662732A	Malaysia	MD,RP	8 Months/M	INJ	.5ML	02Jun2010-02Jun2010	03Jun2010	U/1 Days	Depressed level of consciousness*, Decreased eye contact*, Abnormal behaviour*, Decreased activity*, Pyrexia*	U

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#B0641793A	Netherlands	RA	2 Months/F	INJ	U	31Jul2009-31Jul2009	31Jul2009	U/4 Hours	Depressed level of consciousness*, Depressed level of consciousness*, Respiration abnormal*, Pallor*, Cyanosis*, Hypotonia*, Oligodipsia*, Pyrexia*	R
#B0665677A	Italy	MD,RA	14 Months/F	INJ	U	19Mar2010-19Mar2010	19Mar2010	U/0 Days	Depressed level of consciousness*, Hyperpyrexia*, Hypotonia*, Staring*	R
#B0629752A	Italy	RA	4 Months/M	INJ	U	20Feb2009-20Feb2009	20Feb2009	U/0 Days	Depressed level of consciousness*, Hypotonia*	R
#B0646879A	Netherlands	RA	4 Months/M	INJ	U	22Jul2009-22Jul2009	22Jul2009	U/2 Hours	Depressed level of consciousness*, Hypotonia*, Crying*, Insomnia*, Inflammation*, Pain*	R
#B0657314A	Italy	RA	2 Months/F	INJ	U	22Feb2010-22Feb2010	22Feb2010	U/5 Hours	Depressed level of consciousness*, Hypotonia*, Hyperhidrosis*	U

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#B0667070A	Italy	RA	3 Months/F	INJ	U	U	10Jun2010	U/Unknown	Depressed level of consciousness, Hypotonia, Pallor	R
#B0626503A	Italy	RA	4 Months/F	INJ	U	12May2009-12May2009	12May2009	U/0 Days	Depressed level of consciousness*, Hypotonia*, Pallor*	R
#B0641821A	Italy	RA	2 Months/M	INJ	U	27Jan2010-27Jan2010	27Jan2010	U/0 Days	Depressed level of consciousness*, Hypotonia*, Pallor*	R
#B0676060A	Italy	RA	11 Months/M	INJ	U	30Jun2010-30Jun2010	30Jun2010	U/0 Days	Depressed level of consciousness*, Hypotonia*, Rash*, Decreased appetite*, Pyrexia*	R
#B0627982A	Italy	RA	2 Months/M	INJ	U	1 Days	27Oct2009	U/Unknown	Depressed level of consciousness*, Hypotonia*, Vomiting*	R
#B0679534A	Netherlands	RA	2 Months/M	INJ	U	28Jul2010-28Jul2010	01Jul2010	U/Hours	Depressed level of consciousness, Inflammation, Oligodipsia*, Pyrexia	R

#B0641738A	Netherlands	RA	1 Months/F	INJ	U	03Aug2009-03Aug2009	03Aug2009	U/0 Days	Depressed level of consciousness*, Inflammation*, Pallor*, Oligodipsia*, Pyrexia*	R
#B0662525A	Italy	MD,RA	5 Months/F	INJ	U	09Dec2009-09Dec2009, 30Sep2009-30Sep2009	09Dec2009	U/0 Days, U/U	Depressed level of consciousness*, Microcytic anaemia*, Crying*, Agitation*, Sopor*, Injection site pain*, Hypotonia*	U
#B0665333A	Italy	MD,RA	14 Months/M	INJ	U	03Dec2009-03Dec2009	03Dec2009	U/0 Days	Depressed level of consciousness, Muscular weakness, Pyrexia	R
#B0667970A	Netherlands	RA	3 Months/M	INJ	U	22Feb2010-22Feb2010	01Feb2010	U/Hours	Depressed level of consciousness, Oligodipsia, Pyrexia, Vomiting	R
#B0651952A	Netherlands	RA	1 Months/M	INJ	U	26Oct2009-26Oct2009	26Oct2009	U/0 Days	Depressed level of consciousness*, Pain*, Inflammation*, Pyrexia*	R
#B0616676A	Netherlands	HP,RA	11 Months/M	IM	U	08Jun2009-08Jun2009	01Jun2009	U/7 Hours	Depressed level of consciousness*, Pyrexia*, Inflammation*, Rash*, Pruritus*, Insomnia*	R

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#B0652034A	Netherlands	RA	3 Months/F	INJ	U	21Sep2009-21Sep2009	21Sep2009	U/2 Hours	Depressed level of consciousness*, Rash*, Pyrexia*	R
#B0627290A	Netherlands	RA	3 Months/F	INJ	U	26Nov2009-26Nov2009	26Nov2009	U/2 Hours	Depressed level of consciousness*, Respiratory disorder*, Petechiae*, Hypotonia*, Somnolence*, Diarrhoea*, Crying*, Pyrexia*, Pallor*	R
#B0678021A	Italy	MD,RA	3 Months/M	INJ	U	16Jun2006-16Jun2006, 28Jul2006-28Jul2006, 05Feb2007-05Feb2007	16Jun2006	U/0 Days, U/U, U/U	Encephalopathy	N
#B0649288A	Italy	RA	4 Months/F	INJ	U	22Mar2010-22Mar2010	23Mar2010	U/1 Days	Encephalopathy*, Altered state of consciousness*, Encephalitis*, Hypotonia*, Hyperreflexia*	I
#B0607020A	Czech Republic	MD	5 Months/M	INJ	U	19Oct2009-19Oct2009	26Oct2009	U/7 Days	Epilepsy*	R
#B0680077A	Italy	MD,RA	3 Months/F	INJ	U	26Jul2010-26Jul2010	01Aug2010	U/6 Days	Epilepsy*	N

#B0657965A	Czech Republic	RA	4 Months/F	INJ	U	06May2009-06May2009, 09Jun2009-09Jun2009	09Jun2009	U/0 Days, U/34 Days	Epilepsy*, Loss of consciousness*, Convulsions local*, Methylmalonic aciduria, Vitamin B12 deficiency	S
#B0645066A	Italy	MD,RA	12 Months/F	INJ	U	20Nov2009-20Nov2009	21Nov2009	U/1 Days	Epilepsy*, Partial seizures*, Cerebrovascular disorder*, Apnoea, Joint hyperextension, Pyrexia	I
#B0670231A	Italy	MD,RA	3 Months/F	INJ	U	19Nov2007-19Nov2007		U/0 Days	Febrile convulsion	U
#B0604993A	Czech Republic	RA	5 Months/F	INJ	U	07Oct2009-07Oct2009	08Oct2009	U/1 Days	Febrile convulsion*	R
#D0067139A	Germany	RA	3 Months/F	INJ	.5ML	15Mar2010-15Mar2010	15Mar2010	U/0 Days	Febrile convulsion*	R
#D0067789A	Germany	RA	3 Months/M	INJ	.5ML	09Feb2010-09Feb2010	09Feb2010	U/0 Days	Febrile convulsion*	R

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#D0068084A	Germany	HP,RA	1 Years/F	INJ	U	20May2010-20May2010	20May2010	U/0 Days	Febrile convulsion*	R
#D0068405A	Germany	RA	13 Months/M	INJ	.5ML	05Jul2010-05Jul2010, 29Sep2009-29Sep2009	05Jul2010	U/0 Days, U/U	Febrile convulsion*	R
#B0631029A	Italy	RA	10 Months/M	INJ	U	U	29Dec2009	U/Unknown	Febrile convulsion*	I
#B0643070A	Italy	RA	3 Months/M	INJ	U	08Mar2010-08Mar2010	08Mar2010	U/0 Days	Febrile convulsion*	R
#B0672628A	Italy	MD,RA	4 Months/M	INJ	U	04Aug2010-04Aug2010, 16Jun2010-16Jun2010	07Aug2010	U/3 Days, U/U	Febrile convulsion*	R
#B0617222A	Netherlands	RA	Child/U	INJ	U	19Jan2009-19Jan2009		U/Unknown	Febrile convulsion*	U

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#B0645073A	South Africa	HP	3 Months/U	INJ	U	1 Days		U/Unknown	Febrile convulsion*	U
#B0636815A	Spain	RA	2 Months/F	INJ	U	26Jan2010-26Jan2010	26Jan2010	U/0 Days	Febrile convulsion*	R
#D0068599A	Germany	RA	22 Months/F	INJ	.5ML	23Jul2010-23Jul2010	23Jul2010	U/0 Days	Febrile convulsion*, Convulsion*, Pyrexia*	R
#B0656746A	Italy	RA	12 Months/M	INJ	U	10May2010-10May2010	10May2010	U/0 Days	Febrile convulsion*, Convulsion*, Pyrexia*	R
#B0612159A	France	RA	7 Months/F	INJ	U	23Jun2009-23Jun2009	23Jun2009	U/12 Hours	Febrile convulsion*, C-reactive protein increased*, White blood cell count increased*	R
#B0675844A	Czech Republic	CO,MD,RA	13 Months/F	INJ	U	31Aug2010-31Aug2010	01Sep2010	U/1 Days	Febrile convulsion, Depressed level of consciousness, Convulsion, Epilepsy, Vaccination complication, Fatigue, Crying, Chills,	N

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									Somnolence, Pyrexia	
#D0068664A	Germany	MD	14 Months/M	INJ	.5ML	10Jun2010-10Jun2010	15Jun2010	U/5 Days	Febrile convulsion*, Depressed level of consciousness, Cyanosis, Eye rolling, Posture abnormal, Dyskinesia, Pyrexia, Infection, Pharyngeal erythema	R
#B0650414A	Sweden	RA	12 Months/F	INJ	U	08Apr2010-08Apr2010	08Apr2010	U/0 Days	Febrile convulsion*, Depressed level of consciousness*, Tonic convulsion*, Hypotonia*, Crying*	R
#D0068398A	Germany	MD,RA	8 Months/M	INJ	U	02Jul2010-02Jul2010	03Jul2010	U/1 Days	Febrile convulsion*, Gaze palsy*, Respiratory arrest*, Respiratory tract infection*, Pharyngeal erythema*, Feeling of relaxation*, Skin discolouration*, Vaccination complication*	R
#B0669438A	Poland	MD,RA	16 Months/M	INJ	U	10Jun2010-10Jun2010	11Jun2010	U/1 Days	Febrile convulsion, Gaze palsy, Unresponsive to stimuli, Pyrexia	R

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#B0612164A	France	RA	18 Months/M	INJ	U	16Nov2009-16Nov2009	17Nov2009	U/1 Days	Febrile convulsion*, Grand mal convulsion*, Pyrexia*	R
#D0067937A	Germany	RA	6 Months/F	INJ	.5ML	01Jun2010-01Jun2010, 16Feb2010-16Feb2010	02Jun2010	U/1 Days, U/U	Febrile convulsion*, Hyperpyrexia*	R
#D0067186A	Germany	RA	14 Months/F	INJ	U	18Dec2009-18Dec2009	18Dec2009	U/0 Days	Febrile convulsion*, Loss of consciousness*, Cataplexy*, Gaze palsy*, Pyrexia*, Vaccination complication*	R
#B0656946A	Netherlands	RA	1 Months/M	INJ	U	25Nov2009-25Nov2009	25Nov2009	U/8 Hours	Febrile convulsion*, Loss of consciousness*, Gaze palsy*, Pain*, Skin warm*, Respiration abnormal*, Pyrexia*, Crying*	R
#B0629094A	Italy	RA	11 Months/M	INJ, INJ	U, U	20Aug2009-20Aug2009, U, U	20Aug2009	U/0 Days, U/1 Days, U/U	Febrile convulsion*, Loss of consciousness*, Grand mal convulsion*, Cyanosis*, Tremor*, Staring*, Vomiting*, Pyrexia*	R
#D0067255A	Germany	RA	14 Months/M	INJ	U	23Feb2010-23Feb2010	23Feb2010	U/0 Days	Febrile convulsion*, Muscle twitching*	R

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#B0651935A	Italy	RA	2 Months/F	INJ, INJ	U, U	01Feb2010-01Feb2010, 29Mar2010-29Mar2010	02Feb2010	U/1 Days, U/0 Days	Febrile convulsion*, Nystagmus*, Visual impairment*, Eye movement disorder*, Pyrexia*, Pyrexia*	R
#D0068851A	Germany	MD,RA,RP	3 Months/F	INJ	U	02Sep2010-02Sep2010	02Sep2010	U/5 Hours	Febrile convulsion, Pneumonia aspiration, Depressed level of consciousness, Staring, Rhinitis	U
#D0069021A	Germany	MD,RA	13 Months/F	INJ	U	05Aug2010-05Aug2010	05Aug2010	U/10 Hours	Febrile convulsion, Poor quality sleep, Chills, Eye movement disorder, Pallor, Cyanosis, Ill-defined disorder, Postictal state, Pharyngeal erythema, Pyrexia	U
#B0645518A	Austria	RA	1 Years/M	INJ	U	05Feb2010-05Feb2010	05Feb2010	U/2 Hours	Febrile convulsion*, Pyrexia*	R
#D0063432A	Germany	RA	18 Months/F	INJ	.5ML	22Sep2009-22Sep2009, 28May2008-28May2008, 14Jul2008-14Jul2008, 13Mar2009-13Mar2009	22Sep2009	U/0 Days, U/U, U/U, U/U	Febrile convulsion*, Pyrexia*	R

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#D0068082A	Germany	HP,RA	4 Months/M	INJ	U	14Jun2010-14Jun2010	14Jun2010	U/0 Days	Febrile convulsion*, Pyrexia*	N
#D0069012A	Germany	RA	3 Months/M	INJ	.5ML	22Sep2010-22Sep2010, 25Aug2010-25Aug2010	22Sep2010	U/0 Days, U/U	Febrile convulsion*, Pyrexia*	R
#B0630476A	Italy	RA	11 Months/F	INJ	U	18Jan2010-18Jan2010	19Jan2010	U/1 Days	Febrile convulsion*, Pyrexia*	U
#B0607056A	Poland	RA	12 Months/F	INJ	U	08Oct2009-08Oct2009	09Oct2009	U/1 Days	Febrile convulsion*, Pyrexia*	R
#B0658814A	South Africa	MD	20 Months/M	INJ	U	29May2010-29May2010	29May2010	U/0 Days	Febrile convulsion*, Pyrexia*	R
#B0670625A	Poland	CO,MD,RA	6 Weeks/M	INJ	U	06Aug2010-06Aug2010	06Aug2010	U/2 Hours	Febrile convulsion*, Pyrexia*, Cyanosis*, Somnolence*, Chills*, Decreased appetite*	R

#D0068260A	Germany	MD	23 Months/M	INJ	.5ML	11May2010-11May2010	11May2010	U/0 Days	Febrile convulsion*, Pyrexia*, Diarrhoea*, Gaze palsy*, Grand mal convulsion*, Pallor*, Vomiting*, Gastroenteritis*	R
#D0068440A	Germany	RA	5 Months/M	INJ	.5ML	04Mar2010-04Mar2010	01Feb2010	U/U	Febrile convulsion*, Pyrexia*, Faeces discoloured*, Diarrhoea*, Convulsion*, Musculoskeletal stiffness*, Pancytopenia*, Sleep disorder*	R
#D0068914A	Germany	MD,RA	14 Months/F	INJ	.5ML	16Oct2009-16Oct2009, 20Nov2009-20Nov2009, 07Jan2010-07Jan2010, 20Sep2010-20Sep2010	20Sep2010	U/0 Days, U/U, U/U, U/U	Febrile convulsion*, Pyrexia*, Fatigue*, Gaze palsy*, Loss of consciousness*, Grand mal convulsion*, Oxygen saturation decreased*, Disorientation*, Somnolence*	R
#D0068403A	Germany	RA	14 Months/F	INJ	.5ML	28Jun2010-28Jun2010, 27Jul2009-27Jul2009, 21Sep2009-21Sep2009, 12Nov2009-12Nov2009	28Jun2010	U/0 Days, U/U, U/U, U/U	Febrile convulsion*, Pyrexia*, Grand mal convulsion*, Fatigue*, Abnormal behaviour*	R
#D0066156A	Germany	MD	12 Months/M	INJ	U	14Jan2010-14Jan2010	15Jan2010	U/1 Days	Febrile convulsion*, Pyrexia*, Injection site swelling*, Injection site erythema*	R

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#B0669272A	Italy	OT,RA	17 Months/M	INJ, INJ, INJ	U, U, U	1 Days, 1 Days, 1 Days	14Jun2010	U/Unknown, U/Unknown, U/Unknown	Febrile convulsion, Pyrexia, Pyrexia	U
#B0660128A	Netherlands	RA	11 Months/M	INJ	U	25Mar2010-25Mar2010	25Mar2010	U/30 Minutes	Febrile convulsion*, Respiratory disorder*, Apnoea*, Loss of consciousness*, Pallor*, Cyanosis*, Drooling*, Staring*, Convulsion*, Rash*, Depressed level of consciousness*, Pyrexia*	R
#D0068402A	Germany	RA	8 Weeks/M	INJ	U	15Jun2010-15Jun2010	15Jun2010	U/0 Days	Febrile convulsion*, Status epilepticus*, Fatigue*, Restlessness*, Staring*, Body temperature increased*	R
#D0066596A	Germany	MD	12 Months/M	INJ	.5ML	02Feb2010-02Feb2010	02Feb2010	U/0 Days	Febrile convulsion*, Unresponsive to stimuli*, Pyrexia*, Leukopenia*, Neutropenia*, Decreased appetite*, Decreased appetite*, Bronchitis*, Upper respiratory tract infection*, Rhinitis*, Asthenia*, Hyperpyrexia*	R
#B0616473A	Italy	RA	11 Months/F	INJ	1VIAL	25Nov2009-25Nov2009	25Nov2009	U/0 Days	Febrile convulsion*, Upper respiratory tract inflammation*	R

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#B0605673A	France	MD	3 Months/U	INJ	U	01Jan2009-01Jan2009	01Jan2009	U/1 Weeks	Febrile convulsion*, Wrong technique in drug usage process*	R
#D0066441A	Germany	PH,RA	4 Months/F	INJ	U	14Jan2010-14Jan2010	14Jan2010	U/2 Days	Fontanelle bulging*, Rash macular*, Cerebral ventricle dilatation, Viral infection, Pyrexia*, General physical health deterioration*, Restlessness*, Screaming	U
#B0650525A	Australia	RA	6 Months/F	INJ	.5MG	23Mar2010-23Mar2010	23Mar2010	U/0 Days	Grand mal convulsion*, Chills*, Feeling hot*, Crying*, Pyrexia*	R
#D0067144A	Germany	RA	15 Months/M	INJ	.5ML	25Feb2010-25Feb2010	26Feb2010	U/1 Days	Grand mal convulsion*, Febrile convulsion*, Opisthotonus*, Pyrexia*, Diarrhoea*	R
#B0669299A	Italy	MD,RA	6 Months/M	INJ	U	26May2010-26May2010	26May2010	U/0 Days	Grand mal convulsion, Loss of consciousness, Gaze palsy, Cyanosis, Cyanosis, Pyrexia*, Salivary hypersecretion, Somnolence, Hyperaemia, Escherichia urinary tract infection*, Electroencephalogram abnormal	U

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#B0661753A	Poland	RA	2 Years/F	INJ	U	26Apr2010-26Apr2010	27Apr2010	U/1 Days	Grand mal convulsion*, Loss of consciousness*, Pyrexia*	R
#B0677079A	Italy	RA	2 Months/F	INJ	U	20May2010-20May2010	21May2010	U/0 Days	Grand mal convulsion, Musculoskeletal stiffness, Foaming at mouth, Pyrexia	R
#B0630482A	Italy	RA	3 Months/F	INJ	U	15Jan2010-15Jan2010	15Jan2010	U/0 Days	Grand mal convulsion*, Pyrexia*	R
#B0600406A	Italy	RA	17 Months/F	INJ	U	01Sep2009-01Sep2009	01Sep2009	U/0 Days	Grand mal convulsion*, Pyrexia*, Hypotonia*	R
#B0629291A	Italy	RA	5 Months/F	INJ	.5ML	25Jun2009-25Jun2009	26Jun2009	U/0 Days	Grand mal convulsion*, Pyrexia*, Restlessness*, Vomiting*, Febrile convulsion*	R
D0068384A	Germany	MD	2 Months/M	INJ	U	16Jun2010-16Jun2010	16Jun2010	U/3 Hours	Hyperaesthesia, Pyrexia	R

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#B0642119A	Italy	RA	2 Months/M	INJ	U	11Mar2010-11Mar2010	11Mar2010	U/0 Days	Hypersomnia*, Staring*, Vomiting*	R
#B0623099A	Italy	RA	2 Months/F	INJ	U	06Oct2009-06Oct2009	07Oct2009	U/1 Days	Hypertonia*, Irritability*, Crying*, Dyskinesia*	I
#B0672342A	Italy	MD,RA	4 Months/M	INJ	U	06Aug2010-06Aug2010	06Aug2010	U/4 Hours	Hyporeflexia, Pallor, Protrusion tongue	R
#B0657899A	France	MD	5 Months/M	INJ	U	01Jan2010-01Jan2010	27May2010	U/1 Months	Hypotonia*, Asthenia*, Areflexia*	U
#B0675230A	Spain	PH	4 Months/F	INJ	U	1 Days, 30Jul2010-30Jul2010	30Jul2010	U/0 Days, U/U	Hypotonia*, Atrial septal defect*, Pallor*, Urinary tract infection*, Regurgitation*, Somnolence*, Vomiting*, Pyrexia*	R
#B0670268A	Poland	MD,RA	1 Months/U	INJ	U	21Jul2010-21Jul2010	22Jul2010	U/1 Days	Hypotonia, Cough	R

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B0678742A	Netherlands	HP,RA	2 Months/F	INJ	U	25May2010-25May2010		U/Unknown	Hypotonia, Crying, Pyrexia	R
#B0665519A	Ireland	RA	10 Months/M	INJ, INJ	U, U	19May2010-19May2010, 1 Days	01May2010	U/12 Hours, U/Unknown	Hypotonia*, Hypotonia*, Pyrexia*	R
#B0666464A	Ireland	MD,RA	1 Years/M	INJ	U	09Jul2010-09Jul2010	09Jul2010	U/0 Days	Hypotonia, Injection site inflammation, Injection site erythema, Body temperature increased	R
#B0668864A	Italy	MD,RA	2 Months/M	INJ	U	09Feb2010-09Feb2010	16Feb2010	U/7 Days	Hypotonia*, Muscle spasms*	I
#B0630334A	Poland	RA	5 Months/M	INJ	U	29Dec2009-29Dec2009	29Dec2009	U/11 Hours	Hypotonia*, Pallor*, Hypotonia*	R
#B0680732A	Italy	MD,RA	2 Months/M	INJ	U	09Aug2010-09Aug2010	13Aug2010	U/4 Days	Hypotonia*, Somnolence*, Irritability*, Pyrexia*	R

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#B0632565A	Italy	RA	5 Months/M	INJ	U	28Jan2010-28Jan2010	31Jan2010	U/3 Days	Hypotonia*, Vomiting*, Hypothermia*	R
#B0670546A	Spain	RA	6 Months/F	INJ	U	29Jul2010-29Jul2010	29Jul2010	U/9 Hours	Hypotonic-hyporesponsive episode	R
B0605647A	Brazil	MD,RP	1 Months/M	INJ	U	21Aug2009-21Aug2009	23Aug2009	U/2 Days	Hypotonic-hyporesponsive episode*	R
B0616506A	Brazil	MD	2 Months/M	INJ	.5ML	01Dec2009-01Dec2009	03Dec2009	U/2 Days	Hypotonic-hyporesponsive episode*	R
#B0674108A	France	RA	3 Months/F	INJ	U	02Aug2010-02Aug2010	04Aug2010	U/2 Days	Hypotonic-hyporesponsive episode*	R
D0063431A	Germany	MD	15 Months/M	INJ	U	30Oct2009-30Oct2009	01Nov2009	U/56 Hours	Hypotonic-hyporesponsive episode*	R

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#B0636539A	Poland	RA	3 Months/U	INJ	U	18Jan2010-18Jan2010	18Jan2010	U/0 Days	Hypotonic-hyporesponsive episode*	R
#B0625456A	Spain	RA	2 Months/M	INJ	U	23Nov2009-23Nov2009	23Nov2009	U/0 Days	Hypotonic-hyporesponsive episode*	R
#B0671819A	Poland	MD,RA	4 Months/F	INJ	U	11Aug2010-11Aug2010	12Aug2010	U/22 Hours	Hypotonic-hyporesponsive episode, Apathy, Hypotonia, Somnolence, Vomiting	U
#D0067783A	Germany	RA	4 Months/F	INJ	.5ML	23Apr2010-23Apr2010, 03Mar2010-03Mar2010	23Apr2010	U/0 Days, U/U	Hypotonic-hyporesponsive episode*, Body temperature increased*, Febrile convulsion*	R
#B0619564A	Switzerland	RA	4 Months/M	INJ	U	12Nov2009-12Nov2009	12Nov2009	U/0 Days	Hypotonic-hyporesponsive episode*, Crying*, Pallor*, Feeling of body temperature change*	R
#D0066260A	Germany	RA	3 Months/F	INJ, INJ	.5ML, .5ML	25Nov2009-25Nov2009, 26Oct2009-26Oct2009, 20Jan2010-20Jan2010	25Nov2009	U/8 Hours, U/0 Days, U/U	Hypotonic-hyporesponsive episode*, Crying*, Pallor*, Hypotonia*, Injection site erythema*, Body temperature increased*	U

D0066579A	Germany	MD	2 Months/F	INJ	U	21Dec2009-21Dec2009	21Dec2009	U/0 Days	Hypotonic-hyporesponsive episode*, Crying*, Pallor*, Hypotonia*, Motor dysfunction*, Masked facies*	R
D0068033A	Germany	MD	5 Months/M	INJ	U	05Jun2009-05Jun2009	05Jun2009	U/0 Hours	Hypotonic-hyporesponsive episode*, Crying*, Pallor*, Hypotonia*, Motor dysfunction*, Masked facies*	R
#B0668109A	Poland	CO,MD	4 Months/M	INJ	U	27Jul2010-27Jul2010	27Jul2010	U/Immediate	Hypotonic-hyporesponsive episode*, Cyanosis*, Pallor*, Bradykinesia*	R
#B0632568A	Italy	RA	13 Months/F	INJ	U	03Feb2010-03Feb2010	03Feb2010	U/Immediate	Hypotonic-hyporesponsive episode*, Cyanosis*, Unresponsive to stimuli*, Hypotonia*, Areflexia*	R
#B0640404A	Poland	RA	3 Months/U	INJ	U	27Jan2010-27Jan2010	27Jan2010	U/Immediate	Hypotonic-hyporesponsive episode*, Decreased activity*, Pallor*, Somnolence*	R
#B0662920A	Netherlands	RA	2 Years/F	INJ	.5ML	04Jan2010-04Jan2010	04Jan2010	U/5 Hours	Hypotonic-hyporesponsive episode*, Depressed level of consciousness*, Gaze palsy*, Respiration abnormal*, Injection site inflammation*, Vomiting*,	R

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									Cold sweat*, Injection site pain*, Pallor*, Pyrexia*	
#B0662664A	Brazil	CO,MD	2 Months/M	INJ	U	17Jun2010-17Jun2010	17Jun2010	U/0 Days	Hypotonic-hyporesponsive episode*, Fatigue*, Respiratory disorder*, Pallor*, Pyrexia*	R
#D0067882A	Germany	MD,RA	5 Months/M	INJ	.5ML	21May2010-21May2010	21May2010	U/0 Days	Hypotonic-hyporesponsive episode*, Gaze palsy*, Hypotonia*, Mental impairment*, Feeling abnormal*, Neutropenia*	R
#B0663634A	Ireland	RA	4 Months/F	INJ, INJ	U, U	04Jun2010-04Jun2010, U	04Jun2010	U/8 Hours, U/Unknown	Hypotonic-hyporesponsive episode*, Hypotonic-hyporesponsive episode*	R
B0619284A	France	MD	2 Months/F	INJ	U	08Dec2009-08Dec2009	08Dec2009	U/3 Hours	Hypotonic-hyporesponsive episode*, Pallor*, Crying*, Hypersomnia*	R
#D0064102A	Germany	MD	15 Months/F	INJ	U	13Nov2009-13Nov2009	13Nov2009	U/6 Hours	Hypotonic-hyporesponsive episode*, Pallor*, Depressed level of consciousness*	R

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#B0661768A	France	RA	3 Months/F	INJ	U	04May2010-04May2010	04May2010	U/Hours	Hypotonic-hyporesponsive episode*, Pyrexia, Malaise*, Cyanosis*, General physical health deterioration*, Decreased eye contact*, Agitation*	R
#B0600645A	Poland	RA	2 Months/U	INJ	U	23Sep2009-23Sep2009	23Sep2009	U/0 Days	Hypotonic-hyporesponsive episode*, Restlessness*, Somnolence*	R
#D0068669A	Germany	RA	9 Weeks/F	INJ	.5ML	01Jul2010-01Jul2010	01Jul2010	U/0 Days	Hypotonic-hyporesponsive episode*, Skin discolouration*, Clonus*, Hypotonia*, Flatulence*	R
#D0067330A	Germany	MD	7 Months/F	INJ	U	25Mar2010-25Mar2010	25Mar2010	U/2 Hours	Infantile spasms*, Clonic convulsion*, Infantile spasms*, Gastroenteritis rotavirus*, Bronchitis*	U
#B0613669A	France	CO,MD	2 Months/M	INJ	U	12Aug2009-12Aug2009	01Aug2009	U/1 Weeks	Infantile spasms*, Gaze palsy*, Muscle spasms*, Sleep disorder*, Condition aggravated*, Infantile spasms*, Motor dysfunction*, Hypertonia*	R
#B0674954A	Greece	MD,RP	4 Months/F	INJ	U	U		U/5 Minutes	Loss of consciousness	R

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#B0636914A	Italy	RA	5 Months/F	INJ	U	15Feb2010-15Feb2010	16Feb2010	U/24 Hours	Loss of consciousness*, Cyanosis*, Epilepsy*, Hypotonia*, Asthenia*, Areflexia*, Pyrexia*	R
#B0651462A	Netherlands	RA	2 Months/F	INJ	U	03Nov2009-03Nov2009	03Nov2009	U/6 Hours	Loss of consciousness*, Gaze palsy*, Pallor*, Cyanosis*, Hypotonia*, Vomiting*	R
#B0674217A	Netherlands	RA	4 Months/F	INJ	U	07Jun2010-07Jun2010	07Jun2010	U/0 Minutes	Loss of consciousness*, Hypotonia*, Pallor*, Rash*, Injection site inflammation*, Cold sweat*, Lethargy*, Crying*	R
#B0640594A	Poland	RA	13 Months/M	INJ	U	27Jan2010-27Jan2010	27Jan2010	U/0 Days	Loss of consciousness*, Hypotonic-hyporesponsive episode*	R
#B0658389A	Spain	RA	4 Months/F	INJ	U	26Aug2008-26Aug2008	27Aug2008	U/6 Hours	Loss of consciousness*, Hypotonic-hyporesponsive episode*, Crying*, Hypotonia*, Pallor*	R
#B0663633A	Poland	RA	3 Months/U	INJ	U	27Apr2010-27Apr2010	28Apr2010	U/1 Days	Loss of consciousness*, Hypotonic-hyporesponsive episode*, Hypotonia*	R

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#B0635785A	Italy	RA	4 Months/F	INJ	U	31Mar2009-31Mar2009	04Apr2009	U/4 Days	Loss of consciousness*, Iron deficiency anaemia*, Hypotonia*, Pallor*, Eye disorder*, Muscle spasms*	U
#B0679304A	Italy	MD,RA	4 Months/F	INJ	U	07Sep2010-07Sep2010	07Sep2010	U/0 Days	Loss of consciousness, Pallor, Hypotonia	R
#B0666833A	Netherlands	HP,RA	4 Months/M	INJ	U	07Dec2009-07Dec2009	07Dec2009	U/45 Minutes	Loss of consciousness, Pallor, Hypotonia	R
#B0652045A	Netherlands	RA	3 Years/M	INJ	U	23Nov2009-23Nov2009	23Nov2009	U/7 Hours	Meningism*, Pyrexia, Crying*, Respiration abnormal*, C-reactive protein increased*	R
#B0604823A	Czech Republic	RA	6 Years/F	INJ	U	29Sep2009-29Sep2009	29Sep2009	U/0 Days	Monoparesis*	R
#D0067843A	Germany	MD	3 Months/F	INJ	.5ML	07May2010-07May2010	10May2010	U/3 Days	Monoparesis*, Mobility decreased*	I

#D0067112A	Germany	RA	4 Months/F	INJ	.5ML	05Oct2009-05Oct2009	05Oct2009	U/0 Days	Monoplegia*, Gait disturbance*	R
#D0068441A	Germany	RA	8 Weeks/F	INJ	.5ML	21May2010-21May2010	21May2010	U/0 Days	Motor developmental delay*, Hypotonia*, Fluid intake reduced*, Enteral nutrition*, Hyperpyrexia*, Rash*, Moaning*, Eyelid ptosis*, Fatigue*	N
#B0678411A	Poland	MD,RA	18 Months/U	INJ	U	21Sep2010-21Sep2010	21Sep2010	U/0 Days	Movement disorder, Pain, Injection site haematoma, Injection site oedema, Pyrexia	R
#B0599788A	Italy	RA	1 Years/F	INJ	U	16Oct2009-16Oct2009, 1 Days	16Oct2009	U/0 Days, U/U	Myoclonus*, Rash*, Vomiting*, Pyrexia*	U
#B0679806A	Slovakia	MD	3 Months/M	INJ	U	11Oct2010-11Oct2010	01Oct2010	U/Days	Paresis*	U
#D0068999A	Germany	PH	8 Months/M	INJ	U	25Mar2010-25Mar2010	07May2010	U/43 Days	Paresis cranial nerve, Ophthalmoplegia	R

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#D0068999B	Germany	PH	12 Months/M	INJ	U	21Jul2010-21Jul2010	01Sep2010	U/46 Days	Paresis cranial nerve, Ophthalmoplegia	N
#B0643340A	Poland	RA	17 Months/U	INJ	U	23Feb2010-23Feb2010	24Feb2010	U/1 Days	Paresis*, Pallor*, Tremor*, Injection site reaction*, Pyrexia*, Hypotonic-hyporesponsive episode*, Staring*	R
#B0667520A	Latvia	HP,RA	2 Months/F	INJ	U	08Mar2010-08Mar2010	12Mar2010	U/4 Days	Partial seizures, Convulsion, Dyspnoea	R
#B0664846A	Italy	RA	10 Months/M	INJ	U	06Jul2010-06Jul2010	06Jul2010	U/0 Days	Petit mal epilepsy, Hypotonia, Irritability	R
#B0670341A	Italy	RA	13 Months/M	INJ	U	26Jun2010-26Jun2010	01Jul2010	U/5 Days	Petit mal epilepsy*, Irritability, Eye rolling*	S
#B0599810A	Italy	RA	3 Months/M	INJ	U	17Sep2009-17Sep2009	17Sep2009	U/0 Days	Somnolence*, Decreased appetite*, Pyrexia*	I

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#D0069130A	Germany	MD,RA	24 Months/F	INJ	U	06Oct2010-06Oct2010	08Oct2010	U/2 Days	Somnolence, Fatigue, General physical health deterioration, Musculoskeletal stiffness, Hypotonia	R
#B0679316A	Switzerland	CO,RA	4 Months/M	INJ, INJ, INJ	U, U, U	01Nov2009-01Nov2009, 01Mar2009-01Mar2009, 01May2009-01May2009	01Mar2009	U/24 Hours, U/Unknown, U/Unknown	Speech disorder developmental, Dermatitis atopic, Viral infection, General physical health deterioration, Blister, Pruritus, Crying	N
#D0066581A	Germany	RA	5 Months/M	INJ, INJ, INJ, INJ	U, U, U, U	02Dec2005-02Dec2005, 13Sep2004-13Sep2004, 15Oct2004-15Oct2004, 25Nov2004-25Nov2004	01Dec2004	U/2 Months, U/1 Months, U/0 Months, U/0 Weeks	Speech disorder developmental*, Sensorimotor disorder*, Visual impairment*, Hypermetropia*, Astigmatism*, Anisometropia*, Vomiting*, Restlessness*, Disturbance in attention*, Gastroenteritis norovirus*, Iron deficiency anaemia*, Pneumonia respiratory syncytial viral*, Cough*, Pyrexia*, Fluid intake reduced*, Bronchitis*, Rales*, Pneumonia*, Pyrexia*, Cough*, Fluid intake reduced*	U
#B0641899A	Greece	MD,RA	2 Months/M	INJ	U	05Feb2010-05Feb2010	05Feb2010	U/10 Hours	Status epilepticus*, Grand mal convulsion*, Loss of consciousness*, Cyanosis*, Muscle spasms, Somnolence*, Pyrexia*	R

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#B0665503A	France	RA	16 Months/F	INJ	U	15Apr2010-15Apr2010	16Apr2010	U/1 Days	Status epilepticus*, Hypotonia*, Grand mal convulsion*, Pyrexia*	R
#B0677766A	Netherlands	HP,MD	5 Months/F	INJ	U	22Feb2010-22Feb2010	26Feb2010	U/4 Days	Status epilepticus, Retinal haemorrhage, Subdural effusion, Vomiting, Diarrhoea	N
#B0679695A	Italy	MD,RA	5 Months/M	INJ	U	21Jan2010-21Jan2010	21Jan2010	U/0 Days	Syncope, Loss of consciousness, Cyanosis, Pallor, Hypotonia, Vomiting, Pyrexia	R
#D0069116A	Germany	RA	9 Weeks/F	INJ	.5ML	27Sep2010-27Sep2010	28Sep2010	U/8 Hours	Tonic convulsion*, Cyanosis*	R
D0066180A	Germany	MD,RP	15 Months/M	INJ	U	22Jan2010-22Jan2010	22Jan2010	U/0 Days	Tremor*, Abasia*	R
#B0608538A	Italy	RA	1 Years/F	INJ	U	05Nov2009-05Nov2009	22Nov2009	U/17 Days	Tremor*, Head titubation*	U

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#B0657727A	Poland	RA	39 Days/U	INJ	U	08Feb2010-08Feb2010	08Feb2010	U/4 Hours	Tremor*, Somnolence*, Appetite disorder*, Restlessness*	R
#B0625578A	Czech Republic	RA	4 Months/M	INJ	.5ML	12Aug2009-12Aug2009	13Aug2009	U/1 Days	Unresponsive to stimuli*, Hypotonia*, Dyspnoea*	R
Psychiatric disorders										
#B0646200A	Italy	RA	2 Months/F	INJ	U	07Jan2010-07Jan2010	07Jan2010	U/0 Days	Agitation*, Erythema*, Urticaria*	R
#B0676434A	Ireland	HP,RA	4 Months/M	INJ	U	09Sep2010-09Sep2010	09Sep2010	U/0 Days	Agitation*, Injection site erythema*, Injection site swelling*, Injection site warmth*	R
D0067264A	Germany	HP,RA	U/F	INJ	U	09Sep2008-09Sep2008	09Sep2008	U/4 Hours	Anxiety*, Screaming*, Nervous system disorder*, Anxiety disorder due to a general medical condition*, Delusion*	U

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#B0613565A	Poland	RA	7 Weeks/M	INJ	U	14Oct2009-14Oct2009	26Oct2009	U/12 Days	Insomnia*, Restlessness*, Crying*, Head circumference abnormal*, Psychomotor hyperactivity*, Hypertonia*, Muscle spasticity*	U
D0069060A	Germany	HP,RA	3 Months/M	INJ	U	18Aug2010-18Aug2010	18Aug2010	U/0 Days	Restlessness, Crying, Hyperhidrosis	N
#B0653110A	Poland	RA	6 Months/U	INJ	U	04Mar2010-04Mar2010	04Mar2010	U/0 Days	Restlessness*, Crying*, Pyrexia*	R
#B0636273A	Poland	RA	1 Months/U	INJ	U	13Jan2010-13Jan2010	13Jan2010	U/0 Days	Restlessness*, Thirst decreased*, Pyrexia*, Pallor*, Crying*, Irritability*, Moaning*	I
#B0667682A	Latvia	RA	2 Months/F	INJ	U	20Apr2010-20Apr2010	20Apr2010	U/30 Minutes	Screaming*, Insomnia*, Body temperature increased*	R

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#B0640283A	South Africa	HP	13 Weeks/F	INJ	.5ML	09Feb2010-09Feb2010	10Feb2010	U/1 Days	Screaming*, Pyrexia*, Crying*	R
D0069181A	Germany	MD	Child/U	INJ	U	19Oct2010-19Oct2010	19Oct2010	U/1 Hours	Screaming, Restlessness	N
#B0658791A	Italy	RA	11 Months/F	INJ	U	20Apr2010-20Apr2010	20Apr2010	U/0 Days	Sleep disorder*	R
Respiratory, thoracic and mediastinal disorders										
#B0624662A	Austria	RA	3 Months/M	INJ	U	19Dec2009-19Dec2009	19Dec2009	U/0 Days	Apnoea*	R
#D0068940A	Germany	MD,RA	9 Weeks/F	INJ	U	08Sep2010-08Sep2010	08Sep2010	U/9 Hours	Apnoea*, Bradycardia*	R

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#D0065856A	Germany	RA	3 Months/F	INJ	U	25Sep2009-25Sep2009, 14Aug2009-14Aug2009	25Sep2009	U/4 Hours, U/U	Apnoea*, Convulsion*, Cyanosis*, Crying*, Hypotonia*, Blood lactic acid increased*	R
#B0665574A	Netherlands	RA	3 Months/M	INJ	.5ML	07Jan2010-07Jan2010	07Jan2010	U/4 Hours	Apnoea*, Cough*, Crying*	R
#B0633537A	Romania	RA	2 Months/F	INJ	U	1 Days	09Oct2009	U/Unknown	Apnoea*, Cyanosis*, Cough*	R
#B0661622A	Italy	RA	2 Months/F	INJ	U	03Mar2010-03Mar2010	03Mar2010	U/1 Hours	Apnoea*, Cyanosis, Tremor, Hypotonic-hyporesponsive episode*, Hypotonia*, Pyrexia*, Crying*, Food aversion	R
#B0622409A	Poland	RA	6 Weeks/U	INJ	U	15Sep2009-15Sep2009	15Sep2009	U/0 Days	Apnoea*, Hypotonic-hyporesponsive episode*, Pallor*, Crying*	R
#B0673252A	Netherlands	HP,RA	2 Months/F	INJ	U	01Jun2010-01Jun2010	01Jun2010	U/5 Hours	Apnoea, Loss of consciousness, Respiratory disorder, Cyanosis, Staring, Regurgitation, Crying, Vomiting	R

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#B0630350A	Poland	RA	1 Months/U	INJ	U	29Dec2009-29Dec2009	29Dec2009	U/3 Hours	Apnoea*, Muscle rigidity*, Skin discolouration*, Dyspnoea*, Injection site extravasation*, Somnolence*, Somnolence*, Crying*, Hypotonic-hyporesponsive episode*, Depressed level of consciousness*, Salivary hypersecretion*	R
#B0650954A	Netherlands	RA	53 Days/F	INJ	U	02Nov2009-02Nov2009	02Nov2009	U/10 Hours	Apnoea*, Pyrexia*	R
#D0067156A	Germany	RA	4 Months/M	INJ	U	23Feb2010-23Feb2010	25Feb2010	U/2 Days	Apnoea*, Pyrexia*, Hyperhidrosis*, Respiratory disorder*	R
#B0653466A	Netherlands	HP,RA	2 Months/F	INJ	U	04May2010-04May2010	04May2010	U/3 Minutes	Apparent life threatening event*, Apnoea, Cyanosis, Respiration abnormal, Pallor, Crying, Pyrexia	R
#D0064655B	Germany	MD,RA	3 Months/M	INJ	.5ML	16Nov2009-16Nov2009	16Nov2009	U/0 Days	Apparent life threatening event*, Cyanosis*, Hypotonia*, Gaze palsy*, Fatigue*, Somnolence*, Sleep apnoea syndrome*, Apnoea*, Apathy*, Gastroenteritis rotavirus*	U

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#B0671540A	Italy	MD,RA	11 Weeks/M	INJ, INJ	U, U	17May2010-17May2010, 28Jul2010-28Jul2010	17May2010	U/0 Days, U/Unknown	Apparent life threatening event*, Pyrexia*	R
#D0067792A	Germany	RA	3 Months/F	INJ	.5ML	14May2010-14May2010	15May2010	U/1 Days	Apparent life threatening event*, Resuscitation*, Fatigue*, Lethargy*, Hypotonia*	R
#D0069126A	Germany	RA	10 Weeks/F	INJ	.5ML	13Sep2010-13Sep2010	15Sep2010	U/2 Days	Apparent life threatening event*, Unresponsive to stimuli*, Pallor*, Eyelid disorder*, Dyspnoea*, Hypotonia*, Asthenia*, Crying*	R
#B0662719A	Singapore	MD	2 Months/M	INJ	U	23Jun2010-23Jun2010	23Jun2010	U/Minutes	Choking*, Hypotonic-hyporesponsive episode*, Pallor*, Asthenia*, Oxygen saturation decreased*, Respiratory rate increased*, Heart rate increased*	R
#D0067351A	Germany	MD,RP	5 Months/M	INJ	.5ML	08Apr2010-08Apr2010	08Apr2010	U/0 Minutes	Choking sensation*, Dyskinesia*, Vision blurred*, Aphasia*, Strabismus*, Erythema*, Staring*, Crying*	R

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#B0675850A	Hong Kong	MD	Infant/U	INJ, INJ, INJ	U, U, U	U, U, U		U/Unknown, U/Unknown, U/Unknown	Cough, Rhinorrhoea, Tracheitis, Influenza like illness	U
#B0636885A	South Africa	HP	2 Months/F	INJ	.5ML	23Feb2010-23Feb2010	26Feb2010	U/3 Days	Dyspnoea*, Cold sweat*, Crying*, Pain*, Apnoeic attack*	I
#B0653325A	Netherlands	RA	4 Months/F	INJ	U	19Apr2010-19Apr2010	19Apr2010	U/0 Days	Dyspnoea*, Pyrexia*	R
#B0604562A	Hong Kong	MD	Infant/U	INJ	U	11Nov2009-11Nov2009	11Nov2009	U/0 Days	Dyspnoea*, Pyrexia*, Heart rate increased*, Blood glucose increased*	U
#D0068461A	Germany	RA	4 Months/M	INJ	.5ML	01Jul2010-01Jul2010	04Jul2010	U/3 Days	Hiccups*, Constipation*, Crying*, Fluid intake reduced*, Muscle twitching*, Hypotonia*	I
#D0068597A	Germany	RA	9 Weeks/F	INJ	.5ML	05Jul2010-05Jul2010	08Jul2010	U/3 Days	Infantile apnoeic attack*, Atelectasis*, Pneumonia*, Oxygen saturation decreased*, Mechanical ventilation*, Leukopenia*	R

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#B0649654A	Netherlands	RA	8 Weeks/F	INJ	U	04Jan2010-04Jan2010	04Jan2010	U/2 Hours	Respiration abnormal*, Cyanosis*, Crying*, Pyrexia*, Hypotonia*	U
#B0614538A	Netherlands	RA	2 Months/M	INJ	U	11Jun2009-11Jun2009	11Jun2009	U/5 Hours	Respiration abnormal*, Gaze palsy*, Loss of consciousness*, Pallor*, Cyanosis*, Hypotonia*	R
#D0068462A	Germany	RA	3 Months/M	INJ	.5ML	19Jul2010-19Jul2010	19Jul2010	U/0 Days	Respiratory disorder*, Apnoea*, Dyspnoea*	R
#B0678008A	Poland	MD,RA	1 Months/M	INJ	U	16Sep2010-16Sep2010	18Sep2010	U/2 Days	Rhinitis allergic, Urticaria, Crying	R
Skin and subcutaneous tissue disorders										
#B0605278A	Italy	RA	2 Months/M	INJ	U	21Sep2009-21Sep2009	21Sep2009	U/0 Days	Angioedema*	R

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#B0619722A	Italy	RA	12 Months/M	INJ	U	10Dec2009-10Dec2009	15Dec2009	U/5 Days	Angioedema*	I
#B0636938A	Italy	RA	5 Months/M	INJ	U	11Feb2010-11Feb2010	11Feb2010	U/0 Days	Angioedema*	R
#B0676880A	Italy	MD,RA	5 Months/F	INJ	.5ML	29Mar2010-29Mar2010	29Mar2010	U/3 Hours	Angioedema, Dyspnoea, Cough, Malaise, Urticaria, Hypersensitivity	R
#B0648388A	Italy	RA	5 Months/F	INJ	U	17Feb2010-17Feb2010	19Feb2010	U/2 Days	Angioedema*, Hyperaesthesia*	R
#B0677305A	France	MD	16 Months/F	INJ	U	14Sep2010-14Sep2010	16Sep2010	U/2 Days	Angioedema*, Swelling face, Rash*, Rash macular*	N
#D0064226A	Germany	MD	5 Months/M	INJ	.5ML	01Apr2009-01Apr2009	01Apr2009	U/4 Hours	Angioedema*, Urticaria*	R

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D0065219A	Germany	MD,RA,RP	3 Months/M	INJ	U	08Oct2009-08Oct2009, 26Nov2009-26Nov2009, 26Aug2009-26Aug2009	01Sep2009	U/0 Years, U/U, U/U	Dermatitis atopic*	U
#B0658610A	Spain	RA	2 Months/F	INJ	U	18Nov2009-18Nov2009	25Nov2009	U/7 Days	Dermatitis atopic*	N
#B0658126A	Spain	CO,MD,RA	2 Months/M	INJ	U	28Jan2010-28Jan2010	28Jan2010	U/0 Days	Dermatitis atopic*, Asthma*, Faeces discoloured*, Abnormal faeces*, Lactose intolerance*, Pyrexia*, Crying*, Constipation*, Bronchiolitis*, Milk allergy*, Regurgitation*, Abdominal pain*, Flatulence*, Abdominal pain upper*	N
B0676366A	France	MD	16 Months/M	INJ	U	01Jul2010-01Jul2010	01Jul2010	U/2 Days	Dermatitis atopic, Eczema, Pyrexia	R
#B0630473A	Italy	RA	15 Months/F	INJ	U	23Dec2009-23Dec2009	26Dec2009	U/3 Days	Dermatitis*, Herpes ophthalmic*	I

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B0679199A	France	MD	16 Months/F	INJ	U	06Oct2010-06Oct2010	11Oct2010	U/5 Days	Eczema, Injection site eczema, Injection site induration, Injection site erythema, Pruritus	N
B0608559A	France	MD	5 Months/F	INJ	U	01Jan2009-01Jan2009	01Jan2009	U/0 Days	Eczema*, Rash*	R
B0640315A	Italy	MD	3 Months/U	INJ	U	1 Days		U/Unknown	Erythema*	R
B0640318A	Italy	MD	3 Months/U	INJ	U	1 Days		U/Unknown	Erythema*	R
B0640320A	Italy	MD	5 Months/U	INJ	U	1 Days		U/Unknown	Erythema*	R
B0637196A	France	MD	Infant/F	INJ	U	01Feb2009-01Feb2009	01Feb2009	U/2 Minutes	Erythema*, Feeling hot*, Injection site nodule*, Injection site erythema*, Pyrexia*	R

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D0066916A	Germany	MD	5 Months/F	INJ	U	16Mar2010-16Mar2010	01Mar2010	U/0 Days	Erythema*, Incorrect route of drug administration	U
#B0641879A	Nicaraqua	MD	3 Months/F	INJ	U	05Mar2010-05Mar2010	05Mar2010	U/0 Days	Erythema*, Induration*, Abscess*, Pyrexia*	R
B0647483A	South Africa	HP	3 Months/F	INJ	U	14Apr2010-14Apr2010, 17Mar2010-17Mar2010, 17Feb2010-17Feb2010	14Apr2010	U/5 Minutes, U/U, U/U	Erythema*, Induration*, Oedema peripheral*	R
B0641787A	Poland	MD	22 Months/M	INJ	U	18Mar2010-18Mar2010	18Mar2010	U/0 Days	Erythema*, Injection site extravasation*	R
#B0616513A	Singapore	MD,RP	1 Months/M	INJ	U	04Dec2009-04Dec2009	06Dec2009	U/2 Days	Erythema multiforme*	I
#D0068249A	Germany	MD,RA	22 Months/M	INJ	.5ML	1 Days	29May2010	U/Unknown	Erythema, Oedema peripheral	R

B0627302A	South Africa	HP	9 Months/U	INJ	U	11Jan2010-11Jan2010		U/0 Weeks	Erythema*, Oedema peripheral*	U
#D0069190A	Germany	MD,RA	26 Months/F	INJ	U	23Sep2010-U	24Sep2010	U/U	Erythema, Oedema peripheral, Cellulitis, Blister, Purulence, Skin warm, Ulcer	R
D0069096A	Germany	MD,RA	2 Months/M	INJ	.5ML	19Jul2010-19Jul2010	19Jul2010	U/30 Seconds	Erythema, Rash papular, Extensive swelling of vaccinated limb, Urticaria	R
D0068804A	Germany	MD	3 Months/F	INJ	U	08Sep2010-08Sep2010	08Sep2010	U/0 Days	Erythema, Screaming	R
D0069194A	Germany	MD	U/M	INJ	U	U		U/U	Erythema, Swelling	U
D0066939A	Germany	MD	Child/U	INJ	U	1 Days		U/Unknown	Erythema*, Swelling*, Petechiae*	U

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#D0066937A	Germany	PH,MD,RA	4 Months/F	INJ	U	18Mar2010-18Mar2010, 18Feb2010-18Feb2010, 15Jan2010-15Jan2010	18Mar2010	U/2 Minutes, U/U, U/U	Erythema*, Swelling*, Petechiae*, General physical health deterioration*, Fluid intake reduced*, Crying*, Agitation*, Lividity*, Rash macular*	U
B0613306A	France	MD,RP	15 Months/F	INJ	U	25Nov2009-25Nov2009	26Nov2009	U/1 Days	Generalised erythema*	R
B0622063A	France	PH	5 Months/F	INJ, INJ	U, U	01Nov2008-01Nov2008, 01Nov2009-01Nov2009		U/Unknown, U/Unknown	Hair growth abnormal*, Skin lesion*, Injection site erythema*	N
#D0067815A	Germany	MD	7 Years/M	INJ	U	25May2010-25May2010	25May2010	U/0 Days	Henoch-Schonlein purpura*, Pyrexia*, Nausea*, Vomiting*, Decreased appetite*, Myalgia*, Arthralgia*, Erythema nodosum*, Malaise*, Gait disturbance*, Rash*, Oedema peripheral*, Pain in extremity*, Off label use	R
#B0651979A	Spain	RA	4 Months/M	INJ	U	04Mar2010-04Mar2010	04Mar2010	U/0 Days	Livedo reticularis*, Injection site swelling*, Injection site erythema*, Injection site pain*	R

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D0068757A	Germany	HP,RA	3 Months/M	INJ, INJ	U, U	24Mar2010-24Mar2010, 22Apr2010-22Apr2010	01May2010	U/0 Years, U/0 Years	Neurodermatitis	S
#B0634231A	Austria	RA	2 Months/F	INJ	U	22Jan2010-22Jan2010	22Jan2010	U/3 Hours	Petechiae*	R
D0068680A	Germany	MD	3 Months/M	INJ, INJ	U, U	08Jul2010-08Jul2010, 1 Days	08Jul2010	U/0 Days, U/Unknown	Petechiae, Crying, Oedema peripheral, Erythema, Crying, Oedema peripheral	R
B0673408A	Netherlands	HP,RA	2 Months/F	INJ	.5ML	03Jun2010-03Jun2010	03Jun2010	U/3 Minutes	Petechiae*, Crying*, Somnolence*	R
#B0668854A	Czech Republic	HP,MD,RA	3 Months/M	INJ	U	12Jul2010-12Jul2010	12Jul2010	U/0 Days	Petechiae*, Erythema*, Crying*	R
#D0068750A	Germany	MD	3 Months/M	INJ	.5ML	31Aug2010-31Aug2010	31Aug2010	U/0 Days	Petechiae*, Haematoma*	I

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B0601844A	France	MD	2 Months/F	INJ	U	12Oct2009-12Oct2009	12Oct2009	U/2 Hours	Petechiae*, Oedema peripheral*, Urticaria*, Injection site induration*, Rash erythematous*	N
B0638020A	Czech Republic	MD	7 Months/F	INJ, INJ, INJ	U, U, U	1 Days, 1 Days, 1 Days		U/4 Days, U/4 Days, U/4 Days	Petechiae*, Petechiae*, Petechiae*, Petechiae*	R
D0069114A	Germany	MD,RP	4 Months/F	INJ	U	07Oct2010-07Oct2010	08Oct2010	U/1 Days	Petechiae, Pyrexia	R
#D0068961A	Germany	MD,RP	4 Months/M	INJ	.5ML	28Jun2010-28Jun2010	28Jun2010	U/0 Days	Petechiae*, Pyrexia*, Febrile infection*, Rhinitis*, Leukocytosis*, Thrombocytosis*, Crying*, Restlessness*, Bacterial infection*	R
#D0067257A	Germany	RA	3 Months/F	INJ, INJ	U, U	11Mar2010-11Mar2010, 27Apr2010-27Apr2010	11Mar2010	U/3 Hours, U/0 Days	Petechiae*, Rash*, Injection site induration*, Petechiae*, Injection site induration*, Injection site erythema*, Pyrexia*	U
D0063497A	Germany	MD,RP	2 Months/F	INJ	U	01Jan2009-01Jan2009	01Jan2009	U/3 Days	Purpura*	I

D0068231A	Germany	MD,RA	3 Months/F	INJ	U	08Jul2010-08Jul2010	08Jul2010	U/10 Minutes	Purpura, Oedema peripheral, Haemostasis	R
#B0652855A	France	RA	2 Months/F	INJ	U	01Mar2010-01Mar2010	07Mar2010	U/6 Days	Purpura*, Petechiae*, Thrombocytopenia*	U
B0635649A	Argentina	MD,RP	2 Months/M	INJ	U	06Jan2010-06Jan2010		U/Unknown	Rash*	R
B0657902A	France	MD	2 Months/M	INJ	U	11May2010-11May2010	12May2010	U/1 Days	Rash*	R
D0068238A	Germany	MD	Infant/M	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/2 Days	Rash*	R
B0630264A	South Africa	HP	3 Months/M	INJ	U	01Feb2010-01Feb2010	01Feb2010	U/0 Days	Rash*	U

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B0630271A	South Africa	HP	3 Months/M	INJ	U	01Feb2010-01Feb2010	01Feb2010	U/0 Days	Rash*	U
B0646281A	France	MD	2 Months/F	INJ	U	26Mar2010-26Mar2010	01Apr2010	U/8 Days	Rash erythematous*	R
B0676493A	France	MD	4 Months/M	INJ	U	01Aug2010-01Aug2010	01Aug2010	U/11 Hours	Rash erythematous, Crying	R
B0675114A	France	MD	2 Months/F	INJ	U	01Aug2010-01Aug2010	01Aug2010	U/5 Days	Rash erythematous, Erythema, Face oedema, Hypersensitivity	R
#B0607185A	Ireland	RA	6 Months/F	INJ	U	08Oct2009-08Oct2009	08Oct2009	U/0 Days	Rash erythematous*, Pallor*	R
D0068602A	Germany	HP,RA	3 Months/M	INJ	U	20Jul2010-20Jul2010	20Jul2010	U/5 Minutes	Rash erythematous, Petechiae, Restlessness, Screaming, Swelling, Vomiting, Decreased appetite	R

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B0672447A	South Africa	HP,PH	18 Months/M	INJ	.5ML	12Aug2010-12Aug2010, U	12Aug2010	U/0 Days, U/U	Rash erythematous, Rash erythematous, Rash erythematous	I
B0616926A	South Africa	HP	4 Months/U	INJ	U	01Jan2009-01Jan2009	01Jan2009	U/Days	Rash generalised*	U
#B0643319A	Italy	RA	2 Months/F	INJ	U	01Jan2009-01Jan2009	31Dec2009	U/Unknown	Rash generalised*, Dermatitis allergic*	U
#B0675328A	Slovakia	MD,RA	5 Months/M	INJ	.5ML	11Aug2010-11Aug2010	11Aug2010	U/10 Minutes	Rash generalised, Pallor, Hypertension, Restlessness, Hypersensitivity	R
B0638017A	Belgium	MD	3 Months/F	INJ	U	25Jan2010-25Jan2010	26Jan2010	U/1 Days	Rash generalised*, Pyrexia*, Fatigue*	R
B0612629A	Italy	MD	12 Months/M	INJ	U	U		U/Unknown	Rash*, Hypotonia*, Pyrexia*	U

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#B0636608A	Poland	RA	18 Months/U	INJ	U	15Dec2009-15Dec2009	15Dec2009	U/0 Days	Rash*, Injection site reaction*, Skin hypertrophy*, Mental impairment*, Local swelling*, Pyrexia*, Injection site pain*, Injection site oedema*, Injection site erythema*	U
B0656551A	France	MD	17 Months/M	INJ	U	17May2010-17May2010	19May2010	U/2 Days	Rash macular*, Oedema peripheral*	N
#B0630606A	Spain	RA	9 Months/M	INJ	.5ML	21Jul2009-21Jul2009	21Jul2009	U/0 Days	Rash maculo-papular*	R
#B0657560A	Italy	RA	11 Months/M	INJ	U	20Apr2010-20Apr2010	21Apr2010	U/1 Days	Rash maculo-papular*, Conjunctivitis*, Oedema peripheral*, Oedema peripheral*, Kawasaki's disease*, Pyrexia*	R
B0663797A	Poland	MD,RA	2 Months/U	INJ	U	22Mar2010-22Mar2010	22Mar2010	U/0 Days	Rash maculo-papular, Erythema, Abdominal distension, Vomiting, Crying	R

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#B0679333A	France	RA	2 Months/F	INJ	U	29Jul2010-29Jul2010	29Jul2010	U/Minutes	Rash maculo-papular, Injection site oedema	R
#B0653453A	Ireland	RA	6 Months/F	INJ	.5ML	25Apr2010-25Apr2010	03May2010	U/8 Days	Rash maculo-papular*, Pyrexia*, Urticaria*	R
#D0067923A	Germany	MD	3 Months/M	INJ	.5ML	10Jun2010-10Jun2010	10Jun2010	U/2 Hours	Rash maculo-papular*, Rash generalised*, Lividity*, Oedema peripheral*, Skin discolouration*, Dyspnoea*	R
#B0624916A	France	RA	9 Weeks/M	INJ	U	25Aug2009-25Aug2009	26Aug2009	U/1 Days	Rash morbilliform*, Hyperthermia*	R
D0068609A	Germany	PH	Infant/M	INJ	U	1 Days		U/Unknown	Rash, Neurodermatitis, Erythema, Dry skin, Dry skin, Vaccination complication	U
B0680586A	South Africa	HP	18 Months/F	U	U	12Aug2010-12Aug2010	12Aug2010	U/U	Rash, Pain in extremity, Oedema peripheral	U

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B0664578A	France	MD	17 Months/M	INJ	U	03Jul2010-03Jul2010	03Jul2010	U/Same day	Rash papular*, Pyrexia*	N
B0659711A	Viet Nam	MD	16 Months/F	INJ	U	17Apr2010-17Apr2010	17Apr2010	U/0 Days	Rash*, Pyrexia*	R
#B0664047A	Italy	MD,RA	5 Months/F	INJ	U	24Jun2010-24Jun2010	24Jun2010	U/0 Days	Rash*, Rash*	R
#B0625463A	Poland	RA	U/M	INJ	U	30Nov2009-30Nov2009	30Nov2009	U/0 Days	Rash*, Rash*, Injection site reaction*, Crying*, Pyrexia*	R
B0678148A	Netherlands	HP,RA	2 Months/M	INJ	U	25May2010-25May2010	25May2010	U/4 Hours	Rash, Skin warm, Crying	R
B0673453A	Netherlands	OT,RA	11 Months/M	INJ	.5ML	16Apr2010-16Apr2010	01Apr2010	U/19 Hours	Rash vesicular*, Pruritus*, Pyrexia*	R

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B0672345A	Netherlands	HP,RA	11 Months/M	INJ	U	06May2009-06May2009	06May2009	U/3 Seconds	Skin depigmentation	R
D0068693A	Germany	CO,MD,RA	12 Weeks/F	INJ	U	17Aug2010-17Aug2010	17Aug2010	U/0 Days	Skin discolouration, Pyrexia, Injection site erythema, Hyperaesthesia	R
D0068090A	Germany	CO,MD	4 Months/F	INJ	U	21Jun2010-21Jun2010	23Jun2010	U/2 Days	Spider naevus*	R
B0626777A	France	PH	2 Months/U	INJ	U	1 Days		U/0 Days	Swelling face*	R
D0068660A	Germany	MD	8 Months/F	INJ	U	11Aug2010-11Aug2010	13Aug2010	U/1 Days	Swelling face, Erythema, Rash, Auricular swelling	R
#B0612900A	Italy	RA	U/F	INJ	U	1 Days	02Dec2009	U/Unknown	Urticaria*	U

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D0067576A	Germany	MD,RA	14 Months/M	INJ	U	01Mar2010-01Mar2010	02Mar2010	U/1 Days	Urticaria*, Diarrhoea*, Vomiting*, Pyrexia*, Vaccination site induration*, Vaccination site swelling*, Injection site erythema*	R
B0678536A	France	MD	31 Months/F	INJ	U	31Aug2010-31Aug2010	01Sep2010	U/36 Hours	Urticaria, Pruritus	R
#B0601917A	France	MD	4 Months/M	INJ	U	03Nov2009-03Nov2009	03Nov2009	U/5 Minutes	Urticaria*, Skin discolouration*, Oedema peripheral*, Rash erythematous*, Rash papular*	R
Surgical and medical procedures										
B0672743A	Czech Republic	MD	6 Years/M	INJ	U	27Aug2010-27Aug2010, 14Jan2010-14Jan2010, 27Nov2009-27Nov2009, 30Oct2009-30Oct2009	27Aug2010	U/During, U/U, U/U, U/U	Off label use	X
B0679515A	France	PH	4 Years/F	INJ	U	05Oct2010-05Oct2010	05Oct2010	U/See text	Off label use	X

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B0679979A	France	MD	6 Weeks/F	INJ	U	03Sep2010-03Sep2010	03Sep2010	U/See text	Off label use	X
D0066137A	Germany	MD	47 Months/F	INJ	U	01Aug2008-01Aug2008	01Aug2008	U/0 Days	Off label use	X
D0066585A	Germany	MD	15 Years/F	INJ	U	19Mar2009-19Mar2009	19Mar2009	U/0 Days	Off label use	X
D0068389A	Germany	MD	Child/M	INJ, INJ	U, U	01Jan2009-01Jan2009, 01Jan2009-01Jan2009	01Jan2009	U/0 Days, U/0 Days	Off label use	X
D0068453A	Germany	MD	7 Years/M	INJ	U	25May2010-25May2010	25May2010	U/0 Days	Off label use	X
D0065611A	Germany	MD	12 Years/F	INJ	U	15Dec2009-15Dec2009	15Dec2009	U/0 Days	Off label use*	X

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B0663763A	South Africa	HP	30 Days/M	INJ, INJ	U, U	13May2010-13May2010, 15Jun2010-15Jun2010	13May2010	U/During, U/During	Off label use*, Off label use*	X
Vascular disorders										
#D0068505A	Germany	MD,RP	3 Months/M	INJ	.5ML	20Jul2010-20Jul2010	20Jul2010	U/0 Days	Circulatory collapse*, Pallor*, Cyanosis*, Hypotonia*, Body temperature increased*	R
#B0667354A	Ireland	HP,RA	4 Months/F	INJ	U	21Jul2010-21Jul2010	21Jul2010	U/0 Days	Flushing*, Rash*	R
#D0068575A	Germany	MD	4 Months/M	INJ	U	10Aug2010-10Aug2010	10Aug2010	U/0 Days	Haematoma*, Injection site discolouration*, Injection site vesicles*, Incorrect route of drug administration	R
#D0067074A	Germany	PH	Child/U	INJ	U	18Mar2010-18Mar2010	18Mar2010	U/Immediate	Haemorrhage*, Swelling*, Erythema*	U

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#B0677337A	Italy	MD,RA	13 Months/M	INJ	U	21Sep2010-21Sep2010	21Sep2010	U/0 Days	Hyperaemia, Inflammation, Pyrexia, Crying	R
#B0632160A	Spain	PH,RA	6 Years/M	INJ	U	05Nov2009-05Nov2009	05Nov2009	U/0 Days	Hypotension*, Vomiting*, Diarrhoea*, Pallor*, Somnolence*	R
#D0068409A	Germany	MD,RA	4 Months/U	INJ	U	09Jul2010-09Jul2010, 11Jun2010-11Jun2010	13Jul2010	U/0 Weeks, U/U	Kawasaki's disease, Leukocytosis, Meningitis, Gastroenteritis bacterial, Sepsis, Anaemia, Pyrexia, General physical health deterioration, Hyperaesthesia, Crying, Abnormal faeces, Lymphadenopathy, Pain, Acute tonsillitis, Sinus tachycardia, Rash, Chapped lips, Hypotension, Dysplasia, Dry throat, Lip disorder, Conjunctivitis, Hypoalbuminaemia	U
#B0616059A	Italy	RA	3 Months/F	INJ	U	08Jan2008-08Jan2008	09Jan2008	U/1 Days	Kawasaki's disease*, Macrophage activation*, Pyrexia*, Irritability*, Rash erythematous*, Rash erythematous*, Oedema peripheral*, Pain in extremity*, Hepatic function abnormal*, Hypoalbuminaemia*,	R

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									Serum ferritin increased*, Anaemia*, Histiocytosis haematophagic*, Rash*, Oedema peripheral*	
#B0653827A	Italy	RA	11 Months/M	INJ, INJ	U, U	20Apr2010-20Apr2010, 22Sep2009-22Sep2009, 20Jul2009-20Jul2009	20Apr2010	U/0 Days, U/7 Months, U/9 Months	Kawasaki's disease*, Oedema peripheral*, Rash maculo-papular*, Conjunctivitis*, Oedema peripheral*, Rash*, Cheilitis*, Pyrexia*, Pyrexia*	R
#D0066913A	Germany	MD	4 Months/F	INJ	.5ML	04Jun2009-04Jun2009	07Jun2009	U/3 Days	Kawasaki's disease*, Pyrexia*, Interstitial lung disease*, Crying*, Oligodipsia*, Faeces discoloured*, Dermatitis diaper*, Rash*, Conjunctival hyperaemia*, Cheilitis*, Chapped lips*, Skin exfoliation*, Anaemia*, Thrombocytosis*, Hepatic enzyme increased*	R
#B0656556A	Ireland	RA	5 Months/M	INJ	U	20Apr2010-20Apr2010	20Apr2010	U/0 Days	Pallor*	R
B0665286A	Poland	MD,RA	1 Months/U	INJ	U	19Apr2010-19Apr2010	19Apr2010	U/5 Minutes	Pallor, Decreased activity, Somnolence	R

B0664926A	Netherlands	HP,RA	14 Months/M	INJ	U	04Jan2010-04Jan2010	04Jan2010	U/10 Hours	Pallor, Hypertonia, Crying, Pyrexia	R
B0612641A	Italy	MD	3 Months/M	INJ	U	U		U/Unknown	Pallor*, Hypotonia*	U
D0065122A	Germany	MD	3 Months/M	INJ	U	29Oct2009-29Oct2009	29Oct2009	U/6 Hours	Pallor*, Hypotonic-hyporesponsive episode*	R
#B0651934A	Italy	RA	4 Months/F	INJ	U	24Jun2009-24Jun2009	24Jun2009	U/0 Days	Vasculitis*, Purpura*	R

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APPENDIX 3B : All serious attributable clinical trial cases which were received prior to the period of this PSUR but unblinded during the reporting period (no cases)

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APPENDIX 3C : All non-serious listed cases (excluding consumer and regulatory authority reports)

Appendix 3C: Individual Case Histories of Non-Serious Listed Cases Received in Time Period of PSUR for:

Infanrix hexa

Case No.	Country	Report Source	Age/Sex	Form'n or Route	TDD	Treatment Dates†	Event Onset	TTO / TTOSLD	Events	Outcome	Comments
Gastrointestinal disorders											
B0672121A	South Africa	HP	4 Months/U	INJ	U	26Aug2010-26Aug2010	26Aug2010	U/0 Days	Vomiting	U	
General disorders and administration site conditions											
B0673225A	Austria	PH	4 Years/F	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/Unknown	Pyrexia*	U	
B0602735A	France	MD,RP	2 Months/F	INJ	U	01Sep2009-01Sep2009	01Sep2009	U/0 Days	Pyrexia*	R	

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B0608877A	France	PH	17 Months/U	INJ	U	01Jan2009-01Jan2009	01Jan2009	U/Unknown	Injection site swelling*, Pyrexia*	U
B0632118A	France	HP,MD	17 Months/M	INJ	U	03Feb2010-03Feb2010	03Feb2010	U/2 Hours	Pyrexia*	R
B0632121A	France	HP,MD	17 Months/M	INJ	U	25Jan2010-25Jan2010	25Jan2010	U/1 Days	Pyrexia*	R
B0632195A	France	HP,MD	2 Years/M	INJ	U	26Jan2010-26Jan2010	27Jan2010	U/1 Days	Injection site erythema*	R
B0643589A	France	MD,RP	Infant/U	INJ	U	01Jan2010-01Jan2010	01Jan2010	U/1 Hours	Injection site swelling*, Injection site erythema*, Injection site pain*	R
B0649835A	France	MD	17 Months/F	INJ	U	08Mar2010-08Mar2010		U/Unknown	Pyrexia*	U

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B0664830A	France	MD	2 Months/M	INJ	U	01Jun2010-01Jun2010	01Jun2010	U/Same day	Injection site pain*, Injection site erythema*, Crying*	R
D0063436A	Germany	MD,RP	4 Years/M	INJ	U	19Oct2009-19Oct2009	01Oct2009	U/0 Weeks	Injection site swelling*, Injection site pain*	R
D0063661A	Germany	MD,RP	Infant/M	INJ	U	1 Days		U/Unknown	Injection site swelling*	U
D0065641A	Germany	MD	3 Months/U	INJ	U	17Dec2009-17Dec2009	17Dec2009	U/0 Days	Injection site swelling*, Injection site erythema*	U
D0066442A	Germany	MD	13 Months/F	INJ	U	09Feb2010-09Feb2010	09Feb2010	U/0 Days	Pyrexia*	R
D0067791A	Germany	MD,RA	6 Months/M	INJ	U	03May2010-03May2010	03May2010	U/0 Days	Pyrexia*	R

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D0068837A	Germany	HP,RA	3 Months/M	INJ	.5ML	19Jul2010-19Jul2010	20Jul2010	U/1 Days	Pyrexia	R
D0069026A	Germany	MD	26 Months/M	INJ	U	30Sep2010-30Sep2010	01Oct2010	U/1 Days	Injection site swelling, Injection site erythema	U
D0069087A	Germany	MD,RP	16 Months/M	INJ	.5ML	29Sep2010-29Sep2010	29Sep2010	U/0 Days	Injection site erythema, Extensive swelling of vaccinated limb	R
B0611964A	Italy	MD	5 Months/M	INJ	U	14Sep2009-14Sep2009	14Sep2009	U/0 Days	Pyrexia*	R
B0661395A	Kenya	HP	U/U	INJ	U	17May2010-17May2010	17May2010	U/0 Days	Pyrexia*, Crying*	U
B0671791A	Kenya	HP,MD,RP	Child/U	INJ	U	1 Days		U/Unknown	Pyrexia*, Irritability*, Injection site swelling*	U

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B0671795A	Kenya	HP,MD,RP	Child/U	INJ	U	1 Days	U/Unknown	Pyrexia*, Irritability*, Injection site swelling*	U
B0671796A	Kenya	HP,MD,RP	Child/U	INJ	U	1 Days	U/Unknown	Pyrexia*, Irritability*, Injection site swelling*	U
B0671797A	Kenya	HP,MD,RP	Child/U	INJ	U	1 Days	U/Unknown	Pyrexia*, Irritability*, Injection site swelling*	U
B0671798A	Kenya	HP,MD,RP	Child/U	INJ	U	1 Days	U/Unknown	Pyrexia*, Irritability*, Injection site swelling*	U
B0671799A	Kenya	HP,MD,RP	Child/U	INJ	U	1 Days	U/Unknown	Pyrexia*, Irritability*, Injection site swelling*	U
B0671800A	Kenya	HP,MD,RP	Child/U	INJ	U	1 Days	U/Unknown	Pyrexia*, Irritability*, Injection site swelling*	U

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B0671801A	Kenya	HP,MD,RP	Child/U	INJ	U	1 Days		U/Unknown	Pyrexia*, Irritability*, Injection site swelling*	U
B0671802A	Kenya	HP,MD,RP	Child/U	INJ	U	1 Days		U/Unknown	Pyrexia*, Irritability*, Injection site swelling*	U
B0671803A	Kenya	HP,MD,RP	Child/U	INJ	U	1 Days		U/Unknown	Pyrexia*, Irritability*, Injection site swelling*	U
B0666882A	Netherlands	HP,RA	2 Months/F	INJ	U	08Feb2010-08Feb2010	08Feb2010	U/2 Hours	Pyrexia, Crying, Vomiting	R
B0672352A	Netherlands	HP,RA	2 Months/M	INJ	U	18Jan2010-18Jan2010	18Jan2010	U/5 Hours	Pyrexia, Crying	R
B0668060A	Pakistan	HP,PH,RP	3 Months/M	INJ, INJ	U, U	26Jun2010-26Jun2010, 17Jul2010-17Jul2010, 04May2010-04May2010	28Jun2010	U/2 Days, U/8 Days, U/U	Injection site swelling, Injection site swelling	N

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B0672727A	Philippines	MD	14 Months/F	INJ	U	30Aug2010-30Aug2010	31Aug2010	U/1 Days	Injection site erythema, Injection site swelling	N
B0633360A	Romania	MD	4 Months/F	INJ	U	08Feb2010-08Feb2010	08Feb2010	U/3 Hours	Pyrexia*	R
B0627454A	South Africa	CO,HP	18 Months/F	INJ	U	11Jan2010-11Jan2010	13Jan2010	U/2 Days	Injection site swelling, Injection site erythema*, Injection site pain*	U
B0631805A	South Africa	HP	22 Months/F	INJ	U	03Feb2010-03Feb2010		U/Unknown	Injection site swelling*, Injection site erythema*, Injection site pain*	U
B0667306A	South Africa	HP	14 Weeks/U	INJ	U	1 Days		U/Unknown	Pyrexia	U
B0677088A	South Africa	HP	24 Months/F	INJ	.5ML	14Sep2010-14Sep2010	15Sep2010	U/1 Days	Injection site swelling*, Injection site erythema*	R

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B0651382A	Switzerland	MD	4 Months/F	INJ	.5ML	01Jan2010-01Jan2010	03May2010	U/Unknown	Pyrexia*, Diarrhoea*	N
B0659714A	Viet Nam	MD	17 Months/F	INJ	U	26May2010-26May2010	26May2010	U/0 Days	Pyrexia*	R
Investigations										
D0066082A	Germany	MD	Infant/F	INJ	U	10Dec2009-10Dec2009	10Dec2009	U/0 Days	Body temperature increased*, Body temperature increased*	R
Nervous system disorders										
B0678906A	Belgium	MD	Infant/F	INJ	U	U		U/1 Days	Crying, Pyrexia	U
B0639449A	Italy	MD	U/U	INJ	U	01Jan2010-01Jan2010		U/Unknown	Crying*, Injection site pain*	U

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B0622904A	Netherlands	RA	177 Days/F	IM	1ML	01Jul2009-U		U/6 Hours	Crying*	R
B0626698A	Netherlands	RA	69 Days/M	IM	U	24Jun2009-U		U/4 Hours	Crying*, Pyrexia*, Urticaria*	R
B0652918A	Pakistan	MD	5 Months/F	INJ, INJ	U, U	01Jan2010-01Jan2010, 08May2010-08May2010	01Jan2010	U/Unknown, U/0 Days	Crying*, Crying*, Crying*, Crying*	U
B0660241A	South Africa	HP	8 Weeks/U	INJ	U	15May2010-15May2010		U/Unknown	Crying*	U
B0664601A	South Africa	HP	10 Weeks/M	INJ	U	08Jul2010-08Jul2010	09Jul2010	U/1 Days	Crying*, Diarrhoea*	U

Skin and subcutaneous tissue disorders

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B0679072A	France	MD	4 Months/M	INJ	U	30Sep2010-30Sep2010	01Oct2010	U/1 Days	Urticaria	R
D0066534A	Germany	MD	5 Months/F	INJ	U	12Feb2010-12Feb2010	12Feb2010	U/0 Days	Urticaria*, Urticaria*	R
D0067929A	Germany	MD,RP	4 Months/F	INJ	U	28Apr2010-28Apr2010	28Apr2010	U/0 Days	Urticaria*, Pyrexia*	N
D0069002A	Germany	MD	22 Months/M	INJ	U	08Jun2010-08Jun2010	01Jun2010	U/5 Days	Urticaria	N
B0662680A	Sri Lanka	MD	4 Months/M	INJ	U	26Jun2010-26Jun2010	26Jun2010	U/0 Days	Dermatitis allergic*	R

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APPENDIX 3D : All non-medically verified cases

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Appendix 3D: Individual Case Histories of Non-Medically Verified Cases Received in Time Period of PSUR for:

Infanrix hexa

Case No.	Country	Report Source	Age/Sex	Form'n or Route	TDD	Treatment Dates†	Event Onset	TTO / TTOSLD	Events	Outcome	Comments
Eye disorders											
B0674680A	Poland	CO	5 Months/F	INJ	U	19Aug2010-19Aug2010, 22Apr2010-22Apr2010, 10Jun2010-10Jun2010	21Aug2010	U/2 Days, U/U, U/U	Eye rolling*, Muscle contracture*, Crying*	U	
Gastrointestinal disorders											
B0644102A	Italy	CO	3 Months/F	INJ	U	09Mar2010-09Mar2010	10Mar2010	U/1 Days	Parotid gland enlargement*, Agitation*, Pyrexia*	I	
B0630743A	Poland	CO	8 Weeks/F	INJ	U	02Feb2010-02Feb2010	02Feb2010	U/30 Minutes	Vomiting*	U	

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B0608006A	Spain	CO	2 Months/F	INJ	U	18Nov2009-18Nov2009	18Nov2009	U/0 Days	Vomiting*	R
General disorders and administration site conditions										
B0662808A	France	CO	2 Months/F	INJ	U	23Jun2010-23Jun2010	23Jun2010	U/See text	Incorrect product storage	X
D0067890A	Germany	CO	U/M	INJ	U	1 Days		U/Unknown	Injection site erythema*	U
B0663988A	France	CO,CN	17 Months/M	INJ	U	29Apr2009-29Apr2009	01Jan2009	U/Unknown	Injection site induration*, Injection site pruritus*, Injection site warmth*, Injection site pain*	N
D0066109A	Germany	CO	11 Months/F	INJ	U	U		U/0 Days	Injection site induration*, Injection site scar*	U

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D0067001A	Germany	CO	27 Years/M	INJ	U	25Nov2009-25Nov2009	25Nov2009	U/0 Days	Injection site pain*, Off label use	R
B0660461A	Poland	CO	2 Months/F	INJ	U	09Jun2010-09Jun2010, 21May2010-21May2010	09Jun2010	U/0 Days, U/U	Injection site reaction*, Wrong drug administered*	U
B0664631A	Chile	CO	17 Months/M	INJ	U	07Jul2010-07Jul2010, 22Apr2010-22Apr2010	07Jul2010	U/1 Days, U/U	Injection site warmth, Injection site swelling, Injection site pain	N
B0601131A	Colombia	CO	2 Months/M	INJ	U	29Oct2009-29Oct2009	29Oct2009	U/0 Days	Irritability*, Crying*, Product quality issue*	R
B0660183A	South Africa	CO	U/M	INJ	U	1 Days		U/Unknown	No therapeutic response*	U
#B0666660A	Poland	CO	2 Months/M	INJ	U	08Jul2010-08Jul2010	09Jul2010	U/1 Days	Pyrexia	U

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B0665707A	Greece	CO	2 Months/F	INJ	U	14Jul2010-14Jul2010	14Jul2010	U/6 Hours	Pyrexia*	R
B0602823A	Hong Kong	CO	4 Months/F	INJ	U	01Apr2009-01Apr2009	01Apr2009	U/Unknown	Pyrexia*	R
B0661396A	Kenya	CO	10 Weeks/F	INJ	U	1 Days		U/0 Days	Pyrexia*	U
B0662718A	Kenya	RP	10 Weeks/F	INJ	U	24Jun2010-24Jun2010	24Jun2010	U/0 Days	Pyrexia*	U
B0661816A	Thailand	CO	6 Months/M	INJ	.5ML	10Jun2010-10Jun2010	10Jun2010	U/1 Hours	Pyrexia*	R
B0638208A	France	CO	2 Months/U	INJ	U	01Mar2010-01Mar2010	01Mar2010	U/0 Days	Pyrexia*, Incorrect storage of drug	R

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B0648514A	Argentina	CO	4 Months/M	INJ	U	12Apr2010-12Apr2010	12Apr2010	U/0 Days	Pyrexia*, Irritability*, Wrong technique in drug usage process*	N
B0639181A	Czech Republic	CO	Infant/F	INJ	U	U		U/Unknown	Pyrexia*, Vomiting*, Decreased appetite*	R
B0639603A	Kenya	RP	U/U	INJ	U	U		U/Unknown	Swelling*	U
Infections and infestations										
#D0067703A	Germany	CO,OT	10 Months/M	INJ	.5ML	01Sep2009-01Sep2009	01Feb2010	U/5 Months	Abscess limb*, Nodule on extremity*	I
#D0066769A	Germany	CO	2 Years/F	INJ, INJ, INJ, INJ	U, U, U, U	06Feb2008-06Feb2008, 06Mar2008-06Mar2008, 04Apr2008-04Apr2008, 12Jan2009-12Jan2009	01Feb2010	U/24 Months, U/23 Months, U/22 Months, U/13 Months	Haemophilus infection*, Vaccination failure*, Pneumonia*, Pyrexia*, Fatigue*, Pharyngitis*	R

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#D0066195A	Germany	CO	4 Months/M	INJ	U	1 Days	01Jan2010	U/Unknown	Meningitis pneumococcal*, Pyrexia*, Restlessness*, Muscle spasms*, Respiratory disorder*, Salivary hypersecretion*, Daydreaming*, Hypertension*, Hemiplegia*, Cerebral haemorrhage*, Motor dysfunction*	U
B0601502A	Poland	CO	3 Months/M	INJ	U	28Oct2009-28Oct2009	29Oct2009	U/1 Days	Urinary tract infection*, Pyrexia*	U
Injury, poisoning and procedural complications										
B0676688A	Australia	CO	5 Months/F	INJ	U	02Sep2010-02Sep2010	02Sep2010	U/During	Expired drug administered*	X
B0644428A	France	CO,OT	15 Months/F	INJ	U	U	27May2009	U/U	Inappropriate schedule of drug administration	U

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B0644432A	France	CO,OT	12 Months/F	INJ	U	U	30Jan2009	U/U	Inappropriate schedule of drug administration	U
B0644436A	France	CO,OT	15 Months/M	INJ	U	U	23Jul2008	U/U	Inappropriate schedule of drug administration	U
B0644439A	France	CO,OT	15 Months/M	INJ	U	U	10Oct2008	U/U	Inappropriate schedule of drug administration	U
B0646835A	France	CO,OT	5 Years/M	INJ	U	U	13Nov2008	U/U	Inappropriate schedule of drug administration	U
B0646850A	France	CO,OT	2 Years/M	INJ	U	U	30Sep2009	U/U	Inappropriate schedule of drug administration	U
B0646853A	France	CO,OT	1 Years/M	INJ	U	U	25Sep2009	U/U	Inappropriate schedule of drug administration	U

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B0646860A	France	CO,OT	1 Years/F	INJ	U	U	20Jul2009	U/U	Inappropriate schedule of drug administration	U
B0646861A	France	CO,OT	0 Years/F	INJ	U	U	10Oct2008	U/U	Inappropriate schedule of drug administration	U
B0646864A	France	CO,OT	1 Years/M	INJ	U	U	04May2009	U/U	Inappropriate schedule of drug administration	U
B0646880A	France	CO,OT	1 Years/F	INJ	U	U	06Jul2009	U/U	Inappropriate schedule of drug administration	U
B0646882A	France	CO,OT	1 Years/F	INJ	U	U	04Feb2009	U/U	Inappropriate schedule of drug administration	U
B0646887A	France	CO,OT	1 Years/F	INJ	U	U	13Feb2009	U/U	Inappropriate schedule of drug administration	U

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B0646890A	France	CO,OT	1 Years/F	INJ	U	U	07Oct2009	U/U	Inappropriate schedule of drug administration	U
B0646894A	France	CO,OT	1 Years/F	INJ	U	U	04Nov2008	U/U	Inappropriate schedule of drug administration	U
B0646897A	France	CO,OT	1 Years/F	INJ	U	U	16Dec2008	U/U	Inappropriate schedule of drug administration	U
B0646900A	France	CO,OT	1 Years/F	INJ	U	U	19Aug2008	U/U	Inappropriate schedule of drug administration	U
B0646902A	France	CO,OT	1 Years/F	INJ	U	U	05Nov2008	U/U	Inappropriate schedule of drug administration	U
B0646906A	France	CO,OT	4 Months/M	INJ	U	U	20May2008	U/U	Inappropriate schedule of drug administration	U

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B0646908A	France	CO,OT	4 Months/F	INJ	U	U	23Mar2008	U/U	Inappropriate schedule of drug administration	U
B0646911A	France	CO,OT	22 Months/F	INJ	U	U	06May2009	U/U	Inappropriate schedule of drug administration	U
B0646912A	France	CO,OT	3 Months/M	INJ	U	U	13May2009	U/U	Inappropriate schedule of drug administration	U
B0646915A	France	CO,OT	3 Months/F	INJ	U	U	06Dec2008	U/U	Inappropriate schedule of drug administration	U
B0647082A	France	CO,OT	6 Months/M	INJ	U	U, U	10Jun2008	U/U, U/U	Inappropriate schedule of drug administration	U
B0647092A	France	CO,OT	7 Weeks/M	INJ	U	U	05Nov2008	U/U	Inappropriate schedule of drug administration	U

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B0647100A	France	CO,OT	15 Months/F	INJ	U	U	04Dec2008	U/U	Inappropriate schedule of drug administration	U
B0647115A	France	CO,OT	45 Days/F	INJ	U	U	24Sep2009	U/U	Inappropriate schedule of drug administration	U
B0647118A	France	CO,OT	53 Days/F	INJ	U	U	18Dec2008	U/U	Inappropriate schedule of drug administration	U
B0647120A	France	CO,OT	55 Days/F	INJ	U	U	08Sep2009	U/U	Inappropriate schedule of drug administration	U
B0647197A	France	CO,OT	1 Years/M	INJ	U	U	21Nov2008	U/U	Inappropriate schedule of drug administration	U
B0647200A	France	CO,OT	1 Years/M	INJ	U	U	30Oct2008	U/U	Inappropriate schedule of drug administration	U

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B0647202A	France	CO,OT	11 Years/M	INJ	U	U	03Nov2008	U/U	Inappropriate schedule of drug administration	U
B0647203A	France	CO,OT	11 Years/M	INJ	U	U	23Sep2009	U/U	Inappropriate schedule of drug administration	U
B0647206A	France	CO,OT	1 Years/M	INJ	U	U	29Jan2009	U/U	Inappropriate schedule of drug administration	U
B0647209A	France	CO,OT	1 Years/M	INJ	U	U	25Jun2009	U/U	Inappropriate schedule of drug administration	U
B0647210A	France	CO,OT	1 Years/M	INJ	U	U	05Oct2009	U/U	Inappropriate schedule of drug administration	U
B0647212A	France	CO,OT	1 Years/M	INJ	U	U	27Sep2008	U/U	Inappropriate schedule of drug administration	U

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B0647277A	France	CO,OT	1 Years/M	INJ	U	U	18Jun2004	U/U	Inappropriate schedule of drug administration	U
B0647310A	France	CO,OT	15 Months/M	INJ	U	U	16Feb2009	U/U	Inappropriate schedule of drug administration	U
B0647326A	France	CO,OT	14 Months/M	INJ	U	U	13Mar2009	U/U	Inappropriate schedule of drug administration	U
B0647332A	France	CO,OT	15 Months/M	INJ	U	U	11Sep2008	U/U	Inappropriate schedule of drug administration	U
B0627950A	Poland	CO	2 Months/M	INJ	U	22Dec2009-22Dec2009, 13Jan2010-13Jan2010	13Jan2010	U/During, U/U	Inappropriate schedule of drug administration*	X
B0646485A	France	CO,OT	1 Months/F	U	U	U	08Feb2008	U/U	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	U

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B0646503A	France	CO,OT	2 Months/M	INJ	U	U	26Dec2007	U/U	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	X
B0646512A	France	CO,OT	7 Weeks/M	INJ	U	U	26Jun2007	U/U	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	X
B0646955A	France	CO,OT	1 Months/F	U	U	U	17Aug2007	U/U	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	U
B0647081A	France	CO,OT	3 Months/F	INJ	U	U, U	21Jul2008	U/U, U/U	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	U
B0647329A	France	CO,OT	3 Months/M	INJ	U	U	11Jul2008	U/U	Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	U
B0646668A	France	CO,OT	4 Months/M	U	U	U	13Sep2007	U/U	Inappropriate schedule of drug administration, Incorrect dose administered	U

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B0647107A	France	CO,OT	2 Months/F	INJ	U	U	06Jun2007	U/U	Inappropriate schedule of drug administration, Incorrect dose administered	U
B0647093A	France	CO,OT	6 Weeks/M	INJ, INJ	U, U	U, U	14Nov2008	U/U, U/U	Inappropriate schedule of drug administration, Wrong drug administered	U
B0647097A	France	CO,OT	7 Weeks/M	INJ, INJ	U, U	U, U	08Jul2009	U/U, U/U	Inappropriate schedule of drug administration, Wrong drug administered	U
B0647263A	France	CO,OT	7 Weeks/F	INJ, INJ, INJ	U, U, U	U, U, U, U	20Aug2003	U/U, U/U, U/U, U/U	Inappropriate schedule of drug administration, Wrong drug administered, Incorrect dose administered	U
B0644476A	France	CO,OT	1 Years/F	U	U	U, U	16Dec2009	U/U, U/U	Incorrect dose administered	U

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B0644478A	France	CO,OT	U/F	U	U	U	19Nov2007	U/U	Incorrect dose administered	U
B0646855A	France	CO,OT	1 Years/M	INJ	U	U	24Jul2008	U/U	Incorrect dose administered	U
B0671342A	Australia	CO	8 Months/M	INJ, INJ	U, U	U, U		U/During, U/During	Incorrect storage of drug	X
B0613305A	France	CO	Infant/M	INJ	U	01Nov2009-01Nov2009		U/See text	Incorrect storage of drug*	X
B0614762A	France	CO	3 Months/F	INJ	U	06Nov2009-06Nov2009	01Jan2009	See text/U	Incorrect storage of drug*	X
B0616268A	France	CO	10 Weeks/F	INJ	U	01Dec2009-01Dec2009		U/See text	Incorrect storage of drug*	X

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B0663967A	France	CO	4 Months/F	INJ	U	27Jun2010-27Jun2010	27Jun2010	U/U	Underdose	X
B0680075A	Australia	CO	6 Weeks/M	INJ, INJ	U, U	30Sep2010-30Sep2010, 30Sep2010-30Sep2010	30Sep2010	U/During, U/During	Underdose, Overdose	X
B0659986A	Italy	RP	3 Months/M	INJ	U	1 Days		U/During	Underdose*, Product quality issue*	X
B0643348A	France	CO,OT	11 Years/F	INJ	U	01Feb2006-01Feb2006	01Feb2006	U/See text	Wrong drug administered	X
B0643349A	France	CO,OT	6 Years/F	INJ	U	01Apr2005-01Apr2005	22Jan2000	U/See text	Wrong drug administered	X
B0643350A	France	CO,OT	8 Years/F	INJ	U	09May2001-09May2001	09May2001	U/See text	Wrong drug administered	X

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B0643351A	France	CO,OT	13 Years/M	INJ	U	17May2006-17May2006	17May2006	U/See text	Wrong drug administered	X
B0643352A	France	CO,OT	11 Years/M	INJ	U	06Jan2006-06Jan2006	06Jan2006	U/See text	Wrong drug administered	X
B0643353A	France	CO,OT	11 Years/M	INJ	U	23Apr2004-23Apr2004	23Apr2004	U/See text	Wrong drug administered	X
B0643354A	France	CO,OT	11 Years/F	INJ	U	31Jul2003-31Jul2003	31Jul2003	U/See text	Wrong drug administered	X
B0643355A	France	CO,OT	6 Years/F	INJ	U	09Jan2004-09Jan2004	09Jan2004	U/See text	Wrong drug administered	X
B0643356A	France	CO,OT	11 Years/F	INJ	U	26Jul2006-26Jul2006	26Jul2006	U/See text	Wrong drug administered	X

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B0643357A	France	CO,OT	6 Years/F	INJ, INJ	U, U	10Jul2003-10Jul2003, 24Jul2008-24Jul2008	10Jul2003	U/See text, U/See text	Wrong drug administered	X
B0643358A	France	CO,OT	12 Years/F	INJ	U	27Apr2009-27Apr2009	27Apr2009	U/See text	Wrong drug administered	X
B0643359A	France	CO,OT	12 Years/M	INJ	U	17Oct2008-17Oct2008	17Oct2008	U/See text	Wrong drug administered	X
B0643360A	France	CO,OT	6 Years/F	INJ	U	01Oct2008-01Oct2008	19Nov2003	U/See text	Wrong drug administered	X
B0643361A	France	CO,OT	11 Years/F	INJ	U	01Mar2005-01Mar2005	01Mar2005	U/See text	Wrong drug administered	X
B0643362A	France	CO,OT	10 Years/M	INJ	U	23May2007-23May2007	23May2007	U/See text	Wrong drug administered	X

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B0643363A	France	CO,OT	11 Years/F	INJ	U	23Aug2006-23Aug2006	23Aug2006	U/See text	Wrong drug administered	X
B0643364A	France	CO,OT	12 Years/F	INJ	U	28Aug2004-28Aug2004	28Aug2004	U/See text	Wrong drug administered	X
B0643365A	France	CO,OT	12 Years/F	INJ	U	22Oct2003-22Oct2003	22Oct2003	U/See text	Wrong drug administered	X
B0643366A	France	CO,OT	6 Years/F	INJ	U	19Dec2005-19Dec2005	02Nov2000	U/See text	Wrong drug administered	X
B0644445A	France	CO,OT	U/F	U	U	U, U	09Mar2009	U/U, U/U	Wrong drug administered	U
B0644448A	France	CO,OT	U/F	U	U	U, U	09Feb2009	U/U, U/U	Wrong drug administered	U

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B0644450A	France	CO,OT	4 Months/F	INJ	U	U	16Feb2009	U/U	Wrong drug administered	U
B0644454A	France	CO,OT	U/F	U	U	U, U	03Aug2009	U/U, U/U	Wrong drug administered	U
B0644455A	France	CO,OT	11 Weeks/F	INJ	U	U	16Dec2008	U/U	Wrong drug administered	U
B0644457A	France	CO,OT	11 Weeks/F	INJ	U	U	12Feb2009	U/U	Wrong drug administered	U
B0644461A	France	CO,OT	15 Weeks/F	INJ	U	U	15Oct2008	U/U	Wrong drug administered	U
B0644464A	France	CO,OT	U/F	U	U	U, U	19May2009	U/U, U/U	Wrong drug administered	U

B0644466A	France	CO,OT	U/F	U	U	U, U	11Jul2009	U/U, U/U	Wrong drug administered	U
B0644469A	France	CO,OT	U/F	U	U	U, U	16Nov2007	U/U, U/U	Wrong drug administered	U
B0644484A	France	CO,OT	U/F	U	U	U, U	29Dec2008	U/U, U/U	Wrong drug administered	U
B0644494A	France	CO,OT	U/F	U	U	U, U	06Feb2009	U/U, U/U	Wrong drug administered	U
B0644497A	France	CO,OT	U/F	U	U	U, U	18Feb2009	U/U, U/U	Wrong drug administered	U
B0644498A	France	CO,OT	U/F	U	U	U, U	01Apr2009	U/U, U/U	Wrong drug administered	U

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B0644674A	France	CO,OT	3 Months/M	INJ	U	U	10Aug2009	U/U	Wrong drug administered	U
B0644680A	France	CO,OT	3 Months/M	INJ	U	U	11Aug2008	U/U	Wrong drug administered	U
B0644688A	France	CO,OT	2 Months/M	INJ	U	U	27Nov2008	U/U	Wrong drug administered	U
B0644693A	France	CO,OT	3 Months/M	INJ	U	U	05Nov2008	U/U	Wrong drug administered	U
B0644700A	France	CO,OT	4 Months/M	INJ	U	U	14Aug2008	U/U	Wrong drug administered	U
B0644729A	France	CO,OT	4 Months/M	INJ	U	U	13Dec2008	U/U	Wrong drug administered	U

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B0644736A	France	CO,OT	9 Months/M	INJ	U	U	03Nov2008	U/U	Wrong drug administered	U
B0644762A	France	CO,OT	3 Months/M	INJ	U	U	18Nov2008	U/U	Wrong drug administered	U
B0644764A	France	CO,OT	3 Months/M	INJ	U	U	07Nov2008	U/U	Wrong drug administered	U
B0644765A	France	CO,OT	3 Months/M	INJ	U	U	30Jun2008	U/U	Wrong drug administered	U
B0644768A	France	CO,OT	3 Months/M	INJ	U	U	17Sep2008	U/U	Wrong drug administered	U
B0644772A	France	CO,OT	4 Months/M	INJ	U	U	18Nov2008	U/U	Wrong drug administered	U

B0644774A	France	CO,OT	3 Months/M	INJ	U	U	28Oct2008	U/U	Wrong drug administered	U
B0644780A	France	CO,OT	3 Months/M	INJ	U	U	08Dec2008	U/U	Wrong drug administered	U
B0644782A	France	CO,OT	3 Months/M	INJ	U	U	15Sep2008	U/U	Wrong drug administered	U
B0644786A	France	CO,OT	3 Months/M	INJ	U	U	02Sep2008	U/U	Wrong drug administered	U
B0644788A	France	CO,OT	3 Months/M	INJ	U	U	06Aug2008	U/U	Wrong drug administered	U
B0644794A	France	CO,OT	3 Months/M	INJ	U	U	05Aug2009	U/U	Wrong drug administered	U

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B0644815A	France	CO,OT	4 Months/M	INJ	U	U	15Jun2009	U/U	Wrong drug administered	U
B0644817A	France	CO,OT	3 Months/M	INJ	U	U	11Dec2008	U/U	Wrong drug administered	U
B0644827A	France	CO,OT	3 Months/M	INJ	U	U	09Mar2009	U/U	Wrong drug administered	U
B0644832A	France	CO,OT	2 Months/M	INJ	U	U	25Feb2009	U/U	Wrong drug administered	U
B0644834A	France	CO,OT	3 Months/M	INJ	U	U	30Apr2009	U/U	Wrong drug administered	U
B0644840A	France	CO,OT	3 Months/M	INJ	U	U	27Aug2009	U/U	Wrong drug administered	U

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B0644843A	France	CO,OT	4 Months/M	INJ	U	U	17Jul2009	U/U	Wrong drug administered	U
B0644846A	France	CO,OT	5 Months/M	INJ	U	U	20Nov2008	U/U	Wrong drug administered	U
B0644848A	France	CO,OT	3 Months/M	INJ	U	U	20Jun2009	U/U	Wrong drug administered	U
B0644854A	France	CO,OT	3 Months/M	INJ	U	U	08Apr2009	U/U	Wrong drug administered	U
B0644862A	France	CO,OT	3 Months/M	INJ	U	U	21Jul2009	U/U	Wrong drug administered	U
B0644867A	France	CO,OT	7 Months/M	INJ	U	U	12May2009	U/U	Wrong drug administered	U

B0644870A	France	CO,OT	3 Months/M	INJ	U	U	28Jul2009	U/U	Wrong drug administered	U
B0644873A	France	CO,OT	3 Months/M	INJ	U	U	10Apr2009	U/U	Wrong drug administered	U
B0644935A	France	CO,OT	19 Months/F	INJ	U	U	08Jul2004	U/U	Wrong drug administered	U
B0644947A	France	CO,OT	13 Weeks/M	INJ	U	U	28May2009	U/U	Wrong drug administered	U
B0644948A	France	CO,OT	11 Weeks/M	INJ	U	U	20Jan2009	U/U	Wrong drug administered	U
B0644949A	France	CO,OT	7 Weeks/M	INJ	U	U	27Aug2009	U/U	Wrong drug administered	U

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B0644953A	France	CO,OT	11 Weeks/M	INJ	U	U	30Apr2009	U/U	Wrong drug administered	U
B0645646A	France	CO,OT	13 Weeks/M	INJ	U	U	14May2009	U/U	Wrong drug administered	U
B0645648A	France	CO,OT	3 Months/M	INJ	U	U	18Mar2009	U/U	Wrong drug administered	U
B0645652A	France	CO,OT	4 Months/M	INJ	U	U	25May2009	U/U	Wrong drug administered	U
B0645654A	France	CO,OT	13 Weeks/M	INJ	U	U	21Jul2009	U/U	Wrong drug administered	U
B0645655A	France	CO,OT	3 Months/M	INJ	U	U	17Mar2009	U/U	Wrong drug administered	U

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B0645704A	France	CO,OT	3 Months/M	INJ	U	U	19Feb2009	U/U	Wrong drug administered	U
B0645706A	France	CO,OT	3 Months/M	INJ	U	U	28Apr2009	U/U	Wrong drug administered	U
B0645708A	France	CO,OT	3 Months/M	INJ	U	U	13Jan2009	U/U	Wrong drug administered	U
B0645710A	France	CO,OT	3 Months/M	INJ	U	U	14Jan2009	U/U	Wrong drug administered	U
B0645713A	France	CO,OT	3 Months/M	INJ	U	U	02Jun2009	U/U	Wrong drug administered	U
B0646580A	France	CO,OT	16 Weeks/M	INJ	U	U	09Jan2009	U/U	Wrong drug administered	U

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B0646582A	France	CO,OT	21 Weeks/M	INJ	U	U	17Mar2009	U/U	Wrong drug administered	U
B0646584A	France	CO,OT	11 Weeks/M	INJ	U	U	16Mar2009	U/U	Wrong drug administered	U
B0646586A	France	CO,OT	12 Weeks/M	INJ	U	U	09Mar2009	U/U	Wrong drug administered	U
B0646591A	France	CO,OT	14 Weeks/M	INJ	U	U	03Apr2009	U/U	Wrong drug administered	U
B0646611A	France	CO,OT	12 Weeks/M	INJ	U	U	05May2009	U/U	Wrong drug administered	U
B0646615A	France	CO,OT	12 Weeks/M	INJ	U	U	09Jun2009	U/U	Wrong drug administered	U

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B0646680A	France	CO,OT	4 Months/F	INJ	U	U, U	17Sep2008	U/U, U/U	Wrong drug administered	U
B0646682A	France	CO,OT	5 Months/F	INJ	U	U, U	05Jan2009	U/U, U/U	Wrong drug administered	U
B0646684A	France	CO,OT	4 Months/F	INJ	U	U, U	22Oct2007	U/U, U/U	Wrong drug administered	U
B0646686A	France	CO,OT	3 Months/F	INJ	U	U, U	08Jan2009	U/U, U/U	Wrong drug administered	U
B0647110A	France	CO,OT	16 Weeks/F	INJ	U	U	13Jan2009	U/U	Wrong drug administered	U
B0647123A	France	CO,OT	3 Months/F	INJ	U	U	22Dec2008	U/U	Wrong drug administered	U

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B0647126A	France	CO,OT	3 Months/F	INJ	U	U	10Jul2009	U/U	Wrong drug administered	U
B0647130A	France	CO,OT	3 Months/F	INJ	U	U	20Feb2009	U/U	Wrong drug administered	U
B0647131A	France	CO,OT	11 Weeks/F	INJ	U	U	24Apr2009	U/U	Wrong drug administered	U
B0647174A	France	CO,OT	3 Months/F	INJ	U	U	17Nov2008	U/U	Wrong drug administered	U
B0647208A	France	CO,OT	3 Months/M	INJ	U	U, U	14Nov2003	U/U, U/U	Wrong drug administered	U
B0647211A	France	CO,OT	4 Months/M	INJ	U	U, U	03Mar2003	U/U, U/U	Wrong drug administered	U

B0647219A	France	CO,OT	3 Months/M	INJ	U	U, U	20Jun2003	U/U, U/U	Wrong drug administered	U
B0647279A	France	CO,OT	6 Years/F	INJ	U	U	07Sep2009	U/U	Wrong drug administered	U
B0647280A	France	CO,OT	13 Weeks/F	INJ	U	U	06Sep2007	U/U	Wrong drug administered	U
B0647290A	France	CO,OT	13 Weeks/F	INJ	U	U	24Feb2009	U/U	Wrong drug administered	U
B0647293A	France	CO,OT	13 Weeks/F	INJ	U	U	05Dec2008	U/U	Wrong drug administered	U
B0647302A	France	CO,OT	12 Weeks/F	INJ	U	U	24Aug2009	U/U	Wrong drug administered	U

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B0647411A	France	CO,OT	15 Weeks/F	INJ	U	U	29Aug2009	U/U	Wrong drug administered	U
B0647413A	France	CO,OT	4 Months/F	INJ	U	U	17Aug2009	U/U	Wrong drug administered	U
B0647416A	France	CO,OT	5 Months/F	INJ	U	U	31Jul2009	U/U	Wrong drug administered	U
B0647418A	France	CO,OT	3 Months/F	INJ	U	U	28Jan2009	U/U	Wrong drug administered	U
B0647419A	France	CO,OT	4 Months/F	INJ	U	U	06Aug2009	U/U	Wrong drug administered	U
B0647420A	France	CO,OT	3 Months/F	INJ	U	U	21Feb2009	U/U	Wrong drug administered	U

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B0647422A	France	CO,OT	5 Months/F	INJ	U	U	02Jan2009	U/U	Wrong drug administered	U
B0647423A	France	CO,OT	5 Months/F	INJ	U	U	03Mar2009	U/U	Wrong drug administered	U
B0647425A	France	CO,OT	6 Months/F	INJ	U	U	15Jun2009	U/U	Wrong drug administered	U
B0647426A	France	CO,OT	18 Weeks/F	INJ	U	U	13May2009	U/U	Wrong drug administered	U
B0647461A	France	CO,OT	2 Months/F	U	U	U, U	02Feb2009	U/U, U/U	Wrong drug administered	U
B0647463A	France	CO,OT	2 Months/F	U	U	U, U	29Oct2008	U/U, U/U	Wrong drug administered	U

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B0647465A	France	CO,OT	3 Months/F	U	U	U, U	07Aug2008	U/U, U/U	Wrong drug administered	U
B0647467A	France	CO,OT	4 Months/F	U	U	U, U	05May2009	U/U, U/U	Wrong drug administered	U
B0647477A	France	CO,OT	3 Months/F	U	U	U, U	22May2009	U/U, U/U	Wrong drug administered	U
B0647479A	France	CO,OT	2 Months/F	U	U	U, U	18Aug2008	U/U, U/U	Wrong drug administered	U
B0614722A	France	CO	8 Months/F	INJ	U	01Jan2009-01Jan2009	01Jan2009	U/See text	Wrong drug administered*	X
B0644441A	France	CO,OT	U/F	U	U	U, U	24Apr2009	U/U, U/U	Wrong drug administered, Inappropriate schedule of drug administration	U

B0644446A	France	CO,OT	U/F	U	U	U, U	28May2009	U/U, U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644451A	France	CO,OT	U/F	U	U	U, U	28Aug2009	U/U, U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644452A	France	CO,OT	2 Months/F	INJ	U	U	24Aug2009	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644456A	France	CO,OT	U/F	U	U	U, U	08Jul2009	U/U, U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644460A	France	CO,OT	U/F	U	U	U, U	26Jun2009	U/U, U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644467A	France	CO,OT	10 Weeks/F	INJ	U	U	20Jun2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U

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B0644468A	France	CO,OT	11 Weeks/F	INJ	U	U	29Aug2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644470A	France	CO,OT	11 Weeks/F	INJ	U	U	16Dec2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644472A	France	CO,OT	U/F	U	U	U, U	16Jan2009	U/U, U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644473A	France	CO,OT	3 Months/F	INJ	U	U	26Sep2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644474A	France	CO,OT	3 Months/F	INJ	U	U	22Dec2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644477A	France	CO,OT	14 Weeks/F	INJ	U	U	31Jul2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U

B0644479A	France	CO,OT	3 Months/F	INJ	U	U	05Sep2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644481A	France	CO,OT	3 Months/F	INJ	U	U	23Oct2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644483A	France	CO,OT	3 Months/F	INJ	U	U	30Sep2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644488A	France	CO,OT	11 Weeks/F	INJ	U	U	11Sep2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644491A	France	CO,OT	U/F	U, U	U, U	U, U, U	13May2009	U/U, U/U, U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644696A	France	CO,OT	2 Months/M	INJ	U	U	13Dec2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U

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B0644720A	France	CO,OT	3 Months/M	INJ	U	U	31Jul2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644733A	France	CO,OT	3 Months/M	INJ	U	U	12Sep2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644785A	France	CO,OT	2 Months/M	INJ	U	U	29Oct2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644792A	France	CO,OT	3 Months/M	INJ	U	U	02Mar2009	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644819A	France	CO,OT	3 Months/M	INJ	U	U	20Feb2009	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644828A	France	CO,OT	3 Months/M	INJ	U	U	05Feb2009	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U

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B0644857A	France	CO,OT	3 Months/M	INJ	U	U	30Apr2009	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644874A	France	CO,OT	4 Months/M	INJ	U	U	12Dec2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0645039A	France	CO,OT	3 Months/M	INJ	U	U	14May2009	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0645041A	France	CO,OT	11 Weeks/M	INJ	U	U	31Jul2009	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0646597A	France	CO,OT	9 Weeks/M	INJ	U	U	05Feb2009	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0646600A	France	CO,OT	17 Weeks/M	INJ	U	U	14May2009	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U

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B0646602A	France	CO,OT	12 Weeks/M	INJ	U	U	27Feb2009	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0646875A	France	CO,OT	2 Years/M	INJ	U	U	29Nov2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0646886A	France	CO,OT	2 Years/M	INJ	U	U	20Nov2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0647112A	France	CO,OT	13 Weeks/F	INJ, INJ	U, U	U, U	30Apr2009	U/U, U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0647196A	France	CO,OT	12 Weeks/F	INJ, U	U, U	U, U	13Feb2009	U/U, U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0647198A	France	CO,OT	3 Months/F	INJ	U	U, U	21Jul2003	U/U, U/U	Wrong drug administered, Inappropriate schedule of drug administration	U

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B0647204A	France	CO,OT	5 Years/M	INJ	U	U	12Jan2009	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0647259A	France	CO,OT	5 Years/M	INJ	U	U	29Nov2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0647264A	France	CO,OT	14 Weeks/F	INJ, INJ	U, U	U, U	25Nov2008	U/U, U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0647407A	France	CO,OT	3 Months/F	INJ	U	U	07Jul2009	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0647409A	France	CO,OT	23 Weeks/F	INJ	U	U	14Apr2009	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0647421A	France	CO,OT	10 Weeks/F	INJ	U	U	03Jul2009	U/U	Wrong drug administered, Inappropriate schedule of drug administration	U

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B0647468A	France	CO,OT	2 Months/F	U	U	U, U	10Mar2009	U/U, U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0647472A	France	CO,OT	3 Months/F	U, U	U, U	U, U, U	20Jan2009	U/U, U/U, U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0647481A	France	CO,OT	2 Months/F	U	U	U, U	23Jun2009	U/U, U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0647482A	France	CO,OT	3 Months/F	U	U	U, U	29Jun2009	U/U, U/U	Wrong drug administered, Inappropriate schedule of drug administration	U
B0644097A	France	CO,OT	15 Weeks/F	INJ	U	U	10Jul2009	U/U	Wrong drug administered, Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	U

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B0644776A	France	CO,OT	2 Months/M	INJ	U	U	15Nov2008	U/U	Wrong drug administered, Inappropriate schedule of drug administration, Inappropriate schedule of drug administration	U
B0672050A	France	CO,CN	2 Months/F	INJ	U	06Jul2010-06Jul2010	06Jul2010	U/See text	Wrong technique in drug usage process	X
B0628030A	Argentina	CO	2 Months/M	INJ	U	14Jan2010-14Jan2010	14Jan2010	U/During	Wrong technique in drug usage process*	X
B0661614A	Italy	RP	U/U	INJ	U	1 Days		U/During	Wrong technique in drug usage process*	X
B0603082A	New Zealand	OT	3 Months/U	INJ	U	1 Days		U/During	Wrong technique in drug usage process*	X

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B0603007A	Sweden	CO	3 Months/F	INJ	U	1 Days		U/During	Wrong technique in drug usage process*	X
Investigations										
B0653828A	Latvia	CO	4 Months/U	INJ	U	1 Days		U/4 Days	Body temperature increased	R
Metabolism and nutrition disorders										
B0601932A	France	CO	4 Months/F	INJ	U	26Oct2009-26Oct2009	26Oct2009	U/0 Days	Decreased appetite*, Agitation*, Abdominal pain*, Diarrhoea*	N
B0601930A	France	CO	4 Months/F	INJ, INJ	U, U	26Oct2009-26Oct2009, 01Sep2009-01Sep2009	01Sep2009	U/1 Days, U/1 Days	Decreased appetite*, Agitation*, Abdominal pain*, Diarrhoea*, Decreased appetite*	N
B0680414A	Poland	CO	2 Months/F	INJ, INJ	U, U	19Aug2010-19Aug2010, 05Oct2010-05Oct2010	20Aug2010	U/1 Days, U/1 Days	Decreased appetite, Decreased appetite	U
Nervous system disorders										

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D0068214A	Germany	CO	9 Weeks/F	INJ	U	06Jul2010-06Jul2010	06Jul2010	U/Hours	Crying	U
B0617478A	Poland	CO	U/F	INJ, INJ	U, U	18Aug2009-18Aug2009, 09Dec2009-09Dec2009	18Aug2009	U/0 Days, U/0 Days	Crying*, Pyrexia*	R
B0633074A	Poland	CO	0 Years/M	INJ, INJ	U, U	15Dec2009-15Dec2009, 26Jan2010-26Jan2010	01Feb2010	U/Days, U/Days	Hypertonia*, Crying*, Somnolence*	N
D0067797A	Germany	CO	9 Weeks/F	INJ	.5ML	31May2010-31May2010	31May2010	U/0 Days	Somnolence*, Body temperature increased*	R
B0632971A	Poland	CO	0 Years/F	INJ	U	10Feb2010-10Feb2010	10Feb2010	U/Unknown	Somnolence*, Crying*	N
B0628325A	Poland	CO	18 Months/U	INJ	U	13Jan2010-13Jan2010	14Jan2010	U/1 Days	Tremor*, Anxiety*, Pyrexia*, Tearfulness*	U

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Psychiatric disorders										
B0674292A	Poland	CO	17 Months/M	INJ	U	07Sep2010-07Sep2010, 19May2009-19May2009, 15Jul2009-15Jul2009, 02Sep2009-02Sep2009	07Sep2010	U/0 Days, U/U, U/U, U/U	Apathy, Pyrexia	U
B0668394A	Poland	CO	U/F	INJ	U	U		U/2 Days	Apathy, Somnolence, Decreased appetite	N
D0067892A	Germany	CO	U/M	INJ	U	01Jan2010-01Jan2010		U/Unknown	Screaming*	N
D0066413A	Germany	CO	U/F	INJ	U	05Feb2010-05Feb2010	05Feb2010	U/0 Days	Screaming*, Agitation*	U
Respiratory, thoracic and mediastinal disorders										
B0628262A	Malta	CO	3 Months/M	INJ, INJ	U, U	11Jan2010-11Jan2010, 1 Days	17Jan2010	U/5 Days, U/Unknown	Nasal congestion*, Feeding disorder*, Insomnia*, Nasal congestion*, Feeding disorder*, Insomnia*, Injection site swelling*, Irritability*, Injection site swelling*, Irritability*	N

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Skin and subcutaneous tissue disorders

#D0063329A	Germany	CO	6 Months/M	INJ	.5ML	11Jul2007-11Jul2007, 14Apr2007-14Apr2007, 22May2007-22May2007	01Jul2007	U/14 Days, U/U, U/U	Dermatitis atopic*, Eczema*, Superinfection*, Decreased immune responsiveness*	I
D0066623A	Germany	CO	15 Weeks/M	INJ	U	01Feb2010-01Feb2010	01Feb2010	U/1 Days	Rash*, Agitation*	U
B0626778A	Greece	CO	4 Months/M	INJ	U	01Dec2009-01Dec2009	01Dec2009	U/Days	Rash generalised*	I
B0661786A	Thailand	CO	6 Months/M	INJ	.5ML	10Jun2010-10Jun2010	10Jun2010	U/0 Days	Rash*, Pyrexia*, Urticaria*	R
B0600573A	Peru	CO	6 Months/M	INJ	U	16Oct2009-16Oct2009	18Oct2009	U/2 Days	Rash*, Rash*, Rash*	R

D0063329B	Germany	CO	4 Months/M	INJ	.5ML	16Apr2007-16Apr2007	01May2007	U/4 Weeks	Seborrhoeic dermatitis*, Dermatitis*	R
D0063329C	Germany	CO	4 Months/M	INJ	.5ML	16Apr2007-16Apr2007, 22May2007-22May2007	01May2007	U/1 Weeks, U/U	Seborrhoeic dermatitis*, Dermatitis*	R

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APPENDIX 4A : All reported AEs for cases included in Appendix 3A

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Appendix 4A: Summary Tabulation of Adverse Events Included in the Line Listing for:

Infanrix hexa

N.B. Events are only considered serious if they fulfil GSK medically serious criteria. GSK medically serious criteria are applied automatically only to events from spontaneous, post-marketing or literature case reports. Events arising from Clinical trial cases are not run against the list of GSK medically serious terms. For this reason events may appear as both serious and non-serious. For full explanation see section 6.2.2.

MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Anaemia	No	6	0	6
		Hypochromic anaemia	No	1	0	1
		Iron deficiency anaemia	No	2	0	2
		Microcytic anaemia	No	2	0	2
		Pancytopenia	No	1	0	1
	Haemolyses and related conditions	Jaundice acholuric	No	1	0	1
		Warm type haemolytic anaemia	No	1	0	1
	Platelet disorders	Idiopathic thrombocytopenic purpura	No	6	0	6
		Thrombocytopenia	No	6	0	6
		Thrombocytopenic purpura	No	1	0	1
		Thrombocytosis	No	2	0	2
	Red blood cell disorders	Hypochromasia	No	1	0	1
		Microcytosis	No	1	0	1
	Spleen, lymphatic and	Lymphadenopathy	No	0	8	8

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	reticuloendothelial system disorders					
		Lymph node pain	No	0	1	1
	White blood cell disorders	Eosinophilia	No	0	1	1
		Granulocytopenia	No	1	0	1
		Leukocytosis	No	9	0	9
		Leukopenia	No	2	0	2
		Neutropenia	No	5	0	5
		White blood cell disorder	No	1	0	1
Cardiac disorders	Cardiac arrhythmias	Bradycardia	No	0	3	3
		Cardiac arrest	No	3	0	3
		Sinus tachycardia	No	0	1	1
		Tachycardia	No	0	4	4
	Cardiac disorder signs and symptoms	Cyanosis	No	39	10	48
Congenital, familial and genetic disorders	Blood and lymphatic system disorders congenital	Haemophilia	No	1	0	1
	Cardiac and vascular disorders congenital	Atrial septal defect	No	1	0	1
	Metabolic and nutritional disorders congenital	Methylmalonic aciduria	No	1	0	1
	Musculoskeletal and connective tissue disorders congenital	Microcephaly	No	1	0	1

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	Neurological disorders congenital	Cerebral palsy	No	1	0	1
Ear and labyrinth disorders	External ear disorders (excl congenital)	Auricular swelling	No	0	2	2
Eye disorders	Eye disorders NEC	Eye disorder	No	0	3	3
		Eyelid disorder	No	0	3	3
	Ocular infections, irritations and inflammations	Conjunctival hyperaemia	No	0	2	2
		Conjunctivitis	No	0	3	3
		Eyelid oedema	No	0	1	1
	Ocular neuromuscular disorders	Eyelid ptosis	No	0	1	1
		Eye movement disorder	No	0	4	4
		Gaze palsy	No	23	0	23
		Ophthalmoplegia	No	4	0	4
		Strabismus	No	0	2	2
	Ocular sensory symptoms NEC	Eye rolling	No	0	4	4
	Retina, choroid and vitreous haemorrhages and vascular disorders	Retinal haemorrhage	No	2	0	2
	Vision disorders	Anisometropia	No	0	1	1
		Astigmatism	No	0	1	1
		Diplopia	No	0	1	1
		Hypermetropia	No	0	1	1

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		Vision blurred	No	0	1	1
		Visual impairment	No	0	2	2
Gastrointestinal disorders	Abdominal hernias and other abdominal wall conditions	Inguinal hernia	No	0	1	1
	Gastrointestinal haemorrhages NEC	Haematochezia	No	5	2	7
		Melaena	No	1	0	1
		Rectal haemorrhage	No	3	0	3
	Gastrointestinal inflammatory conditions	Enteritis	No	1	0	1
		Gastritis	No	0	1	1
		Gastrointestinal inflammation	No	0	1	1
		Oesophagitis	No	0	1	1
	Gastrointestinal motility and defaecation conditions	Constipation	No	0	3	3
		Diarrhoea	Yes	0	19	19
		Diarrhoea haemorrhagic	No	1	0	1
		Gastrointestinal hypomotility	No	0	1	1
		Gastrooesophageal reflux disease	No	0	2	2
		Ileus paralytic	No	1	0	1
		Intestinal dilatation	No	0	1	1
	Gastrointestinal signs and symptoms	Abdominal distension	No	0	1	1

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		Abdominal pain	No	0	3	3
		Abdominal pain upper	No	0	1	1
		Abdominal rigidity	No	0	1	1
		Abnormal faeces	No	0	3	3
		Acute abdomen	No	1	0	1
		Dyspepsia	No	0	1	1
		Faeces discoloured	No	0	4	4
		Flatulence	No	0	3	3
		Mucous stools	No	0	2	2
		Nausea	No	0	1	1
		Regurgitation	No	0	4	4
		Vomiting	Yes	0	46	46
	Gastrointestinal stenosis and obstruction	Intestinal obstruction	No	1	0	1
		Intussusception	No	4	0	4
	Oral soft tissue conditions	Chapped lips	No	0	2	2
		Cheilitis	No	0	2	2
		Lip disorder	No	0	1	1
		Lip oedema	No	0	1	1
		Lip swelling	No	0	1	1
		Mouth haemorrhage	No	0	1	1

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	Peritoneal and retroperitoneal conditions	Ascites	No	1	0	1
		Peritoneal disorder	No	0	1	1
		Peritonitis	No	1	0	1
	Salivary gland conditions	Salivary hypersecretion	No	0	3	3
	Tongue conditions	Protrusion tongue	No	0	1	1
General disorders and administration site conditions	Administration site reactions	Application site discolouration	No	0	1	1
		Injected limb mobility decreased	No	0	1	1
		Injection site abscess sterile	No	0	1	1
		Injection site discolouration	No	0	3	3
		Injection site eczema	No	0	2	2
		Injection site erythema	Yes	0	70	70
		Injection site extravasation	No	0	5	5
		Injection site haematoma	No	0	6	6
		Injection site haemorrhage	No	0	2	2
		Injection site hypersensitivity	Yes	0	1	1
		Injection site induration	No	0	40	40
		Injection site inflammation	No	0	18	18
		Injection site mass	No	0	1	1
		Injection site necrosis	No	1	0	1
		Injection site nodule	No	0	24	24

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		Injection site oedema	Yes	0	27	27
		Injection site pain	Yes	0	26	26
		Injection site pallor	No	0	3	3
		Injection site pruritus	No	0	5	5
		Injection site rash	No	0	1	1
		Injection site reaction	No	0	28	28
		Injection site scab	No	0	1	1
		Injection site swelling	Yes	0	51	51
		Injection site vesicles	No	0	4	4
		Injection site warmth	No	0	21	21
		Vaccination site abscess sterile	No	1	0	1
		Vaccination site erythema	Yes	0	1	1
		Vaccination site granuloma	No	0	1	1
		Vaccination site induration	No	0	2	2
		Vaccination site oedema	No	0	3	3
		Vaccination site pain	Yes	0	1	1
		Vaccination site reaction	No	0	1	1
		Vaccination site swelling	No	0	2	2
	Body temperature conditions	Hyperpyrexia	No	0	4	4
		Hyperthermia	No	0	4	4
		Hypothermia	No	0	2	2

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		Pyrexia	Yes	0	233	233
	Device issues	Needle issue	No	0	1	1
	Fatal outcomes	Death	No	5	0	5
		Sudden infant death syndrome	No	8	0	8
	General system disorders NEC	Abasia	No	0	2	2
		Abscess sterile	No	4	0	4
		Asthenia	No	0	10	10
		Chills	No	0	5	5
		Condition aggravated	No	0	2	2
		Developmental delay	No	0	3	3
		Discomfort	No	0	3	3
		Disease recurrence	No	0	1	1
		Extensive swelling of vaccinated limb	Yes	0	5	5
		Face oedema	No	0	1	1
		Fatigue	No	0	17	17
		Feeling abnormal	No	0	1	1
		Feeling cold	No	0	1	1
		Feeling hot	No	0	5	5
		Feeling of body temperature change	No	0	1	1
		Feeling of relaxation	No	0	1	1
		Foaming at mouth	No	0	1	1

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		Gait deviation	No	0	1	1
		Gait disturbance	No	0	7	7
		General physical health deterioration	No	0	9	9
		Granuloma	No	0	2	2
		Ill-defined disorder	No	0	6	6
		Induration	No	0	8	8
		Inflammation	No	0	19	19
		Influenza like illness	No	0	1	1
		Irritability	Yes	0	18	18
		Local reaction	No	0	3	3
		Local swelling	No	0	6	6
		Malaise	No	0	11	11
		Nonspecific reaction	No	0	1	1
		Oedema peripheral	No	0	31	31
		Pain	No	0	19	19
		Swelling	No	0	15	15
		Thirst decreased	No	0	1	1
	Product quality issues	Incorrect product storage	No	0	16	16
		Product quality issue	No	0	15	15
	Therapeutic and nontherapeutic effects (excl toxicity)	Adverse drug reaction	No	0	1	1

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	Tissue disorders NEC	Dysplasia	No	0	1	1
		Fibrosis	No	0	1	1
		Nodule	No	0	1	1
		Ulcer	No	0	1	1
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Hepatic function abnormal	No	0	1	1
		Hepatosplenomegaly	No	0	1	1
		Jaundice	No	1	0	1
Immune system disorders	Allergic conditions	Anaphylactic reaction	Yes	3	0	3
		Anaphylactic shock	Yes	1	0	1
		Hypersensitivity	Yes	0	10	10
		Milk allergy	No	0	2	2
		Type III immune complex mediated reaction	No	0	2	2
	Immune disorders NEC	Immune system disorder	No	0	1	1
	Immunodeficiency syndromes	Selective IgA immunodeficiency	No	0	1	1
Infections and infestations	Bacterial infectious disorders	Bacterial infection	No	0	2	2
		Bronchitis bacterial	No	0	1	1
		Cellulitis	No	7	0	7
		Erysipelas	No	0	1	1
		Escherichia urinary tract infection	No	0	2	2
		Gastroenteritis bacterial	No	1	0	1

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		Haemophilus infection	No	0	3	3
		Injection site cellulitis	No	0	1	1
		Meningitis haemophilus	No	1	0	1
		Pertussis	No	0	21	21
	Infections - pathogen unspecified	Abscess	No	0	3	3
		Acute tonsillitis	No	0	2	2
		Bronchitis	No	0	6	6
		Ear infection	No	0	1	1
		Enteritis infectious	No	1	0	1
		Epiglottitis	No	1	0	1
		Febrile infection	No	0	1	1
		Gastroenteritis	No	6	0	6
		Incision site abscess	No	0	5	5
		Infection	No	0	5	5
		Injection site abscess	No	0	10	10
		Meningitis	No	1	0	1
		Meningitis aseptic	No	1	0	1
		Nasopharyngitis	No	0	3	3
		Osteomyelitis	No	1	0	1
		Otitis media	No	0	1	1

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		Pneumonia	No	4	0	4
		Purulence	No	0	1	1
		Purulent discharge	No	0	1	1
		Rash pustular	No	0	1	1
		Respiratory tract infection	No	0	1	1
		Rhinitis	No	0	8	8
		Sepsis	No	4	0	4
		Soft tissue infection	No	0	1	1
		Tracheitis	No	0	2	2
		Upper respiratory tract infection	No	0	3	3
		Urinary tract infection	No	0	2	2
		Vaccination site abscess	No	2	0	2
		Vaccination site infection	No	0	1	1
		Wound infection	No	0	1	1
	Viral infectious disorders	Bronchiolitis	No	0	2	2
		Croup infectious	No	0	2	2
		Eczema herpeticum	No	0	1	1
		Gastroenteritis norovirus	No	2	0	2
		Gastroenteritis rotavirus	No	4	0	4
		Gastroenteritis viral	No	1	0	1
		Gianotti-Crosti syndrome	No	0	2	2

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		Hepatitis viral	No	0	1	1
		Herpes ophthalmic	No	0	1	1
		Pneumonia respiratory syncytial viral	No	1	0	1
		Rotavirus infection	No	0	1	1
		Viral infection	No	0	5	5
Injury, poisoning and procedural complications	Chemical injury and poisoning	Drug exposure during pregnancy	No	0	1	1
	Injuries NEC	Child maltreatment syndrome	No	0	1	1
		Fall	No	0	2	2
		Laceration	No	0	1	1
	Medication errors	Accidental exposure	No	0	1	1
		Accidental overdose	No	0	4	4
		Drug administered at inappropriate site	No	0	1	1
		Drug administration error	No	0	11	11
		Drug dispensing error	No	0	2	2
		Expired drug administered	No	0	6	6
		Inappropriate schedule of drug administration	No	0	203	203
		Incorrect dose administered	No	0	18	18
		Incorrect route of drug administration	No	0	10	10
		Incorrect storage of drug	No	0	25	25
		Medication error	No	0	1	1

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		Overdose	No	0	11	11
		Underdose	No	0	20	20
		Wrong drug administered	No	0	52	52
		Wrong technique in drug usage process	No	0	80	80
	Procedural related injuries and complications NEC	Vaccination complication	No	0	14	14
		Vaccination failure	Yes	21	0	21
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Heart rate decreased	No	0	1	1
		Heart rate increased	No	0	3	3
		Pulse abnormal	No	0	1	1
		Pulse pressure increased	No	0	1	1
	Haematology investigations (incl blood groups)	White blood cell count increased	No	0	2	2
	Hepatobiliary investigations	Ammonia increased	No	0	1	1
		Hepatic enzyme increased	No	1	0	1
		Transaminases increased	No	3	0	3
	Immunology and allergy investigations	Allergy test positive	Yes	0	1	1
		Blood immunoglobulin E increased	No	0	1	1
		Blood immunoglobulin M decreased	No	0	1	1
	Metabolic, nutritional and	Blood glucose increased	No	0	1	1

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	blood gas investigations					
		Blood lactic acid increased	No	0	1	1
		Oxygen saturation decreased	No	0	6	6
	Microbiology and serology investigations	Clostridium test negative	No	0	1	1
		Corynebacterium test negative	No	0	1	1
		Hepatitis B antibody negative	No	0	1	1
		Hepatitis B antigen positive	No	0	1	1
		Hepatitis B surface antigen positive	No	0	1	1
		Rotavirus test positive	No	0	1	1
		Staphylococcus test positive	No	0	1	1
		Viral test positive	No	0	1	1
	Neurological, special senses and psychiatric investigations	Electroencephalogram abnormal	No	0	1	1
	Physical examination topics	Body temperature decreased	No	0	2	2
		Body temperature increased	Yes	0	10	10
		Head circumference abnormal	No	0	1	1
		Respiratory rate increased	No	0	1	1
		Weight decreased	No	0	4	4
	Protein and chemistry analyses NEC	C-reactive protein increased	No	0	7	7
	Water, electrolyte and mineral investigations	Serum ferritin increased	No	0	1	1

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Metabolism and nutrition disorders	Acid-base disorders	Acidosis	No	1	1	2
		Ketoacidosis	No	0	1	1
		Metabolic acidosis	No	1	0	1
	Appetite and general nutritional disorders	Appetite disorder	No	0	1	1
		Decreased appetite	Yes	0	18	18
	Electrolyte and fluid balance conditions	Dehydration	No	0	2	2
		Fluid intake reduced	No	0	7	7
		Hyponatraemia	No	0	3	3
		Oligodipsia	No	0	10	10
		Polydipsia	No	0	2	2
	Food intolerance syndromes	Lactose intolerance	No	0	2	2
	Glucose metabolism disorders (incl diabetes mellitus)	Type 1 diabetes mellitus	No	1	0	1
	Metabolism disorders NEC	Metabolic disorder	No	0	1	1
	Protein and amino acid metabolism disorders NEC	Hypoalbuminaemia	No	0	2	2
	Vitamin related disorders	Vitamin B12 deficiency	No	0	1	1
Musculoskeletal and connective tissue disorders	Connective tissue disorders (excl congenital)	Myofascitis	No	0	1	1
	Joint disorders	Arthralgia	No	0	1	1
		Arthritis	No	0	2	2

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		Joint hyperextension	No	0	1	1
		Joint stiffness	No	0	1	1
		Joint swelling	No	0	2	2
	Muscle disorders	Muscle disorder	No	0	1	1
		Muscle rigidity	No	0	6	6
		Muscle spasms	No	0	7	7
		Muscle twitching	No	0	5	5
		Muscular weakness	No	0	2	2
		Myalgia	No	0	2	2
		Myositis	No	0	2	2
		Trismus	No	0	1	1
	Musculoskeletal and connective tissue disorders NEC	Mobility decreased	No	0	3	3
		Musculoskeletal stiffness	No	0	5	5
		Pain in extremity	No	0	11	11
		Posture abnormal	No	0	1	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Haematopoietic neoplasms (excl leukaemias and lymphomas)	Histiocytosis haematophagic	No	1	0	1
	Leukaemias	B precursor type acute leukaemia	No	1	0	1
Nervous system disorders	Central nervous system infections and	Encephalitis	No	1	0	1

CONFIDENTIAL

	inflammations					
	Central nervous system vascular disorders	Cerebral haemorrhage	No	1	0	1
		Cerebrovascular disorder	No	1	0	1
	Cranial nerve disorders (excl neoplasms)	Paresis cranial nerve	No	2	0	2
	Demyelinating disorders	Demyelination	No	1	0	1
	Encephalopathies	Encephalopathy	No	2	0	2
		Periventricular leukomalacia	No	1	0	1
	Mental impairment disorders	Autism	No	2	0	2
		Disturbance in attention	No	0	2	2
		Mental impairment	No	0	3	3
		Mental retardation	No	0	1	1
	Movement disorders (incl parkinsonism)	Bradykinesia	No	0	1	1
		Choreoathetosis	No	0	1	1
		Dyskinesia	No	0	4	4
		Dystonia	No	0	1	1
		Head titubation	No	0	1	1
		Hemiparesis	No	1	0	1
		Hypokinesia	No	0	4	4
		Masked facies	No	0	2	2

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		Monoparesis	No	3	0	3
		Monoplegia	No	1	0	1
		Motor developmental delay	No	0	1	1
		Movement disorder	No	0	2	2
		Opisthotonus	No	0	1	1
		Paresis	No	2	0	2
		Postictal paralysis	No	1	0	1
		Psychomotor hyperactivity	No	0	1	1
		Tremor	No	0	8	8
	Neurological disorders NEC	Altered state of consciousness	No	3	0	3
		Aphasia	No	1	0	1
		Areflexia	No	0	3	3
		Ataxia	No	0	2	2
		Balance disorder	No	0	1	1
		Clonus	No	0	1	1
		Crying	Yes	0	116	116
		Depressed level of consciousness	No	39	0	39
		Dizziness	No	0	1	1
		Drooling	No	0	3	3
		Fontanelle bulging	No	0	1	1
		Hyperaesthesia	No	0	5	5

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		Hyperreflexia	No	0	1	1
		Hyporeflexia	No	0	1	1
		Lethargy	No	0	4	4
		Loss of consciousness	No	32	0	32
		Meningism	No	0	1	1
		Motor dysfunction	No	0	3	3
		Myoclonus	No	0	3	3
		Nervous system disorder	No	0	2	2
		Nystagmus	No	0	1	1
		Poor sucking reflex	No	0	1	1
		Postictal state	No	0	1	1
		Presyncope	No	1	1	2
		Psychomotor skills impaired	No	0	1	1
		Sensory loss	No	0	1	1
		Somnolence	Yes	0	28	28
		Speech disorder developmental	No	0	2	2
		Subdural effusion	No	0	1	1
		Syncope	No	1	0	1
		Unresponsive to stimuli	No	6	1	7
	Neuromuscular disorders	Cholinergic syndrome	No	0	1	1
		Hypertonia	No	0	7	7

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		Hypotonia	No	0	79	79
		Hypotonic-hyporesponsive episode	No	0	38	38
		Muscle spasticity	No	0	1	1
		Sensorimotor disorder	No	0	1	1
	Seizures (incl subtypes)	Atonic seizures	No	1	0	1
		Clonic convulsion	No	1	0	1
		Convulsion	No	53	0	53
		Convulsions local	No	1	0	1
		Epilepsy	No	9	0	9
		Febrile convulsion	No	54	0	54
		Grand mal convulsion	No	18	0	18
		Infantile spasms	No	1	1	2
		Partial seizures	No	3	0	3
		Petit mal epilepsy	No	2	0	2
		Status epilepticus	No	4	0	4
		Tonic convulsion	No	3	0	3
	Sleep disturbances (incl subtypes)	Cataplexy	No	1	0	1
		Circadian rhythm sleep disorder	No	0	1	1
		Hypersomnia	No	0	2	2
		Poor quality sleep	No	0	2	2

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	Structural brain disorders	Cerebral atrophy	No	1	0	1
		Cerebral ventricle dilatation	No	1	0	1
Pregnancy, puerperium and perinatal conditions	Neonatal and perinatal conditions	Poor weight gain neonatal	No	0	1	1
	Pregnancy, labour, delivery and postpartum conditions	Live birth	No	0	1	1
Psychiatric disorders	Anxiety disorders and symptoms	Agitation	No	0	10	10
		Anxiety	No	0	1	1
		Anxiety disorder due to a general medical condition	No	0	1	1
		Nervousness	Yes	0	1	1
		Tension	No	0	1	1
	Changes in physical activity	Decreased activity	No	0	3	3
		Restlessness	Yes	0	25	25
	Communication disorders and disturbances	Mutism	No	0	1	1
		Screaming	No	0	10	10
	Deliria (incl confusion)	Disorientation	No	0	2	2
	Depressed mood disorders and disturbances	Tearfulness	Yes	0	1	1
	Dissociative disorders	Dissociation	No	0	1	1
	Disturbances in thinking and perception	Delusion	No	0	1	1
	Eating disorders and disturbances	Food aversion	Yes	0	2	2

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	Mood disorders and disturbances NEC	Apathy	No	0	5	5
		Emotional distress	No	0	1	1
		Moaning	No	0	2	2
	Personality disorders and disturbances in behaviour	Indifference	No	0	1	1
	Psychiatric and behavioural symptoms NEC	Abnormal behaviour	No	0	6	6
		Decreased eye contact	No	0	2	2
		Staring	No	0	13	13
	Sleep disorders and disturbances	Insomnia	No	0	8	8
		Sleep disorder	No	0	4	4
		Sopor	Yes	0	1	1
Renal and urinary disorders	Urinary tract signs and symptoms	Enuresis	No	0	1	1
		Polyuria	No	0	1	1
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Asthma	No	1	0	1
		Bronchospasm	No	0	1	1
	Lower respiratory tract disorders (excl obstruction and infection)	Atelectasis	No	1	0	1
		Interstitial lung disease	No	1	0	1
		Pneumonia aspiration	No	1	0	1

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	Neonatal respiratory disorders	Apparent life threatening event	No	6	0	6
		Infantile apnoeic attack	No	1	0	1
	Respiratory disorders NEC	Apnoea	No	21	0	21
		Apnoeic attack	No	0	3	3
		Asphyxia	No	0	1	1
		Choking	No	1	0	1
		Choking sensation	No	0	1	1
		Cough	No	0	16	16
		Cyanosis central	No	1	0	1
		Dry throat	No	0	1	1
		Dyspnoea	No	0	14	14
		Hiccups	No	0	1	1
		Productive cough	No	0	1	1
		Rales	No	0	1	1
		Respiration abnormal	No	0	8	8
		Respiratory arrest	No	2	0	2
		Respiratory disorder	No	0	6	6
		Rhinorrhoea	No	0	1	1
		Sleep apnoea syndrome	No	0	1	1
		Sneezing	No	0	1	1

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		Tachypnoea	No	0	1	1
		Upper respiratory tract inflammation	No	0	1	1
		Yawning	No	0	1	1
	Upper respiratory tract disorders (excl infections)	Pharyngeal erythema	No	0	4	4
		Rhinitis allergic	No	0	1	1
		Stridor	No	1	0	1
Skin and subcutaneous tissue disorders	Angioedema and urticaria	Angioedema	Yes	8	0	8
		Urticaria	Yes	0	18	18
		Urticaria papular	No	0	1	1
	Cornification and dystrophic skin disorders	Skin hypertrophy	No	0	1	1
	Epidermal and dermal conditions	Blister	No	0	3	3
		Dermatitis	No	0	1	1
		Dermatitis allergic	Yes	0	1	1
		Dermatitis atopic	No	0	6	6
		Dermatitis diaper	No	0	1	1
		Dry skin	No	0	1	1
		Eczema	No	0	5	5
		Erythema	No	0	46	46
		Erythema multiforme	No	1	0	1
		Generalised erythema	No	0	2	2

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		Lichen striatus	No	0	1	1
		Neurodermatitis	No	0	2	2
		Prurigo	No	0	1	1
		Pruritus	No	0	8	8
		Rash	No	0	45	45
		Rash erythematous	No	0	10	10
		Rash generalised	No	0	5	5
		Rash macular	No	0	9	9
		Rash maculo-papular	No	0	9	9
		Rash morbilliform	No	0	1	1
		Rash papular	No	0	4	4
		Rash vesicular	No	0	1	1
		Scar	No	0	1	1
		Skin chapped	No	0	1	1
		Skin discolouration	No	0	13	13
		Skin exfoliation	No	0	1	1
		Skin lesion	No	0	1	1
		Skin warm	No	0	6	6
		Swelling face	No	0	4	4
	Pigmentation disorders	Schamberg's disease	No	0	1	1
		Skin depigmentation	No	0	2	2

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	Skin and subcutaneous tissue disorders NEC	Erythema nodosum	No	0	1	1
		Skin ulcer	No	0	1	1
	Skin appendage conditions	Cold sweat	No	0	3	3
		Hair growth abnormal	No	0	1	1
		Hyperhidrosis	No	0	4	4
	Skin vascular abnormalities	Ecchymosis	No	0	2	2
		Henoch-Schonlein purpura	No	1	0	1
		Livedo reticularis	No	0	3	3
		Lividity	No	0	2	2
		Petechiae	No	0	24	24
		Purpura	No	0	6	6
		Skin oedema	No	0	1	1
		Spider naevus	No	0	1	1
Surgical and medical procedures	Gastrointestinal therapeutic procedures	Colectomy	No	0	1	1
		Ileostomy	No	0	1	1
		Small intestinal resection	No	0	1	1
	Haematological and lymphoid tissue therapeutic procedures	Haemostasis	No	0	1	1
	Respiratory tract therapeutic procedures	Mechanical ventilation	No	0	1	1

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	Skin and subcutaneous tissue therapeutic procedures	Skin lesion excision	No	0	1	1
	Therapeutic procedures and supportive care NEC	Enteral nutrition	No	0	1	1
		Macrophage activation	No	0	1	1
		Off label use	No	0	11	11
		Resuscitation	No	0	3	3
Vascular disorders	Decreased and nonspecific blood pressure disorders and shock	Circulatory collapse	No	1	0	1
		Hypotension	No	0	2	2
	Embolism and thrombosis	Jugular vein thrombosis	No	1	0	1
		Thrombosis	No	1	0	1
	Vascular disorders NEC	Capillary disorder	No	0	1	1
		Flushing	No	0	1	1
		Hyperaemia	No	0	4	4
		Pallor	No	0	67	67
		Vasodilatation	No	0	1	1
	Vascular haemorrhagic disorders	Haematoma	No	0	6	6
		Haemorrhage	No	1	0	1
	Vascular hypertensive disorders	Hypertension	No	0	1	1

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	Vascular inflammations	Kawasaki's disease	No	0	5	5
		Vasculitis	No	1	0	1

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APPENDIX 4B : All reported AEs for cases included in Appendix 3C

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Appendix 4B: Summary Tabulation of Adverse Events for Non-Serious Listed Cases for:

Infanrix hexa

N.B. Events are considered non serious against GSK list of medically serious terms (see section 6.3.)

MedDRA SOC	HLGT	Event PT	Non-serious
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Diarrhoea	2
	Gastrointestinal signs and symptoms	Vomiting	2
General disorders and administration site conditions	Administration site reactions	Injection site erythema	10
		Injection site pain	6
		Injection site swelling	21
	Body temperature conditions	Pyrexia	30
	General system disorders NEC	Extensive swelling of vaccinated limb	1
		Irritability	10
Investigations	Physical examination topics	Body temperature increased	1
Nervous system disorders	Neurological disorders NEC	Crying	11
Skin and subcutaneous tissue disorders	Angioedema and urticaria	Urticaria	5
	Epidermal and dermal conditions	Dermatitis allergic	1

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APPENDIX 4C : All reported AEs from non-medically verified serious cases and non-serious unlisted cases

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Appendix 4C: Summary Tabulation of Adverse Events from Non-Medically Verified, Serious Listed + Unlisted + Non-Serious Unlisted Cases for:

Infanrix hexa

N.B. Events are only considered serious if they fulfil GSK medically serious criteria. GSK medically serious criteria are applied automatically only to events from spontaneous, post-marketing or literature case reports. Events arising from Clinical trial cases are not run against the list of GSK medically serious terms. For this reason events may appear as both serious and non-serious. For full explanation see section 6.2.2.

MedDRA SOC	HLGT	Event (PT)	Listed	Serious	Non-serious	Total Cases for current period
Eye disorders	Ocular sensory symptoms NEC	Eye rolling	No	0	1	1
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Diarrhoea	Yes	0	2	2
	Gastrointestinal signs and symptoms	Abdominal pain	No	0	2	2
	Salivary gland conditions	Parotid gland enlargement	No	0	1	1
		Salivary hypersecretion	No	0	1	1
General disorders and administration site conditions	Administration site reactions	Injection site induration	No	0	2	2
		Injection site pain	Yes	0	3	3
		Injection site pruritus	No	0	1	1
		Injection site reaction	No	0	1	1
		Injection site scar	No	0	1	1
		Injection site swelling	Yes	0	2	2
		Injection site warmth	No	0	2	2

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	Body temperature conditions	Pyrexia	Yes	0	10	10
	General system disorders NEC	Fatigue	No	0	1	1
		Irritability	Yes	0	3	3
		Swelling	No	0	1	1
	Product quality issues	Incorrect product storage	No	0	1	1
		Product quality issue	No	0	2	2
Immune system disorders	Immune disorders NEC	Decreased immune responsiveness	No	0	1	1
Infections and infestations	Bacterial infectious disorders	Haemophilus infection	No	0	1	1
		Meningitis pneumococcal	No	1	0	1
	Infections - pathogen unspecified	Abscess limb	No	0	1	1
		Pharyngitis	No	0	1	1
		Pneumonia	No	1	0	1
		Superinfection	No	0	1	1
		Urinary tract infection	No	0	1	1
Injury, poisoning and procedural complications	Medication errors	Expired drug administered	No	0	1	1
		Inappropriate schedule of drug administration	No	0	102	102
		Incorrect dose administered	No	0	6	6
		Incorrect storage of drug	No	0	5	5

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		Overdose	No	0	1	1
		Underdose	No	0	3	3
		Wrong drug administered	No	0	175	175
		Wrong technique in drug usage process	No	0	6	6
	Procedural related injuries and complications NEC	Vaccination failure	Yes	1	0	1
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Decreased appetite	Yes	0	3	3
		Feeding disorder	No	0	1	1
Musculoskeletal and connective tissue disorders	Muscle disorders	Muscle spasms	No	0	1	1
	Musculoskeletal and connective tissue disorders NEC	Muscle contracture	No	0	1	1
		Nodule on extremity	No	0	1	1
Nervous system disorders	Central nervous system vascular disorders	Cerebral haemorrhage	No	1	0	1
	Movement disorders (incl parkinsonism)	Hemiplegia	No	1	0	1
		Tremor	No	0	1	1
	Neurological disorders NEC	Crying	Yes	0	3	3
		Motor dysfunction	No	0	1	1
		Somnolence	Yes	0	2	2

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	Neuromuscular disorders	Hypertonia	No	0	1	1
Psychiatric disorders	Anxiety disorders and symptoms	Agitation	No	0	5	5
		Anxiety	No	0	1	1
	Changes in physical activity	Restlessness	Yes	0	1	1
	Cognitive and attention disorders and disturbances	Daydreaming	No	0	1	1
	Communication disorders and disturbances	Screaming	No	0	2	2
	Depressed mood disorders and disturbances	Tearfulness	Yes	0	1	1
	Mood disorders and disturbances NEC	Apathy	No	0	2	2
	Sleep disorders and disturbances	Insomnia	No	0	1	1
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory disorder	No	0	1	1
	Upper respiratory tract disorders (excl infections)	Nasal congestion	No	0	1	1
Skin and subcutaneous tissue disorders	Angioedema and urticaria	Urticaria	Yes	0	1	1
	Epidermal and dermal conditions	Dermatitis	No	0	2	2
		Dermatitis atopic	No	0	1	1
		Eczema	No	0	1	1

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		Rash	No	0	3	3
		Rash generalised	No	0	1	1
		Seborrhoeic dermatitis	No	0	2	2
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Off label use	No	0	1	1
Vascular disorders	Vascular hypertensive disorders	Hypertension	No	0	1	1

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APPENDIX 4D : All reported AEs from non-medically verified non-serious listed cases

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Appendix 4D: Summary Tabulation of Adverse Events from Non-Medically Verified, Non-Serious Listed Cases for:

Infanrix hexa

N.B. Events are considered non serious against GSK list of medically serious terms (see section 6.3.)

MedDRA SOC	HLGT	Event (PT)	Non-serious
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Vomiting	3
General disorders and administration site conditions	Administration site reactions	Injection site erythema	1
	Body temperature conditions	Pyrexia	7
	Therapeutic and nontherapeutic effects (excl toxicity)	No therapeutic response	1
Investigations	Physical examination topics	Body temperature increased	2
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Decreased appetite	2
Nervous system disorders	Neurological disorders NEC	Crying	3
		Somnolence	2

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APPENDIX 4E : Cumulative tabulation of all unlisted events from serious unlisted spontaneous reports and all serious unlisted reactions from clinical trial cases reported since launch

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Cumulative count
23oct2000 to 22oct2010
Drug PTT decode : IGA182
Date of Refresh : 08Nov2010

MedDRA SOC	MedDRA HLGT	MedDRA PT	Number of AEs	Event level Seriousness
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Anaemia	1	No
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Anaemia	24	Yes
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Aplastic anaemia	1	Yes
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Bicytopenia	1	Yes
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Haemorrhagic anaemia	3	Yes
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Hypochromic anaemia	3	Yes
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Iron deficiency anaemia	4	Yes
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Microcytic anaemia	3	Yes
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Pancytopenia	3	Yes
Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Protein deficiency anaemia	1	Yes
Blood and lymphatic system disorders	Coagulopathies and bleeding diatheses (excl thrombocytopenic)	Coagulopathy	3	Yes
Blood and lymphatic system disorders	Coagulopathies and bleeding diatheses (excl thrombocytopenic)	Disseminated intravascular coagulation	5	Yes
Blood and lymphatic system disorders	Coagulopathies and bleeding diatheses (excl thrombocytopenic)	Haemorrhagic diathesis	2	Yes
Blood and lymphatic system disorders	Haematological disorders NEC	Hypergammaglobulinaemia	1	Yes
Blood and lymphatic system disorders	Haemolyses and related conditions	Anaemia haemolytic autoimmune	3	Yes
Blood and lymphatic system disorders	Haemolyses and related conditions	Haemolysis	4	Yes
Blood and lymphatic system disorders	Haemolyses and related conditions	Haemolytic anaemia	3	Yes
Blood and lymphatic system disorders	Haemolyses and related conditions	Haemolytic uraemic syndrome	1	Yes
Blood and lymphatic system disorders	Haemolyses and related conditions	Jaundice acholuric	1	Yes
Blood and lymphatic system disorders	Haemolyses and related conditions	Warm type haemolytic anaemia	1	Yes
Blood and lymphatic system disorders	Platelet disorders	Autoimmune thrombocytopenia	7	Yes

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Blood and lymphatic system disorders	Platelet disorders	Idiopathic thrombocytopenic purpura	21	Yes
Blood and lymphatic system disorders	Platelet disorders	Thrombocytopenia	1	No
Blood and lymphatic system disorders	Platelet disorders	Thrombocytopenia	33	Yes
Blood and lymphatic system disorders	Platelet disorders	Thrombocytopenic purpura	8	Yes
Blood and lymphatic system disorders	Platelet disorders	Thrombocytosis	7	Yes
Blood and lymphatic system disorders	Red blood cell disorders	Hypochromasia	1	Yes
Blood and lymphatic system disorders	Red blood cell disorders	Microcytosis	2	Yes
Blood and lymphatic system disorders	Spleen, lymphatic and reticuloendothelial system disorders	Lymphadenitis	5	No
Blood and lymphatic system disorders	Spleen, lymphatic and reticuloendothelial system disorders	Lymphadenitis	1	Yes
Blood and lymphatic system disorders	Spleen, lymphatic and reticuloendothelial system disorders	Lymphadenopathy	20	No
Blood and lymphatic system disorders	Spleen, lymphatic and reticuloendothelial system disorders	Lymphadenopathy	2	Yes
Blood and lymphatic system disorders	Spleen, lymphatic and reticuloendothelial system disorders	Lymphatic disorder	1	Yes
Blood and lymphatic system disorders	Spleen, lymphatic and reticuloendothelial system disorders	Lymph node pain	1	No
Blood and lymphatic system disorders	Spleen, lymphatic and reticuloendothelial system disorders	Splenitis	1	Yes
Blood and lymphatic system disorders	Spleen, lymphatic and reticuloendothelial system disorders	Splenomegaly	4	Yes
Blood and lymphatic system disorders	White blood cell disorders	Agranulocytosis	2	Yes
Blood and lymphatic system disorders	White blood cell disorders	Autoimmune neutropenia	1	Yes
Blood and lymphatic system disorders	White blood cell disorders	Eosinophilia	5	No
Blood and lymphatic system disorders	White blood cell disorders	Febrile neutropenia	2	Yes
Blood and lymphatic system disorders	White blood cell disorders	Granulocytopenia	5	Yes
Blood and lymphatic system disorders	White blood cell disorders	Leukocytosis	1	No
Blood and lymphatic system disorders	White blood cell disorders	Leukocytosis	28	Yes
Blood and lymphatic system disorders	White blood cell disorders	Leukopenia	3	Yes
Blood and lymphatic system disorders	White blood cell disorders	Lymphocytic infiltration	1	No
Blood and lymphatic system disorders	White blood cell disorders	Lymphocytosis	7	Yes
Blood and lymphatic system disorders	White blood cell disorders	Lymphopenia	2	Yes

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Blood and lymphatic system disorders	White blood cell disorders	Monocytosis	2	Yes
Blood and lymphatic system disorders	White blood cell disorders	Neutropenia	14	Yes
Blood and lymphatic system disorders	White blood cell disorders	Neutrophilia	1	Yes
Blood and lymphatic system disorders	White blood cell disorders	White blood cell disorder	1	Yes
Cardiac disorders	Cardiac arrhythmias	Arrhythmia	3	No
Cardiac disorders	Cardiac arrhythmias	Atrioventricular block	1	Yes
Cardiac disorders	Cardiac arrhythmias	Bradycardia	32	No
Cardiac disorders	Cardiac arrhythmias	Cardiac arrest	9	Yes
Cardiac disorders	Cardiac arrhythmias	Cardio-respiratory	5	Yes
Cardiac disorders	Cardiac arrhythmias	Extrasystoles	1	No
Cardiac disorders	Cardiac arrhythmias	Sinus arrhythmia	1	No
Cardiac disorders	Cardiac arrhythmias	Sinus bradycardia	1	Yes
Cardiac disorders	Cardiac arrhythmias	Sinus tachycardia	1	No
Cardiac disorders	Cardiac arrhythmias	Tachycardia	25	No
Cardiac disorders	Cardiac arrhythmias	Tachycardia	1	Yes
Cardiac disorders	Cardiac arrhythmias	Ventricular asystole	1	Yes
Cardiac disorders	Cardiac arrhythmias	Ventricular flutter	1	Yes
Cardiac disorders	Cardiac arrhythmias	Ventricular tachycardia	1	Yes
Cardiac disorders	Cardiac arrhythmias	Wolff-Parkinson-White	2	Yes
Cardiac disorders	Cardiac disorder signs and symptoms	Cardiovascular disorder	8	No
Cardiac disorders	Cardiac disorder signs and symptoms	Cardiovascular disorder	1	Yes
Cardiac disorders	Cardiac disorder signs and symptoms	Cardiovascular insufficiency	1	Yes
Cardiac disorders	Cardiac disorder signs and symptoms	Cyanosis	32	No
Cardiac disorders	Cardiac disorder signs and symptoms	Cyanosis	180	Yes
Cardiac disorders	Cardiac valve disorders	Aortic valve incompetence	1	Yes
Cardiac disorders	Cardiac valve disorders	Mitral valve disease	2	No
Cardiac disorders	Cardiac valve disorders	Pulmonary valve stenosis	1	Yes
Cardiac disorders	Cardiac valve disorders	Supravalvular aortic stenosis	1	No
Cardiac disorders	Coronary artery disorders	Arteritis coronary	2	Yes
Cardiac disorders	Coronary artery disorders	Coronary artery	1	Yes
Cardiac disorders	Coronary artery disorders	Coronary artery	2	No
Cardiac disorders	Coronary artery disorders	Coronary artery disease	1	No

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Cardiac disorders	Coronary artery disorders	Myocardial infarction	3	Yes
Cardiac disorders	Endocardial disorders	Endocardial fibrosis	1	No
Cardiac disorders	Heart failures	Cardiac failure	5	Yes
Cardiac disorders	Heart failures	Cardiac failure acute	1	Yes
Cardiac disorders	Heart failures	Cardiopulmonary failure	3	Yes
Cardiac disorders	Myocardial disorders	Atrial septal defect	1	No
Cardiac disorders	Myocardial disorders	Cardiomegaly	2	No
Cardiac disorders	Myocardial disorders	Congestive cardiomyopath	2	Yes
Cardiac disorders	Myocardial disorders	Hypertrophic cardiomyopath	1	Yes
Cardiac disorders	Myocardial disorders	Myocarditis	3	Yes
Cardiac disorders	Pericardial disorders	Pericardial effusion	4	Yes
Congenital, familial and genetic disorders	Blood and lymphatic system disorders congenital	Haemophilia	1	Yes
Congenital, familial and genetic disorders	Blood and lymphatic system disorders congenital	Infantile genetic agranulocytosi	2	Yes
Congenital, familial and genetic disorders	Cardiac and vascular disorders congenital	Atrial septal defect	5	Yes
Congenital, familial and genetic disorders	Chromosomal abnormalities and abnormal gene carriers	Cytogenetic abnormality	1	Yes
Congenital, familial and genetic disorders	Congenital and hereditary disorders NEC	Familial mediterranean fever	1	Yes
Congenital, familial and genetic disorders	Cytoplasmic disorders congenital	Mitochondrial encephalomyopathy	1	Yes
Congenital, familial and genetic disorders	Gastrointestinal tract disorders congenital	Pyloric stenosis	1	No
Congenital, familial and genetic disorders	Immune system disorders congenital	Thymus hypoplasia	1	Yes
Congenital, familial and genetic disorders	Metabolic and nutritional disorders congenital	Glycogen storage disorder	1	Yes
Congenital, familial and genetic disorders	Metabolic and nutritional disorders congenital	Leukodystrophy	2	Yes
Congenital, familial and genetic disorders	Metabolic and nutritional disorders congenital	Methylmalonic aciduria	1	Yes
Congenital, familial and genetic disorders	Metabolic and nutritional disorders congenital	Rett's disorder	1	Yes
Congenital, familial and genetic disorders	Musculoskeletal and connective tissue disorders congenital	Dysmorphism	1	Yes
Congenital, familial and genetic disorders	Musculoskeletal and connective tissue disorders congenital	Microcephaly	3	Yes

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Congenital, familial and genetic disorders	Musculoskeletal and connective tissue disorders congenital	Plagiocephaly	2	Yes
Congenital, familial and genetic disorders	Musculoskeletal and connective tissue disorders congenital	Skull malformation	1	No
Congenital, familial and genetic disorders	Neurological disorders congenital	Aicardi's syndrome	1	Yes
Congenital, familial and genetic disorders	Neurological disorders congenital	Benign familial neonatal convulsions	1	Yes
Congenital, familial and genetic disorders	Neurological disorders congenital	Cerebral palsy	4	Yes
Congenital, familial and genetic disorders	Neurological disorders congenital	Lissencephaly	1	Yes
Congenital, familial and genetic disorders	Neurological disorders congenital	Microencephal y	1	Yes
Congenital, familial and genetic disorders	Neurological disorders congenital	Tuberous sclerosis	2	Yes
Congenital, familial and genetic disorders	Renal and urinary tract disorders congenital	Renal hypoplasia	1	Yes
Congenital, familial and genetic disorders	Reproductive tract and breast disorders congenital	Hydrocele	2	No
Ear and labyrinth disorders	Aural disorders NEC	Ear pain	1	No
Ear and labyrinth disorders	Aural disorders NEC	Ear pain	1	Yes
Ear and labyrinth disorders	External ear disorders (excl congenital)	Auricular perichondritis	1	No
Ear and labyrinth disorders	External ear disorders (excl congenital)	Auricular swelling	1	No
Ear and labyrinth disorders	External ear disorders (excl congenital)	Auricular swelling	1	Yes
Ear and labyrinth disorders	Hearing disorders	Deafness	2	Yes
Ear and labyrinth disorders	Hearing disorders	Deafness neurosensory	1	Yes
Ear and labyrinth disorders	Hearing disorders	Hyperacusis	1	No
Ear and labyrinth disorders	Inner ear and VIIIth cranial nerve disorders	Vertigo	1	No
Ear and labyrinth disorders	Middle ear disorders (excl congenital)	Otosalpingitis	1	No
Ear and labyrinth disorders	Middle ear disorders (excl congenital)	Tympanic membrane hyperaemia	5	No
Endocrine disorders	Endocrine and glandular disorders NEC	Endocrine pancreatic disorder	1	No
Endocrine disorders	Thyroid gland disorders	Hypothyroidis	3	Yes
Eye disorders	Eye disorders NEC	Eye disorder	16	No
Eye disorders	Eye disorders NEC	Eyelid disorder	6	No
Eye disorders	Eye disorders NEC	Eye swelling	1	No

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Eye disorders	Eye disorders NEC	Lacrimation increased	4	No
Eye disorders	Eye disorders NEC	Periorbital oedema	1	No
Eye disorders	Ocular haemorrhages and vascular disorders NEC	Conjunctival haemorrhage	2	No
Eye disorders	Ocular haemorrhages and vascular disorders NEC	Corneal bleeding	1	Yes
Eye disorders	Ocular infections, irritations and inflammations	Conjunctival hyperaemia	3	No
Eye disorders	Ocular infections, irritations and inflammations	Conjunctivitis	12	No
Eye disorders	Ocular infections, irritations and inflammations	Eye discharge	1	No
Eye disorders	Ocular infections, irritations and inflammations	Eyelid oedema	7	No
Eye disorders	Ocular infections, irritations and inflammations	Ocular hyperaemia	1	No
Eye disorders	Ocular neuromuscular disorders	Binocular eye movement disorder	2	No
Eye disorders	Ocular neuromuscular disorders	Blepharospas m	2	No
Eye disorders	Ocular neuromuscular disorders	Excessive eye blinking	1	No
Eye disorders	Ocular neuromuscular disorders	Eyelid function disorder	1	No
Eye disorders	Ocular neuromuscular disorders	Eyelid ptosis	3	No
Eye disorders	Ocular neuromuscular disorders	Eye movement disorder	24	No
Eye disorders	Ocular neuromuscular disorders	Gaze palsy	49	Yes
Eye disorders	Ocular neuromuscular disorders	Mydriasis	1	No
Eye disorders	Ocular neuromuscular disorders	Oculogyric crisis	1	Yes
Eye disorders	Ocular neuromuscular disorders	Ophthalmople gia	3	Yes
Eye disorders	Ocular neuromuscular disorders	Opsoclonus myoclonus	2	No
Eye disorders	Ocular neuromuscular disorders	Pupil fixed	1	No
Eye disorders	Ocular neuromuscular disorders	Pupillary reflex impaired	1	No
Eye disorders	Ocular neuromuscular disorders	Pupils unequal	1	No
Eye disorders	Ocular neuromuscular disorders	Saccadic eye movement	1	No
Eye disorders	Ocular neuromuscular disorders	Strabismus	16	No
Eye disorders	Ocular sensory symptoms NEC	Asthenopia	1	No
Eye disorders	Ocular sensory symptoms NEC	Eye rolling	48	No
Eye disorders	Ocular sensory symptoms NEC	Eye rolling	3	Yes
Eye disorders	Ocular sensory symptoms NEC	Photophobia	2	No
Eye disorders	Retina, choroid and vitreous haemorrhages and vascular disorders	Retinal haemorrhage	4	Yes
Eye disorders	Vision disorders	Anisometropia	1	No

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Eye disorders	Vision disorders	Astigmatism	1	No
Eye disorders	Vision disorders	Diplopia	1	No
Eye disorders	Vision disorders	Hypermetropia	2	No
Eye disorders	Vision disorders	Vision blurred	2	No
Eye disorders	Vision disorders	Visual impairment	4	No
Gastrointestinal disorders	Abdominal hernias and other abdominal wall conditions	Inguinal hernia	2	No
Gastrointestinal disorders	Abdominal hernias and other abdominal wall conditions	Umbilical hernia	1	No
Gastrointestinal disorders	Gastrointestinal conditions NEC	Anal fistula	1	No
Gastrointestinal disorders	Gastrointestinal conditions NEC	Disbacteriosis	1	No
Gastrointestinal disorders	Gastrointestinal conditions NEC	Gastrointestinal disorder	1	No
Gastrointestinal disorders	Gastrointestinal conditions NEC	Hyperchlorhydria	1	No
Gastrointestinal disorders	Gastrointestinal conditions NEC	Intestinal mucosal hypertrophy	1	No
Gastrointestinal disorders	Gastrointestinal haemorrhages NEC	Gastrointestinal	2	Yes
Gastrointestinal disorders	Gastrointestinal haemorrhages NEC	Haematochezia	7	No
Gastrointestinal disorders	Gastrointestinal haemorrhages NEC	Haematochezia	6	Yes
Gastrointestinal disorders	Gastrointestinal haemorrhages NEC	Melaena	2	Yes
Gastrointestinal disorders	Gastrointestinal haemorrhages NEC	Rectal haemorrhage	3	Yes
Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Colitis	3	Yes
Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Duodenitis	2	No
Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Enteritis	8	Yes
Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Enterocolitis	1	Yes
Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Eosinophilic colitis	1	Yes
Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Gastritis	2	No
Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Gastroenteritis eosinophilic	2	Yes
Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Gastrointestinal	1	No
Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Oesophagitis	2	No
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Constipation	10	No
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Diarrhoea	1	No
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Diarrhoea haemorrhagic	10	Yes
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Dyskinesia oesophageal	1	No
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Gastrointestinal hypomotility	1	No

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Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Gastrointestinal motility	1	Yes
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Gastrooesophageal reflux disease	14	No
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Ileus paralytic	2	Yes
Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Intestinal dilatation	2	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Abdominal discomfort	1	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Abdominal distension	5	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Abdominal pain	11	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Abdominal pain	1	Yes
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Abdominal pain upper	1	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Abdominal rigidity	1	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Abnormal faeces	9	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Abnormal faeces	1	Yes
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Acute abdomen	1	Yes
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Aphagia	1	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Dyspepsia	2	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Dysphagia	5	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Faecal incontinence	1	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Faecal incontinence	1	Yes
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Faeces discoloured	10	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Flatulence	4	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Gastrointestinal sounds abnormal	1	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Mucous stools	5	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Nausea	6	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Nausea	1	Yes
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Regurgitation	5	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Vomiting	1	No
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Vomiting	1	Yes
Gastrointestinal disorders	Gastrointestinal stenosis and obstruction	Intestinal obstruction	1	Yes
Gastrointestinal disorders	Gastrointestinal stenosis and obstruction	Intussusception	8	Yes

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Gastrointestinal disorders	Gastrointestinal stenosis and obstruction	Subileus	1	Yes
Gastrointestinal disorders	Malabsorption conditions	Malabsorption	1	No
Gastrointestinal disorders	Malabsorption conditions	Steatorrhoea	1	No
Gastrointestinal disorders	Oral soft tissue conditions	Aphthous stomatitis	6	No
Gastrointestinal disorders	Oral soft tissue conditions	Chapped lips	2	No
Gastrointestinal disorders	Oral soft tissue conditions	Cheilitis	3	No
Gastrointestinal disorders	Oral soft tissue conditions	Lip disorder	2	No
Gastrointestinal disorders	Oral soft tissue conditions	Lip oedema	3	No
Gastrointestinal disorders	Oral soft tissue conditions	Lip swelling	2	No
Gastrointestinal disorders	Oral soft tissue conditions	Mouth haemorrhage	4	No
Gastrointestinal disorders	Oral soft tissue conditions	Oral discharge	1	No
Gastrointestinal disorders	Oral soft tissue conditions	Stomatitis	3	No
Gastrointestinal disorders	Oral soft tissue conditions	Stomatitis	1	Yes
Gastrointestinal disorders	Oral soft tissue conditions	Stomatitis haemorrhagic	1	Yes
Gastrointestinal disorders	Peritoneal and retroperitoneal conditions	Ascites	4	Yes
Gastrointestinal disorders	Peritoneal and retroperitoneal conditions	Peritoneal disorder	1	No
Gastrointestinal disorders	Peritoneal and retroperitoneal conditions	Peritonitis	1	Yes
Gastrointestinal disorders	Salivary gland conditions	Salivary hypersecretion	30	No
Gastrointestinal disorders	Tongue conditions	Protrusion tongue	2	No
Gastrointestinal disorders	Tongue conditions	Swollen tongue	1	No
Gastrointestinal disorders	Tongue conditions	Tongue discolouration	1	No
General disorders and administration site conditions	Administration site reactions	Application site discolouration	1	No
General disorders and administration site conditions	Administration site reactions	Application site rash	1	No
General disorders and administration site conditions	Administration site reactions	Embolia cutis medicamentosa	4	Yes
General disorders and administration site conditions	Administration site reactions	Injected limb mobility decreased	4	No
General disorders and administration site conditions	Administration site reactions	Injection site abscess sterile	6	No
General disorders and administration site conditions	Administration site reactions	Injection site abscess sterile	1	Yes

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General disorders and administration site conditions	Administration site reactions	Injection site atrophy	1	Yes
General disorders and administration site conditions	Administration site reactions	Injection site dermatitis	1	No
General disorders and administration site conditions	Administration site reactions	Injection site discolouration	5	No
General disorders and administration site conditions	Administration site reactions	Injection site erythema	1	No
General disorders and administration site conditions	Administration site reactions	Injection site extravasation	12	No
General disorders and administration site conditions	Administration site reactions	Injection site haematoma	12	No
General disorders and administration site conditions	Administration site reactions	Injection site haemorrhage	3	No
General disorders and administration site conditions	Administration site reactions	Injection site induration	64	No
General disorders and administration site conditions	Administration site reactions	Injection site induration	3	Yes
General disorders and administration site conditions	Administration site reactions	Injection site inflammation	9	No
General disorders and administration site conditions	Administration site reactions	Injection site mass	1	No
General disorders and administration site conditions	Administration site reactions	Injection site necrosis	6	Yes
General disorders and administration site conditions	Administration site reactions	Injection site nodule	21	No
General disorders and administration site conditions	Administration site reactions	Injection site nodule	3	Yes
General disorders and administration site conditions	Administration site reactions	Injection site pain	1	No
General disorders and administration site conditions	Administration site reactions	Injection site pallor	1	No
General disorders and administration site conditions	Administration site reactions	Injection site pruritus	2	No
General disorders and administration site conditions	Administration site reactions	Injection site rash	5	No
General disorders and administration site conditions	Administration site reactions	Injection site reaction	48	No
General disorders and administration site conditions	Administration site reactions	Injection site scab	1	No
General disorders and administration site conditions	Administration site reactions	Injection site scar	1	No

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General disorders and administration site conditions	Administration site reactions	Injection site swelling	1	No
General disorders and administration site conditions	Administration site reactions	Injection site swelling	1	Yes
General disorders and administration site conditions	Administration site reactions	Injection site urticaria	3	No
General disorders and administration site conditions	Administration site reactions	Injection site vesicles	9	No
General disorders and administration site conditions	Administration site reactions	Injection site warmth	30	No
General disorders and administration site conditions	Administration site reactions	Injection site warmth	1	Yes
General disorders and administration site conditions	Administration site reactions	Vaccination site abscess sterile	1	Yes
General disorders and administration site conditions	Body temperature conditions	Hyperpyrexia	25	No
General disorders and administration site conditions	Body temperature conditions	Hyperpyrexia	2	Yes
General disorders and administration site conditions	Body temperature conditions	Hyperthermia	6	No
General disorders and administration site conditions	Body temperature conditions	Hyperthermia	1	Yes
General disorders and administration site conditions	Body temperature conditions	Hypothermia	8	No
General disorders and administration site conditions	Body temperature conditions	Pyrexia	4	No
General disorders and administration site conditions	Device issues	Device dislocation	1	No
General disorders and administration site conditions	Fatal outcomes	Brain death	2	Yes
General disorders and administration site conditions	Fatal outcomes	Death	1	No
General disorders and administration site conditions	Fatal outcomes	Death	17	Yes
General disorders and administration site conditions	Fatal outcomes	Sudden cardiac death	1	Yes
General disorders and administration site conditions	Fatal outcomes	Sudden death	7	Yes
General disorders and administration site conditions	Fatal outcomes	Sudden infant death syndrome	67	Yes
General disorders and administration site conditions	General system disorders NEC	Abasia	1	No

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General disorders and administration site conditions	General system disorders NEC	Abscess sterile	15	Yes
General disorders and administration site conditions	General system disorders NEC	Asthenia	45	No
General disorders and administration site conditions	General system disorders NEC	Asthenia	2	Yes
General disorders and administration site conditions	General system disorders NEC	Chest discomfort	1	No
General disorders and administration site conditions	General system disorders NEC	Chest pain	1	No
General disorders and administration site conditions	General system disorders NEC	Chills	18	No
General disorders and administration site conditions	General system disorders NEC	Condition aggravated	3	No
General disorders and administration site conditions	General system disorders NEC	Developmental delay	30	No
General disorders and administration site conditions	General system disorders NEC	Developmental delay	3	Yes
General disorders and administration site conditions	General system disorders NEC	Discomfort	4	No
General disorders and administration site conditions	General system disorders NEC	Disease recurrence	1	No
General disorders and administration site conditions	General system disorders NEC	Face oedema	3	No
General disorders and administration site conditions	General system disorders NEC	Fatigue	54	No
General disorders and administration site conditions	General system disorders NEC	Fatigue	1	Yes
General disorders and administration site conditions	General system disorders NEC	Feeling abnormal	5	No
General disorders and administration site conditions	General system disorders NEC	Feeling cold	2	No
General disorders and administration site conditions	General system disorders NEC	Feeling hot	7	No
General disorders and administration site conditions	General system disorders NEC	Feeling of body temperature	1	No
General disorders and administration site conditions	General system disorders NEC	Feeling of relaxation	3	No
General disorders and administration site conditions	General system disorders NEC	Feeling of relaxation	1	Yes
General disorders and administration site conditions	General system disorders NEC	Foaming at mouth	14	No

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General disorders and administration site conditions	General system disorders NEC	Foreign body reaction	1	No
General disorders and administration site conditions	General system disorders NEC	Gait disturbance	13	No
General disorders and administration site conditions	General system disorders NEC	Gait disturbance	1	Yes
General disorders and administration site conditions	General system disorders NEC	General physical health deterioration	45	No
General disorders and administration site conditions	General system disorders NEC	General physical health deterioration	3	Yes
General disorders and administration site conditions	General system disorders NEC	General symptom	1	No
General disorders and administration site conditions	General system disorders NEC	Granuloma	2	No
General disorders and administration site conditions	General system disorders NEC	Ill-defined disorder	44	No
General disorders and administration site conditions	General system disorders NEC	Ill-defined disorder	1	Yes
General disorders and administration site conditions	General system disorders NEC	Induration	7	No
General disorders and administration site conditions	General system disorders NEC	Induration	1	Yes
General disorders and administration site conditions	General system disorders NEC	Inflammation	23	No
General disorders and administration site conditions	General system disorders NEC	Influenza like illness	2	No
General disorders and administration site conditions	General system disorders NEC	Irritability	1	No
General disorders and administration site conditions	General system disorders NEC	Irritability	1	Yes
General disorders and administration site conditions	General system disorders NEC	Localised oedema	2	No
General disorders and administration site conditions	General system disorders NEC	Local reaction	10	No
General disorders and administration site conditions	General system disorders NEC	Local swelling	5	No
General disorders and administration site conditions	General system disorders NEC	Malaise	27	No
General disorders and administration site conditions	General system disorders NEC	Mucosal dryness	1	No
General disorders and administration site conditions	General system disorders NEC	Mucosal haemorrhage	1	Yes

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General disorders and administration site conditions	General system disorders NEC	Multi-organ failure	6	Yes
General disorders and administration site conditions	General system disorders NEC	No adverse event	2	No
General disorders and administration site conditions	General system disorders NEC	Nonspecific reaction	2	No
General disorders and administration site conditions	General system disorders NEC	Oedema	4	No
General disorders and administration site conditions	General system disorders NEC	Oedema peripheral	69	No
General disorders and administration site conditions	General system disorders NEC	Oedema peripheral	9	Yes
General disorders and administration site conditions	General system disorders NEC	Pain	32	No
General disorders and administration site conditions	General system disorders NEC	Pneumatosis	1	No
General disorders and administration site conditions	General system disorders NEC	Sense of oppression	1	No
General disorders and administration site conditions	General system disorders NEC	Swelling	17	No
General disorders and administration site conditions	General system disorders NEC	Systemic inflammatory response syndrome	2	Yes
General disorders and administration site conditions	General system disorders NEC	Thirst decreased	1	No
General disorders and administration site conditions	Product quality issues	Product quality issue	25	No
General disorders and administration site conditions	Therapeutic and nontherapeutic effects (excl toxicity)	Adverse drug reaction	1	No
General disorders and administration site conditions	Therapeutic and nontherapeutic effects (excl toxicity)	Adverse event	1	No
General disorders and administration site conditions	Tissue disorders NEC	Atrophy	1	Yes
General disorders and administration site conditions	Tissue disorders NEC	Cyst	1	Yes
General disorders and administration site conditions	Tissue disorders NEC	Dysplasia	2	No
General disorders and administration site conditions	Tissue disorders NEC	Hyperplasia	3	No
General disorders and administration site conditions	Tissue disorders NEC	Hypertrophy	1	No

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General disorders and administration site conditions	Tissue disorders NEC	Mass	1	No
General disorders and administration site conditions	Tissue disorders NEC	Necrosis	4	Yes
General disorders and administration site conditions	Tissue disorders NEC	Nodule	1	No
General disorders and administration site conditions	Tissue disorders NEC	Ulcer	1	No
Hepatobiliary disorders	Gallbladder disorders	Cholelithiasis	1	No
Hepatobiliary disorders	Gallbladder disorders	Gallbladder disorder	1	No
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Acute hepatic failure	1	Yes
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Cholestasis	1	Yes
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Hepatic failure	2	Yes
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Hepatic function abnormal	2	No
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Hepatic steatosis	1	Yes
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Hepatitis acute	1	Yes
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Hepatitis neonatal	1	Yes
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Hepatomegaly	1	No
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Hepatospleno megaly	1	No
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Jaundice	7	Yes
Hepatobiliary disorders	Hepatic and hepatobiliary disorders	Liver disorder	4	No
Immune system disorders	Allergic conditions	Allergy to metals	1	No
Immune system disorders	Allergic conditions	Anaphylactic reaction	1	Yes
Immune system disorders	Allergic conditions	Atopy	1	No
Immune system disorders	Allergic conditions	Food allergy	3	No
Immune system disorders	Allergic conditions	Hypersensitivit y	1	Yes
Immune system disorders	Allergic conditions	Milk allergy	2	No
Immune system disorders	Allergic conditions	Multiple allergies	1	No
Immune system disorders	Allergic conditions	Serum sickness	1	No
Immune system disorders	Allergic conditions	Type III immune complex mediated reaction	2	No

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Immune system disorders	Immune disorders NEC	Decreased immune responsivenes	1	No
Immune system disorders	Immune disorders NEC	Immunisation reaction	1	No
Immune system disorders	Immune disorders NEC	Immunisation reaction	1	Yes
Immune system disorders	Immunodeficiency syndromes	Hypogammaglobulinaemia	1	No
Infections and infestations	Bacterial infectious disorders	Bacterial infection	4	No
Infections and infestations	Bacterial infectious disorders	Bacterial pyelonephritis	1	Yes
Infections and infestations	Bacterial infectious disorders	Bacterial tracheitis	1	Yes
Infections and infestations	Bacterial infectious disorders	Bronchitis bacterial	2	No
Infections and infestations	Bacterial infectious disorders	Cellulitis	26	Yes
Infections and infestations	Bacterial infectious disorders	Clostridial infection	1	No
Infections and infestations	Bacterial infectious disorders	Conjunctivitis bacterial	1	No
Infections and infestations	Bacterial infectious disorders	Erysipelas	6	No
Infections and infestations	Bacterial infectious disorders	Erysipelas	1	Yes
Infections and infestations	Bacterial infectious disorders	Erythema migrans	1	No
Infections and infestations	Bacterial infectious disorders	Escherichia infection	3	No
Infections and infestations	Bacterial infectious disorders	Escherichia urinary tract infection	2	No
Infections and infestations	Bacterial infectious disorders	Gastroenteritis bacterial	1	Yes
Infections and infestations	Bacterial infectious disorders	Haemophilus infection	8	No
Infections and infestations	Bacterial infectious disorders	Haemophilus sepsis	3	No
Infections and infestations	Bacterial infectious disorders	Injection site cellulitis	5	No
Infections and infestations	Bacterial infectious disorders	Injection site cellulitis	2	Yes
Infections and infestations	Bacterial infectious disorders	Meningitis bacterial	3	Yes
Infections and infestations	Bacterial infectious disorders	Meningitis haemophilus	7	Yes
Infections and infestations	Bacterial infectious disorders	Meningitis pneumococcal	4	Yes
Infections and infestations	Bacterial infectious disorders	Meningococcal sepsis	1	No
Infections and infestations	Bacterial infectious disorders	Meningoencephalitis bacterial	1	Yes
Infections and infestations	Bacterial infectious disorders	Necrotising ulcerative gingivostomatitis	1	Yes
Infections and infestations	Bacterial infectious disorders	Neuroborreliosis	1	Yes

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Infections and infestations	Bacterial infectious disorders	Pertussis	62	No
Infections and infestations	Bacterial infectious disorders	Pertussis	1	Yes
Infections and infestations	Bacterial infectious disorders	Pharyngitis streptococcal	1	No
Infections and infestations	Bacterial infectious disorders	Pneumococcal infection	1	No
Infections and infestations	Bacterial infectious disorders	Pneumococcal sepsis	1	No
Infections and infestations	Bacterial infectious disorders	Pneumonia pneumococcal	1	Yes
Infections and infestations	Bacterial infectious disorders	Proteus infection	1	Yes
Infections and infestations	Bacterial infectious disorders	Scarlet fever	1	No
Infections and infestations	Bacterial infectious disorders	Staphylococcal abscess	1	No
Infections and infestations	Bacterial infectious disorders	Staphylococcal abscess	1	Yes
Infections and infestations	Bacterial infectious disorders	Staphylococcal infection	5	No
Infections and infestations	Bacterial infectious disorders	Staphylococcal infection	1	Yes
Infections and infestations	Bacterial infectious disorders	Staphylococcal scalded skin syndrome	1	No
Infections and infestations	Bacterial infectious disorders	Staphylococcal sepsis	2	Yes
Infections and infestations	Bacterial infectious disorders	Streptococcal infection	1	No
Infections and infestations	Bacterial infectious disorders	Superinfection bacterial	1	No
Infections and infestations	Bacterial infectious disorders	Waterhouse-Friderichsen syndrome	1	Yes
Infections and infestations	Fungal infectious disorders	Candida nappy rash	3	No
Infections and infestations	Fungal infectious disorders	Candidiasis	3	No
Infections and infestations	Fungal infectious disorders	Genital candidiasis	3	No
Infections and infestations	Fungal infectious disorders	Oral candidiasis	4	No
Infections and infestations	Infections - pathogen unspecified	Abscess	12	No
Infections and infestations	Infections - pathogen unspecified	Abscess	5	Yes
Infections and infestations	Infections - pathogen unspecified	Abscess limb	8	No
Infections and infestations	Infections - pathogen unspecified	Abscess soft tissue	1	No
Infections and infestations	Infections - pathogen unspecified	Acute tonsillitis	3	No
Infections and infestations	Infections - pathogen unspecified	Bacteraemia	1	Yes
Infections and infestations	Infections - pathogen unspecified	Bronchitis	20	No
Infections and infestations	Infections - pathogen unspecified	Bronchitis	2	Yes

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Infections and infestations	Infections - pathogen unspecified	Bronchopneumonia	7	Yes
Infections and infestations	Infections - pathogen unspecified	Conjunctivitis infective	1	No
Infections and infestations	Infections - pathogen unspecified	Device related sepsis	1	Yes
Infections and infestations	Infections - pathogen unspecified	Ear infection	8	No
Infections and infestations	Infections - pathogen unspecified	Eczema infected	1	No
Infections and infestations	Infections - pathogen unspecified	Empyema	1	No
Infections and infestations	Infections - pathogen unspecified	Enteritis infectious	2	No
Infections and infestations	Infections - pathogen unspecified	Enteritis infectious	2	Yes
Infections and infestations	Infections - pathogen unspecified	Epiglottitis	1	Yes
Infections and infestations	Infections - pathogen unspecified	Febrile infection	13	No
Infections and infestations	Infections - pathogen unspecified	Febrile infection	1	Yes
Infections and infestations	Infections - pathogen unspecified	Gastroenteritis	3	No
Infections and infestations	Infections - pathogen unspecified	Gastroenteritis	34	Yes
Infections and infestations	Infections - pathogen unspecified	Gastrointestinal infection	3	No
Infections and infestations	Infections - pathogen unspecified	Groin abscess	1	No
Infections and infestations	Infections - pathogen unspecified	Incision site abscess	6	No
Infections and infestations	Infections - pathogen unspecified	Infection	16	No
Infections and infestations	Infections - pathogen unspecified	Infection	3	Yes
Infections and infestations	Infections - pathogen unspecified	Injection site abscess	39	No
Infections and infestations	Infections - pathogen unspecified	Injection site abscess	10	Yes
Infections and infestations	Infections - pathogen unspecified	Injection site infection	2	No
Infections and infestations	Infections - pathogen unspecified	Laryngitis	2	No
Infections and infestations	Infections - pathogen unspecified	Localised infection	1	No
Infections and infestations	Infections - pathogen unspecified	Lymph node abscess	1	No
Infections and infestations	Infections - pathogen unspecified	Mastoiditis	3	No
Infections and infestations	Infections - pathogen unspecified	Meningitis	12	Yes
Infections and infestations	Infections - pathogen unspecified	Meningitis aseptic	1	Yes
Infections and infestations	Infections - pathogen unspecified	Nasopharyngitis	18	No
Infections and infestations	Infections - pathogen unspecified	Nasopharyngitis	2	Yes
Infections and infestations	Infections - pathogen unspecified	Necrotising fasciitis	1	Yes

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Infections and infestations	Infections - pathogen unspecified	Orchitis	1	No
Infections and infestations	Infections - pathogen unspecified	Osteomyelitis	3	Yes
Infections and infestations	Infections - pathogen unspecified	Otitis media	11	No
Infections and infestations	Infections - pathogen unspecified	Otitis media	1	Yes
Infections and infestations	Infections - pathogen unspecified	Otitis media acute	1	No
Infections and infestations	Infections - pathogen unspecified	Peritonsillar abscess	1	No
Infections and infestations	Infections - pathogen unspecified	Pharyngitis	12	No
Infections and infestations	Infections - pathogen unspecified	Pharyngitis	1	Yes
Infections and infestations	Infections - pathogen unspecified	Pharyngotonsil litis	2	No
Infections and infestations	Infections - pathogen unspecified	Pneumonia	1	No
Infections and infestations	Infections - pathogen unspecified	Pneumonia	27	Yes
Infections and infestations	Infections - pathogen unspecified	Pseudocroup	2	No
Infections and infestations	Infections - pathogen unspecified	Purulence	1	No
Infections and infestations	Infections - pathogen unspecified	Pyelonephritis	4	Yes
Infections and infestations	Infections - pathogen unspecified	Pyelonephritis acute	1	Yes
Infections and infestations	Infections - pathogen unspecified	Rash pustular	5	No
Infections and infestations	Infections - pathogen unspecified	Respiratory tract infection	9	No
Infections and infestations	Infections - pathogen unspecified	Rhinitis	32	No
Infections and infestations	Infections - pathogen unspecified	Sepsis	29	Yes
Infections and infestations	Infections - pathogen unspecified	Sepsis syndrome	2	No
Infections and infestations	Infections - pathogen unspecified	Sinusitis	1	No
Infections and infestations	Infections - pathogen unspecified	Skin infection	1	No
Infections and infestations	Infections - pathogen unspecified	Soft tissue infection	5	No
Infections and infestations	Infections - pathogen unspecified	Soft tissue infection	1	Yes
Infections and infestations	Infections - pathogen unspecified	Subcutaneous abscess	1	No
Infections and infestations	Infections - pathogen unspecified	Superinfection	4	No
Infections and infestations	Infections - pathogen unspecified	Tonsillitis	7	No
Infections and infestations	Infections - pathogen unspecified	Tonsillitis	1	Yes
Infections and infestations	Infections - pathogen unspecified	Tracheitis	2	No

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Infections and infestations	Infections - pathogen unspecified	Upper respiratory tract infection	27	No
Infections and infestations	Infections - pathogen unspecified	Upper respiratory tract infection	2	Yes
Infections and infestations	Infections - pathogen unspecified	Urinary tract infection	5	No
Infections and infestations	Infections - pathogen unspecified	Vaccination site abscess	2	Yes
Infections and infestations	Infections - pathogen unspecified	Vaccination site infection	1	No
Infections and infestations	Infections - pathogen unspecified	Viraemia	1	Yes
Infections and infestations	Infections - pathogen unspecified	Wound infection	1	No
Infections and infestations	Viral infectious disorders	Adenovirus infection	1	No
Infections and infestations	Viral infectious disorders	Bronchiolitis	6	No
Infections and infestations	Viral infectious disorders	Coxsackie viral infection	1	No
Infections and infestations	Viral infectious disorders	Croup infectious	2	No
Infections and infestations	Viral infectious disorders	Cytomegalovirus infection	3	No
Infections and infestations	Viral infectious disorders	Cytomegalovirus infection	1	Yes
Infections and infestations	Viral infectious disorders	Eczema herpeticum	1	No
Infections and infestations	Viral infectious disorders	Encephalitis herpes	2	Yes
Infections and infestations	Viral infectious disorders	Encephalitis viral	1	Yes
Infections and infestations	Viral infectious disorders	Enterovirus infection	1	No
Infections and infestations	Viral infectious disorders	Epstein-Barr virus infection	1	No
Infections and infestations	Viral infectious disorders	Exanthema subitum	4	No
Infections and infestations	Viral infectious disorders	Exanthema subitum	3	Yes
Infections and infestations	Viral infectious disorders	Gastroenteritis adenovirus	3	Yes
Infections and infestations	Viral infectious disorders	Gastroenteritis norovirus	6	Yes
Infections and infestations	Viral infectious disorders	Gastroenteritis rotavirus	14	Yes
Infections and infestations	Viral infectious disorders	Gastroenteritis viral	2	Yes
Infections and infestations	Viral infectious disorders	Gianotti-Crosti syndrome	3	No
Infections and infestations	Viral infectious disorders	Gianotti-Crosti syndrome	1	Yes
Infections and infestations	Viral infectious disorders	Hepatitis B	1	No
Infections and infestations	Viral infectious disorders	Hepatitis viral	1	No
Infections and infestations	Viral infectious disorders	Herpes ophthalmic	1	No

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Infections and infestations	Viral infectious disorders	Herpes simplex	1	No
Infections and infestations	Viral infectious disorders	Human herpesvirus 6 infection	2	No
Infections and infestations	Viral infectious disorders	Influenza	3	No
Infections and infestations	Viral infectious disorders	Meningitis viral	3	Yes
Infections and infestations	Viral infectious disorders	Pneumonia respiratory syncytial viral	1	Yes
Infections and infestations	Viral infectious disorders	Pneumonia viral	1	Yes
Infections and infestations	Viral infectious disorders	Respiratory syncytial virus bronchiolitis	2	No
Infections and infestations	Viral infectious disorders	Respiratory syncytial virus infection	5	No
Infections and infestations	Viral infectious disorders	Respiratory tract infection viral	1	Yes
Infections and infestations	Viral infectious disorders	Rotavirus infection	5	No
Infections and infestations	Viral infectious disorders	Varicella	1	No
Infections and infestations	Viral infectious disorders	Viral infection	25	No
Infections and infestations	Viral infectious disorders	Viral infection	2	Yes
Infections and infestations	Viral infectious disorders	Viral pharyngitis	1	No
Infections and infestations	Viral infectious disorders	Viral rash	1	No
Infections and infestations	Viral infectious disorders	Viral upper respiratory tract infection	1	No
Injury, poisoning and procedural complications	Bone and joint injuries	Forearm fracture	1	Yes
Injury, poisoning and procedural complications	Bone and joint injuries	Joint dislocation	2	Yes
Injury, poisoning and procedural complications	Bone and joint injuries	Limb injury	1	No
Injury, poisoning and procedural complications	Bone and joint injuries	Skull fracture	1	Yes
Injury, poisoning and procedural complications	Chemical injury and poisoning	Carbon monoxide poisoning	1	No
Injury, poisoning and procedural complications	Chemical injury and poisoning	Drug toxicity	1	No
Injury, poisoning and procedural complications	Chemical injury and poisoning	Poisoning	1	No
Injury, poisoning and procedural complications	Injuries NEC	Child maltreatment syndrome	2	No

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Injury, poisoning and procedural complications	Injuries NEC	Contusion	4	No
Injury, poisoning and procedural complications	Injuries NEC	Eschar	1	No
Injury, poisoning and procedural complications	Injuries NEC	Excoriation	1	No
Injury, poisoning and procedural complications	Injuries NEC	Fall	10	No
Injury, poisoning and procedural complications	Injuries NEC	Injury	1	No
Injury, poisoning and procedural complications	Injuries NEC	Subdural haematoma	2	Yes
Injury, poisoning and procedural complications	Injuries NEC	Traumatic brain injury	1	Yes
Injury, poisoning and procedural complications	Medication errors	Drug administration error	1	No
Injury, poisoning and procedural complications	Medication errors	Expired drug administered	1	No
Injury, poisoning and procedural complications	Medication errors	Inappropriate schedule of drug administration	9	No
Injury, poisoning and procedural complications	Medication errors	Incorrect route of drug administration	11	No
Injury, poisoning and procedural complications	Medication errors	Medication error	1	No
Injury, poisoning and procedural complications	Medication errors	Overdose	3	No
Injury, poisoning and procedural complications	Medication errors	Wrong drug administered	1	No
Injury, poisoning and procedural complications	Medication errors	Wrong technique in drug usage process	4	No
Injury, poisoning and procedural complications	Procedural related injuries and complications NEC	Seroma	1	No
Injury, poisoning and procedural complications	Procedural related injuries and complications NEC	Vaccination complication	41	No
Injury, poisoning and procedural complications	Procedural related injuries and complications NEC	Vaccination complication	2	Yes
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Blood pressure decreased	1	No
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Blood pressure immeasurable	1	Yes

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Investigations	Cardiac and vascular investigations (excl enzyme tests)	Cardiac murmur	8	No
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Heart rate decreased	3	No
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Heart rate increased	6	No
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Heart sounds abnormal	1	No
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Pulse abnormal	1	No
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Pulse absent	1	No
Investigations	Cardiac and vascular investigations (excl enzyme tests)	Pulse pressure increased	1	No
Investigations	Enzyme investigations NEC	Blood alkaline phosphatase increased	1	No
Investigations	Enzyme investigations NEC	Blood creatine phosphokinase increased	1	No
Investigations	Enzyme investigations NEC	Blood lactate dehydrogenase increased	2	No
Investigations	Haematology investigations (incl blood groups)	Activated partial thromboplastin time prolonged	1	No
Investigations	Haematology investigations (incl blood groups)	Bleeding time prolonged	1	Yes
Investigations	Haematology investigations (incl blood groups)	Blood thromboplastin decreased	1	No
Investigations	Haematology investigations (incl blood groups)	Coombs test positive	1	No
Investigations	Haematology investigations (incl blood groups)	Haematocrit decreased	1	Yes
Investigations	Haematology investigations (incl blood groups)	Haemoglobin decreased	4	No
Investigations	Haematology investigations (incl blood groups)	Haemoglobin decreased	1	Yes
Investigations	Haematology investigations (incl blood groups)	Lymphocyte count	1	No
Investigations	Haematology investigations (incl blood groups)	Neutrophil toxic granulation	1	No
Investigations	Haematology investigations (incl blood groups)	Platelet count abnormal	2	No
Investigations	Haematology investigations (incl blood groups)	Platelet count decreased	3	No
Investigations	Haematology investigations (incl blood groups)	Platelet count increased	2	No
Investigations	Haematology investigations (incl blood groups)	Prothrombin time prolonged	1	No
Investigations	Haematology investigations (incl blood groups)	Red blood cell count	1	No

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Investigations	Haematology investigations (incl blood groups)	Red blood cell sedimentation rate increased	2	No
Investigations	Haematology investigations (incl blood groups)	Shift to the left	1	No
Investigations	Haematology investigations (incl blood groups)	White blood cell count decreased	1	No
Investigations	Haematology investigations (incl blood groups)	White blood cell count	5	No
Investigations	Haematology investigations (incl blood groups)	White blood cell count	1	Yes
Investigations	Hepatobiliary investigations	Alanine aminotransferase increased	9	Yes
Investigations	Hepatobiliary investigations	Ammonia increased	2	No
Investigations	Hepatobiliary investigations	Aspartate aminotransferase increased	7	Yes
Investigations	Hepatobiliary investigations	Blood bilirubin increased	1	Yes
Investigations	Hepatobiliary investigations	Hepatic enzyme increased	5	Yes
Investigations	Hepatobiliary investigations	Liver function test abnormal	1	Yes
Investigations	Hepatobiliary investigations	Transaminases increased	13	Yes
Investigations	Immunology and allergy investigations	Blood immunoglobulin A increased	1	Yes
Investigations	Immunology and allergy investigations	Blood immunoglobulin E increased	1	No
Investigations	Immunology and allergy investigations	Blood immunoglobulin M increased	1	No
Investigations	Immunology and allergy investigations	Blood immunoglobulin M increased	1	Yes
Investigations	Lipid analyses	Carnitine decreased	1	No
Investigations	Metabolic, nutritional and blood gas investigations	Blood glucose increased	1	No
Investigations	Metabolic, nutritional and blood gas investigations	Blood lactic acid increased	2	No
Investigations	Metabolic, nutritional and blood gas investigations	Blood pH decreased	1	No
Investigations	Metabolic, nutritional and blood gas investigations	Oxygen saturation decreased	26	No
Investigations	Microbiology and serology investigations	Bordetella test negative	1	No
Investigations	Microbiology and serology investigations	Hepatitis B antibody negative	2	No
Investigations	Microbiology and serology investigations	Hepatitis B surface antigen	1	No

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Investigations	Microbiology and serology investigations	Mycoplasma test positive	1	No
Investigations	Microbiology and serology investigations	Rotavirus test positive	3	No
Investigations	Microbiology and serology investigations	Staphylococcus test positive	1	No
Investigations	Microbiology and serology investigations	Viral test positive	5	No
Investigations	Neurological, special senses and psychiatric investigations	Electroenceph alogram abnormal	7	No
Investigations	Neurological, special senses and psychiatric investigations	Nerve stimulation test abnormal	3	No
Investigations	Neurological, special senses and psychiatric investigations	Otoacoustic emissions test abnormal	1	No
Investigations	Physical examination topics	Body height below normal	2	No
Investigations	Physical examination topics	Body mass index decreased	1	No
Investigations	Physical examination topics	Body temperature	1	No
Investigations	Physical examination topics	Body temperature decreased	4	No
Investigations	Physical examination topics	Breath sounds abnormal	3	No
Investigations	Physical examination topics	Head circumference abnormal	1	No
Investigations	Physical examination topics	Liver palpable subcostal	1	No
Investigations	Physical examination topics	Lymph node palpable	1	No
Investigations	Physical examination topics	Respiratory rate decreased	3	No
Investigations	Physical examination topics	Respiratory rate increased	4	No
Investigations	Physical examination topics	Skin turgor decreased	1	No
Investigations	Physical examination topics	Weight decreased	12	No
Investigations	Protein and chemistry analyses NEC	C-reactive protein increased	23	No
Investigations	Protein and chemistry analyses NEC	C-reactive protein increased	2	Yes
Investigations	Protein and chemistry analyses NEC	Protein total abnormal	1	No
Investigations	Protein and chemistry analyses NEC	Protein total increased	1	No
Investigations	Renal and urinary tract investigations and urinalyses	Glucose urine present	1	No
Investigations	Renal and urinary tract investigations and urinalyses	Urine output decreased	1	No

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Investigations	Toxicology and therapeutic drug monitoring	Anticonvulsant drug level above therapeutic	1	No
Investigations	Water, electrolyte and mineral investigations	Blood iron decreased	1	No
Investigations	Water, electrolyte and mineral investigations	Blood osmolarity increased	1	No
Investigations	Water, electrolyte and mineral investigations	Blood sodium decreased	1	No
Investigations	Water, electrolyte and mineral investigations	Serum ferritin increased	1	No
Metabolism and nutrition disorders	Acid-base disorders	Acidosis	4	No
Metabolism and nutrition disorders	Acid-base disorders	Acidosis	1	Yes
Metabolism and nutrition disorders	Acid-base disorders	Alkalosis	1	No
Metabolism and nutrition disorders	Acid-base disorders	Ketoacidosis	1	Yes
Metabolism and nutrition disorders	Acid-base disorders	Lactic acidosis	1	Yes
Metabolism and nutrition disorders	Acid-base disorders	Metabolic acidosis	4	Yes
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Appetite disorder	2	No
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Decreased appetite	5	No
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Decreased appetite	3	Yes
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Failure to thrive	2	Yes
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Feeding disorder neonatal	3	No
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Feeding disorder of infancy or early childhood	5	No
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Increased appetite	1	No
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Malnutrition	2	No
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Underweight	3	No
Metabolism and nutrition disorders	Appetite and general nutritional disorders	Weight gain poor	2	No
Metabolism and nutrition disorders	Bone, calcium, magnesium and phosphorus metabolism disorders	Tetany	2	Yes
Metabolism and nutrition disorders	Diabetic complications	Diabetic ketoacidosis	2	Yes
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Dehydration	21	No
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Dehydration	2	Yes
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Electrolyte imbalance	1	No
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Fluid intake reduced	16	No

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Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Hypernatraemia	1	No
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Hypokalaemia	4	Yes
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Hyponatraemia	6	No
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Hypovolaemia	1	No
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Oligodipsia	24	No
Metabolism and nutrition disorders	Electrolyte and fluid balance conditions	Polydipsia	4	No
Metabolism and nutrition disorders	Food intolerance syndromes	Cow's milk intolerance	1	No
Metabolism and nutrition disorders	Food intolerance syndromes	Disaccharide metabolism disorder	1	No
Metabolism and nutrition disorders	Food intolerance syndromes	Lactose intolerance	2	No
Metabolism and nutrition disorders	Glucose metabolism disorders (incl diabetes mellitus)	Hyperglycaemia	3	No
Metabolism and nutrition disorders	Glucose metabolism disorders (incl diabetes mellitus)	Hyperinsulinaemia	1	No
Metabolism and nutrition disorders	Glucose metabolism disorders (incl diabetes mellitus)	Hypoglycaemia	4	Yes
Metabolism and nutrition disorders	Glucose metabolism disorders (incl diabetes mellitus)	Type 1 diabetes mellitus	6	Yes
Metabolism and nutrition disorders	Iron and trace metal metabolism disorders	Haemosiderosis	1	No
Metabolism and nutrition disorders	Iron and trace metal metabolism disorders	Iron deficiency	1	No
Metabolism and nutrition disorders	Lipid metabolism disorders	Hypercholesterolaemia	1	No
Metabolism and nutrition disorders	Lipid metabolism disorders	Hyperlipidaemia	1	No
Metabolism and nutrition disorders	Lipid metabolism disorders	Hypertriglyceridaemia	1	No
Metabolism and nutrition disorders	Metabolism disorders NEC	Enzyme abnormality	1	No
Metabolism and nutrition disorders	Metabolism disorders NEC	Metabolic disorder	3	No
Metabolism and nutrition disorders	Metabolism disorders NEC	Mitochondrial cytopathy	1	Yes
Metabolism and nutrition disorders	Protein and amino acid metabolism disorders NEC	Hyperammonaemia	2	No
Metabolism and nutrition disorders	Protein and amino acid metabolism disorders NEC	Hypoalbuminaemia	4	No
Metabolism and nutrition disorders	Purine and pyrimidine metabolism disorders	Hyperuricaemia	1	No
Metabolism and nutrition disorders	Vitamin related disorders	Vitamin B12 deficiency	2	No
Metabolism and nutrition disorders	Vitamin related disorders	Vitamin K deficiency	2	No
Musculoskeletal and connective tissue disorders	Bone disorders (excl congenital and fractures)	Bone disorder	1	No
Musculoskeletal and connective tissue disorders	Bone disorders (excl congenital and fractures)	Bone pain	1	No

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Musculoskeletal and connective tissue disorders	Bone disorders (excl congenital and fractures)	Osteitis	1	Yes
Musculoskeletal and connective tissue disorders	Connective tissue disorders (excl congenital)	Myofascitis	1	No
Musculoskeletal and connective tissue disorders	Connective tissue disorders (excl congenital)	Myofascitis	1	Yes
Musculoskeletal and connective tissue disorders	Joint disorders	Arthralgia	1	No
Musculoskeletal and connective tissue disorders	Joint disorders	Arthritis	3	No
Musculoskeletal and connective tissue disorders	Joint disorders	Arthritis	1	Yes
Musculoskeletal and connective tissue disorders	Joint disorders	Arthropathy	1	No
Musculoskeletal and connective tissue disorders	Joint disorders	Joint contracture	1	No
Musculoskeletal and connective tissue disorders	Joint disorders	Joint hyperextensio n	2	No
Musculoskeletal and connective tissue disorders	Joint disorders	Joint range of motion decreased	1	No
Musculoskeletal and connective tissue disorders	Joint disorders	Joint swelling	4	No
Musculoskeletal and connective tissue disorders	Joint disorders	Juvenile arthritis	1	Yes
Musculoskeletal and connective tissue disorders	Joint disorders	Polyarthritis	1	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Floppy infant	1	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Hypotonia neonatal	4	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Muscle disorder	3	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Muscle hypertrophy	2	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Muscle rigidity	5	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Muscle rigidity	2	Yes
Musculoskeletal and connective tissue disorders	Muscle disorders	Muscle spasms	34	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Muscle spasms	1	Yes

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Musculoskeletal and connective tissue disorders	Muscle disorders	Muscle twitching	26	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Muscle twitching	1	Yes
Musculoskeletal and connective tissue disorders	Muscle disorders	Muscular weakness	11	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Myalgia	4	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Myopathy	1	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Myosclerosis	1	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Myositis	4	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Myositis	1	Yes
Musculoskeletal and connective tissue disorders	Muscle disorders	Nuchal rigidity	2	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Rhabdomyolysis	1	Yes
Musculoskeletal and connective tissue disorders	Muscle disorders	Torticollis	3	No
Musculoskeletal and connective tissue disorders	Muscle disorders	Trismus	2	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)	Delayed fontanelle closure	1	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)	Limb asymmetry	1	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)	Lordosis	1	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Groin pain	1	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Growth retardation	1	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Mobility decreased	7	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Muscle contracture	1	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Musculoskeletal pain	1	No

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Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Musculoskeletal stiffness	31	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Nodule on extremity	3	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Pain in extremity	19	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Pain in extremity	1	Yes
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Posture abnormal	5	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Soft tissue disorder	2	No
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Soft tissue disorder	1	Yes
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Soft tissue haemorrhage	1	Yes
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders NEC	Soft tissue necrosis	1	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Haematopoietic neoplasms (excl leukaemias and lymphomas)	Histiocytosis haematophagic	1	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Leukaemias	B precursor type acute leukaemia	1	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Leukaemias	Myelodysplastic syndrome	1	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Lymphomas NEC	Lymphoma	1	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Miscellaneous and site unspecified neoplasms benign	Haemangioma	3	No
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Nervous system neoplasms benign	Cerebral hygroma	2	No
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Nervous system neoplasms malignant and unspecified NEC	Neuroblastoma	2	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Nervous system neoplasms malignant and unspecified NEC	Optic nerve glioma	1	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Skeletal neoplasms malignant and unspecified	Ewing's sarcoma	1	Yes

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Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Soft tissue neoplasms benign	Lymphangiom a	1	Yes
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Soft tissue neoplasms malignant and unspecified (excl sarcomas)	Soft tissue neoplasm	2	Yes
Nervous system disorders	Central nervous system infections and inflammations	Encephalitis	1	No
Nervous system disorders	Central nervous system infections and inflammations	Encephalitis	15	Yes
Nervous system disorders	Central nervous system infections and inflammations	Encephalitis haemorrhagic	1	Yes
Nervous system disorders	Central nervous system infections and inflammations	Encephalomye litis	1	Yes
Nervous system disorders	Central nervous system vascular disorders	Blood brain barrier defect	1	Yes
Nervous system disorders	Central nervous system vascular disorders	Brain stem thrombosis	1	Yes
Nervous system disorders	Central nervous system vascular disorders	Cerebral haemorrhage	5	Yes
Nervous system disorders	Central nervous system vascular disorders	Cerebral infarction	1	Yes
Nervous system disorders	Central nervous system vascular disorders	Cerebral ischaemia	2	Yes
Nervous system disorders	Central nervous system vascular disorders	Cerebrovascul ar accident	1	Yes
Nervous system disorders	Central nervous system vascular disorders	Cerebrovascul ar disorder	1	Yes
Nervous system disorders	Central nervous system vascular disorders	Subarachnoid haemorrhage	3	Yes
Nervous system disorders	Central nervous system vascular disorders	Vasculitis cerebral	1	Yes
Nervous system disorders	Cranial nerve disorders (excl neoplasms)	Facial paresis	7	Yes
Nervous system disorders	Cranial nerve disorders (excl neoplasms)	Facial spasm	1	No
Nervous system disorders	Cranial nerve disorders (excl neoplasms)	Paresis cranial nerve	1	No
Nervous system disorders	Cranial nerve disorders (excl neoplasms)	Paresis cranial nerve	2	Yes
Nervous system disorders	Cranial nerve disorders (excl neoplasms)	Tongue paralysis	1	Yes
Nervous system disorders	Cranial nerve disorders (excl neoplasms)	VIIth nerve paralysis	1	Yes
Nervous system disorders	Cranial nerve disorders (excl neoplasms)	VIth nerve paralysis	1	Yes
Nervous system disorders	Demyelinating disorders	Acute disseminated encephalomye litis	3	Yes
Nervous system disorders	Demyelinating disorders	Demyelination	4	Yes
Nervous system disorders	Encephalopathies	Encephalopath y	14	Yes
Nervous system disorders	Encephalopathies	Hypoxic-ischaemic encephalopath	7	Yes
Nervous system disorders	Encephalopathies	Leukoencepha lopathy	2	Yes

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Nervous system disorders	Encephalopathies	Periventricular leukomalacia	2	Yes
Nervous system disorders	Headaches	Headache	1	No
Nervous system disorders	Increased intracranial pressure and hydrocephalus	Brain oedema	11	Yes
Nervous system disorders	Increased intracranial pressure and hydrocephalus	Hydrocephalus	4	Yes
Nervous system disorders	Increased intracranial pressure and hydrocephalus	Intracranial pressure increased	4	Yes
Nervous system disorders	Mental impairment disorders	Autism	1	No
Nervous system disorders	Mental impairment disorders	Autism	5	Yes
Nervous system disorders	Mental impairment disorders	Cognitive disorder	1	No
Nervous system disorders	Mental impairment disorders	Disturbance in attention	2	No
Nervous system disorders	Mental impairment disorders	Memory impairment	1	No
Nervous system disorders	Mental impairment disorders	Mental impairment	6	No
Nervous system disorders	Mental impairment disorders	Mental retardation	5	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Athetosis	1	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Bradykinesia	1	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Choreoathetosis	2	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Dyskinesia	31	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Dyskinesia	1	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Dystonia	3	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Dystonia	1	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Extrapyramidal disorder	2	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Head titubation	6	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Hemiparesis	6	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Hemiplegia	4	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Hypokinesia	10	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Hypokinesia	2	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Monoparesis	5	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Monoplegia	5	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Motor developmental delay	5	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Movement disorder	14	No

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Nervous system disorders	Movement disorders (incl parkinsonism)	Opisthotonus	13	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Opisthotonus	1	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Paralysis	3	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Paralysis flaccid	1	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Paraplegia	1	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Paresis	4	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Postictal paralysis	1	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Psychomotor hyperactivity	8	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Quadriparesis	4	Yes
Nervous system disorders	Movement disorders (incl parkinsonism)	Tardive dyskinesia	1	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Tremor	43	No
Nervous system disorders	Movement disorders (incl parkinsonism)	Tremor	3	Yes
Nervous system disorders	Neurological disorders NEC	Altered state of	11	Yes
Nervous system disorders	Neurological disorders NEC	Aphasia	3	Yes
Nervous system disorders	Neurological disorders NEC	Areflexia	7	No
Nervous system disorders	Neurological disorders NEC	Ataxia	4	No
Nervous system disorders	Neurological disorders NEC	Ataxia	1	Yes
Nervous system disorders	Neurological disorders NEC	Balance disorder	4	No
Nervous system disorders	Neurological disorders NEC	Cerebral disorder	4	No
Nervous system disorders	Neurological disorders NEC	Cerebral disorder	1	Yes
Nervous system disorders	Neurological disorders NEC	Clonus	13	No
Nervous system disorders	Neurological disorders NEC	Coma	7	Yes
Nervous system disorders	Neurological disorders NEC	Coordination abnormal	7	No
Nervous system disorders	Neurological disorders NEC	Coordination abnormal	1	Yes
Nervous system disorders	Neurological disorders NEC	Crying	19	No
Nervous system disorders	Neurological disorders NEC	Depressed level of consciousness	96	Yes
Nervous system disorders	Neurological disorders NEC	Dizziness	3	No
Nervous system disorders	Neurological disorders NEC	Drooling	8	No
Nervous system disorders	Neurological disorders NEC	Dysaesthesia	1	No

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Nervous system disorders	Neurological disorders NEC	Fontanelle bulging	9	No
Nervous system disorders	Neurological disorders NEC	Fontanelle bulging	1	Yes
Nervous system disorders	Neurological disorders NEC	Fontanelle depressed	2	No
Nervous system disorders	Neurological disorders NEC	Grimacing	1	No
Nervous system disorders	Neurological disorders NEC	Hyperaesthesia	16	No
Nervous system disorders	Neurological disorders NEC	Hyperreflexia	2	No
Nervous system disorders	Neurological disorders NEC	Hyporeflexia	2	No
Nervous system disorders	Neurological disorders NEC	Lethargy	13	No
Nervous system disorders	Neurological disorders NEC	Lethargy	1	Yes
Nervous system disorders	Neurological disorders NEC	Loss of consciousness	132	Yes
Nervous system disorders	Neurological disorders NEC	Meningism	5	No
Nervous system disorders	Neurological disorders NEC	Motor dysfunction	7	No
Nervous system disorders	Neurological disorders NEC	Motor dysfunction	1	Yes
Nervous system disorders	Neurological disorders NEC	Myoclonus	22	No
Nervous system disorders	Neurological disorders NEC	Myoclonus	2	Yes
Nervous system disorders	Neurological disorders NEC	Nerve degeneration	1	No
Nervous system disorders	Neurological disorders NEC	Nervous system	10	No
Nervous system disorders	Neurological disorders NEC	Neurodegenerative disorder	1	No
Nervous system disorders	Neurological disorders NEC	Neurological symptom	1	No
Nervous system disorders	Neurological disorders NEC	Neurotoxicity	1	Yes
Nervous system disorders	Neurological disorders NEC	Nystagmus	10	No
Nervous system disorders	Neurological disorders NEC	Pleocytosis	1	No
Nervous system disorders	Neurological disorders NEC	Poor sucking reflex	1	No
Nervous system disorders	Neurological disorders NEC	Postictal state	1	No
Nervous system disorders	Neurological disorders NEC	Presyncope	2	No
Nervous system disorders	Neurological disorders NEC	Presyncope	16	Yes
Nervous system disorders	Neurological disorders NEC	Psychomotor skills impaired	10	No
Nervous system disorders	Neurological disorders NEC	Reflexes abnormal	1	No
Nervous system disorders	Neurological disorders NEC	Sensory loss	1	No
Nervous system disorders	Neurological disorders NEC	Slow response to stimuli	97	Yes

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Nervous system disorders	Neurological disorders NEC	Somnolence	4	No
Nervous system disorders	Neurological disorders NEC	Somnolence	2	Yes
Nervous system disorders	Neurological disorders NEC	Speech disorder	1	No
Nervous system disorders	Neurological disorders NEC	Speech disorder developmental	4	No
Nervous system disorders	Neurological disorders NEC	Stupor	1	Yes
Nervous system disorders	Neurological disorders NEC	Subdural effusion	3	No
Nervous system disorders	Neurological disorders NEC	Syncope	33	Yes
Nervous system disorders	Neurological disorders NEC	Unresponsive to stimuli	11	No
Nervous system disorders	Neurological disorders NEC	Unresponsive to stimuli	17	Yes
Nervous system disorders	Neuromuscular disorders	Autonomic nervous system	1	No
Nervous system disorders	Neuromuscular disorders	Cholinergic syndrome	1	No
Nervous system disorders	Neuromuscular disorders	Hypertonia	35	No
Nervous system disorders	Neuromuscular disorders	Hypertonia	2	Yes
Nervous system disorders	Neuromuscular disorders	Hypotonia	347	No
Nervous system disorders	Neuromuscular disorders	Hypotonia	5	Yes
Nervous system disorders	Neuromuscular disorders	Hypotonic-hyporesponsive episode	133	No
Nervous system disorders	Neuromuscular disorders	Hypotonic-hyporesponsive episode	3	Yes
Nervous system disorders	Neuromuscular disorders	Muscle contractions involuntary	4	No
Nervous system disorders	Neuromuscular disorders	Muscle spasticity	1	No
Nervous system disorders	Neuromuscular disorders	Neuromyopathy	1	No
Nervous system disorders	Neuromuscular disorders	Sensorimotor disorder	1	No
Nervous system disorders	Peripheral neuropathies	Guillain-Barre syndrome	3	Yes
Nervous system disorders	Seizures (incl subtypes)	Atonic seizures	6	Yes
Nervous system disorders	Seizures (incl subtypes)	Clonic convulsion	5	Yes
Nervous system disorders	Seizures (incl subtypes)	Complex partial	2	Yes
Nervous system disorders	Seizures (incl subtypes)	Convulsion	275	Yes
Nervous system disorders	Seizures (incl subtypes)	Convulsions local	1	Yes

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Nervous system disorders	Seizures (incl subtypes)	Epilepsy	60	Yes
Nervous system disorders	Seizures (incl subtypes)	Febrile convulsion	217	Yes
Nervous system disorders	Seizures (incl subtypes)	Grand mal convulsion	66	Yes
Nervous system disorders	Seizures (incl subtypes)	Infantile spasms	46	No
Nervous system disorders	Seizures (incl subtypes)	Infantile spasms	9	Yes
Nervous system disorders	Seizures (incl subtypes)	Myoclonic epilepsy	6	Yes
Nervous system disorders	Seizures (incl subtypes)	Partial seizures	1	No
Nervous system disorders	Seizures (incl subtypes)	Partial seizures	22	Yes
Nervous system disorders	Seizures (incl subtypes)	Petit mal epilepsy	11	Yes
Nervous system disorders	Seizures (incl subtypes)	Post-traumatic epilepsy	1	Yes
Nervous system disorders	Seizures (incl subtypes)	Status epilepticus	13	Yes
Nervous system disorders	Seizures (incl subtypes)	Tonic clonic movements	3	No
Nervous system disorders	Seizures (incl subtypes)	Tonic convulsion	10	Yes
Nervous system disorders	Sleep disturbances (incl subtypes)	Cataplexy	1	Yes
Nervous system disorders	Sleep disturbances (incl subtypes)	Circadian rhythm sleep disorder	2	No
Nervous system disorders	Sleep disturbances (incl subtypes)	Hypersomnia	11	No
Nervous system disorders	Sleep disturbances (incl subtypes)	Poor quality sleep	5	No
Nervous system disorders	Sleep disturbances (incl subtypes)	Sleep phase rhythm disturbance	1	No
Nervous system disorders	Spinal cord and nerve root disorders	Nerve root lesion	1	No
Nervous system disorders	Spinal cord and nerve root disorders	Radiculitis brachial	2	No
Nervous system disorders	Spinal cord and nerve root disorders	Spinal cord compression	1	No
Nervous system disorders	Spinal cord and nerve root disorders	Tethered cord syndrome	1	Yes
Nervous system disorders	Structural brain disorders	Brain injury	2	Yes
Nervous system disorders	Structural brain disorders	Cerebral atrophy	1	No
Nervous system disorders	Structural brain disorders	Cerebral atrophy	5	Yes
Nervous system disorders	Structural brain disorders	Cerebral ventricle dilatation	1	Yes
Nervous system disorders	Structural brain disorders	Subdural hygroma	1	No
Psychiatric disorders	Anxiety disorders and symptoms	Agitation	28	No

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Psychiatric disorders	Anxiety disorders and symptoms	Agitation neonatal	1	No
Psychiatric disorders	Anxiety disorders and symptoms	Anxiety	8	No
Psychiatric disorders	Anxiety disorders and symptoms	Fear	2	No
Psychiatric disorders	Anxiety disorders and symptoms	Tension	2	No
Psychiatric disorders	Changes in physical activity	Decreased activity	5	No
Psychiatric disorders	Changes in physical activity	Restlessness	5	No
Psychiatric disorders	Changes in physical activity	Stereotypy	1	Yes
Psychiatric disorders	Changes in physical activity	Tic	1	No
Psychiatric disorders	Cognitive and attention disorders and disturbances	Attention deficit/hyperactivity disorder	1	No
Psychiatric disorders	Cognitive and attention disorders and disturbances	Daydreaming	3	No
Psychiatric disorders	Communication disorders and disturbances	Communication disorder	1	No
Psychiatric disorders	Communication disorders and disturbances	Dysphemia	1	Yes
Psychiatric disorders	Communication disorders and disturbances	Mutism	1	No
Psychiatric disorders	Communication disorders and disturbances	Screaming	26	No
Psychiatric disorders	Deliria (incl confusion)	Confusional state	1	No
Psychiatric disorders	Deliria (incl confusion)	Delirium	1	Yes
Psychiatric disorders	Deliria (incl confusion)	Disorientation	6	No
Psychiatric disorders	Depressed mood disorders and disturbances	Morose	2	No
Psychiatric disorders	Depressed mood disorders and disturbances	Psychomotor retardation	7	No
Psychiatric disorders	Developmental disorders NEC	Autism spectrum disorder	1	No
Psychiatric disorders	Dissociative disorders	Dissociation	1	No
Psychiatric disorders	Disturbances in thinking and perception	Illusion	1	No
Psychiatric disorders	Disturbances in thinking and perception	Illusion	1	Yes
Psychiatric disorders	Eating disorders and disturbances	Eating disorder	4	No
Psychiatric disorders	Eating disorders and disturbances	Eating disorder	1	Yes
Psychiatric disorders	Eating disorders and disturbances	Food aversion	4	No
Psychiatric disorders	Eating disorders and disturbances	Food aversion	1	Yes
Psychiatric disorders	Eating disorders and disturbances	Merycism	1	No
Psychiatric disorders	Mood disorders and disturbances NEC	Apathy	55	No

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Psychiatric disorders	Mood disorders and disturbances NEC	Apathy	3	Yes
Psychiatric disorders	Mood disorders and disturbances NEC	Emotional distress	1	No
Psychiatric disorders	Mood disorders and disturbances NEC	Inappropriate affect	1	No
Psychiatric disorders	Mood disorders and disturbances NEC	Listless	10	No
Psychiatric disorders	Mood disorders and disturbances NEC	Moaning	12	No
Psychiatric disorders	Mood disorders and disturbances NEC	Moaning	1	Yes
Psychiatric disorders	Mood disorders and disturbances NEC	Mood altered	3	No
Psychiatric disorders	Personality disorders and disturbances in behaviour	Aggression	1	No
Psychiatric disorders	Personality disorders and disturbances in behaviour	Aggression	4	Yes
Psychiatric disorders	Personality disorders and disturbances in behaviour	Antisocial behaviour	2	No
Psychiatric disorders	Personality disorders and disturbances in behaviour	Impatience	1	No
Psychiatric disorders	Personality disorders and disturbances in behaviour	Indifference	2	No
Psychiatric disorders	Personality disorders and disturbances in behaviour	Personality change	5	No
Psychiatric disorders	Personality disorders and disturbances in behaviour	Personality disorder	1	No
Psychiatric disorders	Personality disorders and disturbances in behaviour	Social avoidant	7	No
Psychiatric disorders	Psychiatric and behavioural symptoms NEC	Abnormal behaviour	12	No
Psychiatric disorders	Psychiatric and behavioural symptoms NEC	Abnormal behaviour	1	Yes
Psychiatric disorders	Psychiatric and behavioural symptoms NEC	Breath holding	8	No
Psychiatric disorders	Psychiatric and behavioural symptoms NEC	Breath holding	3	Yes
Psychiatric disorders	Psychiatric and behavioural symptoms NEC	Decreased eye contact	4	No
Psychiatric disorders	Psychiatric and behavioural symptoms NEC	Regressive behaviour	1	No
Psychiatric disorders	Psychiatric and behavioural symptoms NEC	Staring	70	No
Psychiatric disorders	Psychiatric and behavioural symptoms NEC	Staring	1	Yes
Psychiatric disorders	Psychiatric disorders NEC	Mental disorder	1	No
Psychiatric disorders	Sexual dysfunctions, disturbances and gender identity disorders	Excessive masturbation	1	No
Psychiatric disorders	Sleep disorders and disturbances	Initial insomnia	1	No
Psychiatric disorders	Sleep disorders and disturbances	Insomnia	22	No
Psychiatric disorders	Sleep disorders and disturbances	Sleep disorder	16	No
Psychiatric disorders	Suicidal and self-injurious behaviours NEC	Intentional self-injury	1	Yes

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Renal and urinary disorders	Genitourinary tract disorders NEC	Urinary tract disorder	1	No
Renal and urinary disorders	Nephropathies	Nephritic syndrome	1	No
Renal and urinary disorders	Nephropathies	Nephrotic syndrome	2	No
Renal and urinary disorders	Nephropathies	Nephrotic syndrome	1	Yes
Renal and urinary disorders	Renal disorders (excl nephropathies)	Anuria	1	Yes
Renal and urinary disorders	Renal disorders (excl nephropathies)	Hydronephrosis	1	No
Renal and urinary disorders	Renal disorders (excl nephropathies)	Oliguria	4	No
Renal and urinary disorders	Renal disorders (excl nephropathies)	Pyelocaliectasis	1	No
Renal and urinary disorders	Renal disorders (excl nephropathies)	Renal failure	1	No
Renal and urinary disorders	Renal disorders (excl nephropathies)	Renal failure	2	Yes
Renal and urinary disorders	Renal disorders (excl nephropathies)	Renal failure acute	3	Yes
Renal and urinary disorders	Renal disorders (excl nephropathies)	Renal hypertension	1	No
Renal and urinary disorders	Urinary tract signs and symptoms	Chromaturia	1	No
Renal and urinary disorders	Urinary tract signs and symptoms	Enuresis	2	No
Renal and urinary disorders	Urinary tract signs and symptoms	Haematuria	3	No
Renal and urinary disorders	Urinary tract signs and symptoms	Incontinence	1	Yes
Renal and urinary disorders	Urinary tract signs and symptoms	Leukocyturia	1	No
Renal and urinary disorders	Urinary tract signs and symptoms	Polyuria	2	No
Renal and urinary disorders	Urinary tract signs and symptoms	Proteinuria	1	No
Renal and urinary disorders	Urinary tract signs and symptoms	Urinary incontinence	1	No
Reproductive system and breast disorders	Breast disorders	Lactation disorder	1	No
Reproductive system and breast disorders	Male reproductive tract infections and inflammations	Balanitis	1	No
Reproductive system and breast disorders	Penile and scrotal disorders (excl infections and inflammations)	Acquired phimosis	1	Yes
Reproductive system and breast disorders	Reproductive tract disorders NEC	Oedema genital	2	No
Reproductive system and breast disorders	Testicular and epididymal disorders	Testicular retraction	1	No
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Asthma	1	No
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Asthma	7	Yes

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Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Bronchial hyperreactivity	1	No
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Bronchial obstruction	1	No
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Bronchitis chronic	1	No
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Bronchospas m	9	No
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Obstructive airways disorder	2	No
Respiratory, thoracic and mediastinal disorders	Bronchial disorders (excl neoplasms)	Wheezing	3	No
Respiratory, thoracic and mediastinal disorders	Lower respiratory tract disorders (excl obstruction and infection)	Acute respiratory distress syndrome	1	Yes
Respiratory, thoracic and mediastinal disorders	Lower respiratory tract disorders (excl obstruction and infection)	Atelectasis	1	No
Respiratory, thoracic and mediastinal disorders	Lower respiratory tract disorders (excl obstruction and infection)	Atelectasis	1	Yes
Respiratory, thoracic and mediastinal disorders	Lower respiratory tract disorders (excl obstruction and infection)	Emphysema	2	No
Respiratory, thoracic and mediastinal disorders	Lower respiratory tract disorders (excl obstruction and infection)	Interstitial lung disease	3	Yes
Respiratory, thoracic and mediastinal disorders	Lower respiratory tract disorders (excl obstruction and infection)	Lung infiltration	1	No
Respiratory, thoracic and mediastinal disorders	Lower respiratory tract disorders (excl obstruction and infection)	Pneumonia aspiration	6	Yes
Respiratory, thoracic and mediastinal disorders	Lower respiratory tract disorders (excl obstruction and infection)	Pneumonitis	1	Yes
Respiratory, thoracic and mediastinal disorders	Lower respiratory tract disorders (excl obstruction and infection)	Pulmonary oedema	5	Yes
Respiratory, thoracic and mediastinal disorders	Neonatal respiratory disorders	Apparent life threatening event	2	No
Respiratory, thoracic and mediastinal disorders	Neonatal respiratory disorders	Apparent life threatening event	28	Yes
Respiratory, thoracic and mediastinal disorders	Neonatal respiratory disorders	Infantile apnoeic attack	1	Yes
Respiratory, thoracic and mediastinal disorders	Pleural disorders	Haemothorax	1	No
Respiratory, thoracic and mediastinal disorders	Pleural disorders	Pleural effusion	1	Yes

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Respiratory, thoracic and mediastinal disorders	Pulmonary vascular disorders	Pulmonary embolism	1	Yes
Respiratory, thoracic and mediastinal disorders	Pulmonary vascular disorders	Pulmonary hypertension	1	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Acute respiratory failure	1	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Apnoea	109	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Apnoeic attack	8	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Apnoeic attack	2	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Asphyxia	4	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Asphyxia	1	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Aspiration	9	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Aspiration	2	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Bradypnoea	2	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Choking	5	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Choking sensation	3	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Cough	66	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Cough	2	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Cyanosis central	2	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Cyanosis central	1	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Dry throat	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Dysphonia	4	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Dyspnoea	57	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Dyspnoea	2	Yes

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Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Hiccups	2	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Hyperventilation	1	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Hypoventilation	4	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Hypoventilation	1	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Hypoxia	3	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Kussmaul respiration	1	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Oropharyngeal pain	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Productive cough	4	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Rales	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiration abnormal	24	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory acidosis	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory alkalosis	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory arrest	29	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory disorder	21	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory disorder	1	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory distress	4	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory failure	7	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Respiratory tract inflammation	4	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Rhinorrhoea	3	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Sleep apnoea syndrome	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Sleep apnoea syndrome	1	Yes

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Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Sneezing	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Sputum increased	2	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Suffocation feeling	2	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Tachypnoea	8	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Tachypnoea	1	Yes
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Upper airway obstruction	1	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Upper respiratory tract	2	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Use of accessory respiratory muscles	2	No
Respiratory, thoracic and mediastinal disorders	Respiratory disorders NEC	Yawning	1	No
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract disorders (excl infections)	Epistaxis	2	No
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract disorders (excl infections)	Laryngeal oedema	1	Yes
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract disorders (excl infections)	Laryngospasm	3	No
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract disorders (excl infections)	Pharyngeal disorder	2	No
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract disorders (excl infections)	Pharyngeal erythema	23	No
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract disorders (excl infections)	Rhinitis allergic	1	No
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract disorders (excl infections)	Stridor	5	Yes
Respiratory, thoracic and mediastinal disorders	Upper respiratory tract disorders (excl infections)	Tonsillar hypertrophy	2	No
Skin and subcutaneous tissue disorders	Angioedema and urticaria	Circumoral oedema	1	No
Skin and subcutaneous tissue disorders	Angioedema and urticaria	Urticaria papular	1	No
Skin and subcutaneous tissue disorders	Angioedema and urticaria	Urticaria pressure	1	No

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Skin and subcutaneous tissue disorders	Cornification and dystrophic skin disorders	Hyperkeratosis	1	No
Skin and subcutaneous tissue disorders	Cornification and dystrophic skin disorders	Skin hypertrophy	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Blister	11	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Blister	1	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Dermatitis	3	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Dermatitis atopic	8	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Dermatitis atopic	1	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Dermatitis bullous	6	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Dermatitis contact	1	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Dermatitis diaper	7	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Dermatitis exfoliative	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Drug eruption	2	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Dry skin	3	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Eczema	8	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Erythema	80	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Erythema	3	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Erythema multiforme	13	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Exfoliative rash	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Generalised erythema	4	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Lichenification	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Lichen striatus	1	No

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Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Neurodermatitis	8	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Neurodermatitis	3	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Palmar erythema	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Papule	4	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Peau d'orange	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Pemphigoid	1	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Photosensitivity reaction	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Pruritus	12	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash	86	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash	2	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash erythematous	6	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash generalised	15	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash macular	16	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash maculo-papular	16	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash morbilliform	3	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash papular	6	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash pruritic	2	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Rash vesicular	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Scab	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Scab	1	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Scar	6	No

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Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin chapped	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin discolouration	32	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin discolouration	1	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin disorder	6	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin exfoliation	4	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin induration	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin irritation	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin lesion	2	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin necrosis	2	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin odour abnormal	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin reaction	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin warm	13	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Skin warm	1	Yes
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Swelling face	5	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Toxic skin eruption	1	No
Skin and subcutaneous tissue disorders	Epidermal and dermal conditions	Yellow skin	3	Yes
Skin and subcutaneous tissue disorders	Pigmentation disorders	Melanodermia	1	No
Skin and subcutaneous tissue disorders	Pigmentation disorders	Schamberg's disease	1	No
Skin and subcutaneous tissue disorders	Pigmentation disorders	Skin depigmentation	1	No
Skin and subcutaneous tissue disorders	Skin and subcutaneous tissue disorders NEC	Erythema nodosum	2	No
Skin and subcutaneous tissue disorders	Skin and subcutaneous tissue disorders NEC	Palmar-plantar erythrodysaesthesia	1	No

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Skin and subcutaneous tissue disorders	Skin and subcutaneous tissue disorders NEC	Skin ulcer	2	No
Skin and subcutaneous tissue disorders	Skin appendage conditions	Cold sweat	7	No
Skin and subcutaneous tissue disorders	Skin appendage conditions	Heat rash	1	No
Skin and subcutaneous tissue disorders	Skin appendage conditions	Hirsutism	1	No
Skin and subcutaneous tissue disorders	Skin appendage conditions	Hyperhidrosis	29	No
Skin and subcutaneous tissue disorders	Skin appendage conditions	Hyperhidrosis	1	Yes
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Cutaneous vasculitis	1	Yes
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Ecchymosis	12	No
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Ecchymosis	1	Yes
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Haemorrhage subcutaneous	1	No
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Henoch-Schonlein purpura	5	Yes
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Leukocytoclastic vasculitis	2	Yes
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Livedo reticularis	9	No
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Lividity	12	No
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Petechiae	73	No
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Petechiae	4	Yes
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Purpura	19	No
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Purpura	1	Yes
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Skin haemorrhage	1	No
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Skin haemorrhage	1	Yes
Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Skin oedema	1	No

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Skin and subcutaneous tissue disorders	Skin vascular abnormalities	Vasculitic rash	1	Yes
Social circumstances	Lifestyle issues	Immobile	1	No
Social circumstances	Lifestyle issues	Mentally late developer	1	No
Social circumstances	Lifestyle issues	Walking disability	1	No
Surgical and medical procedures	Gastrointestinal therapeutic procedures	Colectomy	1	No
Surgical and medical procedures	Gastrointestinal therapeutic procedures	Ileostomy	1	No
Surgical and medical procedures	Gastrointestinal therapeutic procedures	Small intestinal	1	No
Surgical and medical procedures	Haematological and lymphoid tissue therapeutic procedures	Haemostasis	2	No
Surgical and medical procedures	Male genital tract therapeutic procedures	Orchidectomy	1	Yes
Surgical and medical procedures	Respiratory tract therapeutic procedures	Mechanical ventilation	3	No
Surgical and medical procedures	Respiratory tract therapeutic procedures	Oxygen supplementati on	2	No
Surgical and medical procedures	Skin and subcutaneous tissue therapeutic procedures	Skin lesion excision	1	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Abscess drainage	1	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Emergency care	1	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Enteral nutrition	1	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Hyperthermia therapy	1	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Light anaesthesia	1	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Macrophage activation	1	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Off label use	1	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Resuscitation	11	No
Surgical and medical procedures	Therapeutic procedures and supportive care NEC	Surgery	2	No
Vascular disorders	Aneurysms and artery dissections	Aneurysm	1	Yes
Vascular disorders	Arteriosclerosis, stenosis, vascular insufficiency and necrosis	Ischaemia	1	No
Vascular disorders	Arteriosclerosis, stenosis, vascular insufficiency and necrosis	Peripheral coldness	11	No
Vascular disorders	Arteriosclerosis, stenosis, vascular insufficiency and necrosis	Poor peripheral circulation	1	Yes
Vascular disorders	Arteriosclerosis, stenosis, vascular insufficiency and necrosis	Vasospasm	1	No
Vascular disorders	Decreased and nonspecific blood pressure disorders and shock	Circulatory collapse	31	Yes

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Vascular disorders	Decreased and nonspecific blood pressure disorders and shock	Hypotension	11	No
Vascular disorders	Decreased and nonspecific blood pressure disorders and shock	Hypotension	1	Yes
Vascular disorders	Decreased and nonspecific blood pressure disorders and shock	Hypovolaemic shock	1	Yes
Vascular disorders	Decreased and nonspecific blood pressure disorders and shock	Peripheral circulatory failure	1	Yes
Vascular disorders	Decreased and nonspecific blood pressure disorders and shock	Shock	7	Yes
Vascular disorders	Embolism and thrombosis	Embolism arterial	1	Yes
Vascular disorders	Embolism and thrombosis	Jugular vein thrombosis	1	Yes
Vascular disorders	Embolism and thrombosis	Thrombosis	2	Yes
Vascular disorders	Lymphatic vessel disorders	Lymphoedema	2	No
Vascular disorders	Vascular disorders NEC	Angiopathy	2	Yes
Vascular disorders	Vascular disorders NEC	Capillary disorder	1	No
Vascular disorders	Vascular disorders NEC	Flushing	5	No
Vascular disorders	Vascular disorders NEC	Hyperaemia	11	No
Vascular disorders	Vascular disorders NEC	Hyperaemia	1	Yes
Vascular disorders	Vascular disorders NEC	Pallor	317	No
Vascular disorders	Vascular disorders NEC	Pallor	5	Yes
Vascular disorders	Vascular disorders NEC	Peripheral vascular disorder	1	No
Vascular disorders	Vascular disorders NEC	Vasodilatation	3	No
Vascular disorders	Vascular haemorrhagic disorders	Extravasation blood	1	No
Vascular disorders	Vascular haemorrhagic disorders	Haematoma	24	No
Vascular disorders	Vascular haemorrhagic disorders	Haematoma	1	Yes
Vascular disorders	Vascular haemorrhagic disorders	Haemorrhage	4	Yes
Vascular disorders	Vascular hypertensive disorders	Hypertension	5	No
Vascular disorders	Vascular inflammations	Kawasaki's disease	16	No
Vascular disorders	Vascular inflammations	Kawasaki's disease	2	Yes
Vascular disorders	Vascular inflammations	Vasculitis	23	Yes

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APPENDIX 5A : NARRATIVES OF FATAL CASES IN TIME PERIOD OF PSUR

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Netherlands	04Jun2009		F	16Oct2009

7. & 13. DESCRIBE EVENT(S)

Death, Adverse drug reaction,

This case was reported by a healthcare professional and described the occurrence of death nos in a 4-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevenar) for prophylaxis.

On 15 October 2009, the subject received 3rd dose of Infanrix hexa (unknown route), 3rd dose of Prevenar (unknown route).

On 26 October 2009, 11 days after vaccination with Infanrix hexa and Prevenar, the subject experienced death nos.

The subject died on 26 October 2009, cause of death was not reported. It was unknown whether an autopsy was performed.

Follow up information received on 5 November 2009:

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA530A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 05Oct2009-05Oct2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar Injection D66977 (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 05Oct2009-05Oct2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0599802A NL2009/02217

24c. DATE RECEIVED: 29MAR2010

DATE OF REPORT: 01APR2010

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

This case was also reported by a regulatory authority (NL-College ter Beoordeling van Geneesmiddelen # NL-LRB-92430).

On 16 October 2009, 11 days after vaccination with Infanrix hexa and Prevenar, the subject experienced adverse drug reaction. The subject was found dead in her bed after her afternoon nap.

The subject died on 16 October 2009. No autopsy was performed.

Follow up on 12 March 2010:

Despite several attempts, no further information could be obtained.
The case has been closed.

Follow up information on 29 March 2010:

The subject had no concomitant medication and no relevant medical history.
The subject was transferred to hospital. Hospital report was pending.
The regulatory authority was not able to assess the causality in that case.

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INTERNATIONAL EVENT REPORT

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I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Netherlands		3 M	F	23Oct2009

7. & 13. DESCRIBE EVENT(S)

Sudden infant death syndrome,

This case was reported by a healthcare professional and described the occurrence of cot death in a 3-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-GSK) (Prevenar) for prophylaxis.

On an unspecified date, the subject received 2nd dose of Infanrix hexa (unknown route of administration), 2nd dose of Prevenar (unknown route of administration).

On an unspecified date, at an unspecified time after vaccination with Infanrix hexa and Prevenar, the subject died, cause of death was not specified. It was unknown whether an autopsy was performed.

No active follow-up possible.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA530A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 21Oct2009-21Oct2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar Injection 66977 (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 21Oct2009-21Oct2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0601431A NL2009/02233

24c. DATE RECEIVED: 23APR2010

DATE OF REPORT: 27APR2010

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

Follow up information received from regulatory authority (NL-College ter Beoordeling van Geneesmiddelen # NL-LRB-92684) on 12 November 2009:

On 21 October 2009, the subject received 2nd dose of Infanrix hexa (unknown route of administration), 2nd dose of Prevenar (unknown route of administration).

On 23 October 2009, 2 days after vaccination with Infanrix hexa and Prevenar, the subject died.

Follow up information received from regulatory authority on 23 April 2010:

Baby died during sleep in bed. The baby was found by parents lying on belly with face in mattress. Autopsy did not reveal any cause of death: cot death. Causality: unlikely.

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INTERNATIONAL EVENT REPORT

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I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
PRIVACY	Italy	23May2009		F	10Aug2009

7. & 13. DESCRIBE EVENT(S)

Cardiac arrest, Convulsion, Hypokinesia,

This case was reported by a regulatory authority (IT-Agenzia Italiana del Farmaco # 106091) and described the occurrence of cardiac arrest in a 2-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline) for prophylaxis.

On 10 August 2009, the subject received unspecified dose of Infanrix hexa (unknown route and injection site).

On 10 August 2009, less than one day after vaccination with Infanrix hexa, the subject experienced convulsions.

The subject was hospitalised from 14 August until 19 August 2009.

At discharge, therapy with luminale.

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [x] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA579A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 10Aug2009-10Aug2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADMINISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [ ] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [ ] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0605003A IT2009/02495

24c. DATE RECEIVED: 01JUN2010

DATE OF REPORT: 03JUN2010

24d. REPORT SOURCE: [ ] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

At the time of reporting, the event was resolved with sequelae.

The regulatory authority reported that the event was possibly related to vaccination with Infanrix hexa.

Follow up information received on 14 December 2009 :
Last convulsion episode was on 18 October 2009.
The baby showed a regular growth but a light motor retardation in respect of the age.
Her weight was 7.10 Kg.
Diagnostic tests as Karyotype, Ultrasonography, Computerized axial tomography and Nuclear magnetic resonance were negative.
She was treated with Luminalette 15 mg 3 times per day.

Follow up information received on 01 June 2010 :
The subject died due to a cardiac arrest.

Target Folllow Up Questionaire has been sent together with questions from medical review.

As no further details could be obtained from AIFA, the case has been closed.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Computerized axial tomography		Negative		
Karyotype analysis		Negative		
Nuclear magnetic resonance imaging		Negative		
Ultrasound scan		Negative		

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Netherlands		14 W	U	16Nov2009

7. & 13. DESCRIBE EVENT(S)

Death,

This case was reported by a healthcare professional and described the occurrence of death nos in a 14-week-old subject of unspecified gender who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevenar) for prophylaxis.

On 12 November 2009 the subject received unspecified dose of Infanrix hexa (unknown route, unknown injection site), unspecified dose of Prevenar (unknown route, unknown injection site).

On 16 November 2009, 4 days after vaccination with Infanrix hexa and Prevenar, the subject experienced death (unspecified).

The subject died on 16 November 2009, cause of death was not reported. It was unknown whether an autopsy was performed.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA530A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 12Nov2009-12Nov2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar Injection D91963 (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 12Nov2009-12Nov2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0608494A NL2009/02314

24c. DATE RECEIVED: 16JUL2010

DATE OF REPORT: 16JUL2010

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

Despite several attempts, no additional information could be obtained.
The case has therefore been closed.

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INTERNATIONAL EVENT REPORT

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I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
PRIVACY	Singapore	11Jan2009		F	05Mar2010

7. & 13. DESCRIBE EVENT(S)

Sudden infant death syndrome, Asphyxia,

This case was reported by a physician and described the occurrence of sudden infant death in a 7-week-old female subject who was vaccinated with live attenuated human rotavirus vaccine (Rotarix, GlaxoSmithKline), combined diphtheria, tetanus-acellular pertussis, hepatitis B and inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa) for prophylaxis.

On 1 March 2010, the subject received unspecified dose of Rotarix (oral), unspecified dose of Infanrix hexa (intramuscular, right thigh). Lot numbers not provided.

On 5 March 2010, 4 days after vaccination with Infanrix hexa and Rotarix, the subject experienced sudden infant death.

The subject died on 5 March 2010, cause of death was not reported. It was unknown whether an autopsy was performed.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Rotarix Unknown (Rotavirus vaccine) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Oral

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 01Mar2010-01Mar2010

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Infanrix hexa Injection (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 01Mar2010-01Mar2010

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0639243A SG2010/00015

24c. DATE RECEIVED: 02JUL2010

DATE OF REPORT: 02JUL2010

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

Follow up information received on 19 March 2010:

The reporter insisted that the events were unrelated to vaccination with Infanrix hexa and Rotarix. The subject experienced suffocation during sleep.

Despite several attempts, no additional information could be obtained.
The case has therefore been closed.

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
PRIVACY	Australia	22Feb2010		M	27Apr2010

7. & 13. DESCRIBE EVENT(S)

Sudden infant death syndrome, Apnoeic attack, Pallor, Oxygen saturation decreased, Heart rate decreased,

This case was reported by a healthcare professional and described the occurrence of sudden infant death syndrome in a 2-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), rotavirus vaccine (non-GSK) (RotaTeq) and pneumococcal vaccines (non-GSK) (Prevenar) for prophylaxis.

Concurrent medical conditions included premature birth at 26 weeks gestation.

On 27 April 2010, at 09:30, the subject received unspecified dose of Infanrix hexa (unknown route), unspecified dose of RotaTeq (unknown route), unspecified dose of Prevenar (unknown route).

On 27 April 2010, 12 hours after vaccination with Infanrix hexa,

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [x] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) 1) Infanrix hexa Injection A21CA672B (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 27Apr2010-27Apr2010

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) 2) RotaTeq Unknown 0485Y (Rotavirus vaccine Non-GSK) Other

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 27Apr2010-27Apr2010

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0657890A AU2010/00368

24c. DATE RECEIVED: 15JUL2010

DATE OF REPORT: 15JUL2010

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

CONFIDENTIAL

INTERNATIONAL EVENT REPORT

DESK COPY (Page 2 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
PRIVACY	Australia	22Feb2010		M	27Apr2010

7. & 13. DESCRIBE EVENT(S)

Prevenar and RotaTeq, the subject went dusky and experienced apnea attack, reduced oxygen saturation and decreased heart rate.

The subject was hospitalised.

Relevant test results included: Heart Rate: more than 100 bpm; Pulse Oximetry: more than 94 %; Cranial ultrasound: normal, Ophtalmological examination: normal;

The subject was treated with mechanical ventilation.

The subject stayed under observation for 48 hours in the Special Care Neonate Unit and was discharged.

The subject had another episode of apnea at home 3 days after discharged and could not be resuscitated.

The subject died from sudden infant death syndrome 5 days after vaccination with with Infanrix hexa, Prevenar and RotaTeq.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT DIED AS OUTCOME OF EVENT
- ☐ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) 3) Prevenar Injection E02919 (Pneumococcal vac NonGSK) Other

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 27Apr2010-27Apr2010

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. IDENTIFIED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADMINISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

B0657890A AU2010/00368

24c. DATE RECEIVED: 15JUL2010

DATE OF REPORT: 15JUL2010

24d. REPORT SOURCE: ☐ HEALTH PROFESSIONAL ☐ STUDY ☐ LITERATURE

25a. REPORT TYPE: ☐ INITIAL ☐ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

This case has been reported to regulatory authority and to other manufacturers.

Despite several attemps, no further information could be obtained.
The case has therefore been closed.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Cranial ultrasound scan	Apr2010	normal		
Heart rate	Apr2010	more than 100bpm		
Ophthalmological examination	Apr2010	normal		
Pulse oximetry	Apr2010	more than 94%		

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
PREMATURE BIRTH	Unknown	Unknown	No

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Spain	13Sep2009		M	25Mar2010

7. & 13. DESCRIBE EVENT(S)

Metabolic disorder, Ataxia, Balance disorder, Diplopia, Strabismus, Nervous system disorder,

This case was reported by a physician via a GSK employee and described the occurrence of ataxia in a 6-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-GSK) (Prevenar) for prophylaxis.

The subject's medical history included episodes of shaking of head and arms and legs several times a day.
These episodes occurred previous the 5-month vaccinations and lasted a few days.

On an unspecified date, the subject received 3rd dose of Infanrix hexa (intramuscular, unknown injection site), 3rd dose of Prevenar (intramuscular, unknown injection site) according to the national immunization schedule.

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [x] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [x] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): Mar2010-Mar2010

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar Injection (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): Mar2010-Mar2010

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

Infanrix hexa (GlaxoSmithKline) Unknown
(Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax)

Prevenar (Other) Unknown
(Pneumococcal vac NonGSK)

Meningococcal B C vaccine (Non-GSK) (Other) Unknown
(Meningococcal B C vaccine)

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0661542A ES2010/00560

24c. DATE RECEIVED: 19AUG2010

DATE OF REPORT: 24AUG2010

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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B0661542A	DESK COPY	(Page 2 of 3)

7. & 13. DESCRIBE EVENT(S)

5 days after vaccination with Infanrix hexa and Prevenar, the subject experienced ataxia, instability and diplopia.
The physician suspected a possible neurological alteration.

The subject was hospitalized and some relevant tests were performed and showed normal results.

Two or three days later, the symptoms resolved but the baby still had some instability.
One week later, the subject experienced another episode of ataxia and diplopia, and one month later again.
When the episodes occurred, the baby was always awake.

All the examinations made were normal: NMR, ECG, CSF, Laboratory tests, nasopharyngeal exudates.
The only test pending was the catecholamine.

At the time of reporting, the events were unresolved, the ataxia was still present but in lower intensity.

According to the reporter opinion, the events were unlikely to be related to the vaccinations, but the relationship could not be ruled out by the moment.

Follow up information received on 30 June 2010:

When the patient was 5 months old he presented paroxistic episodes with head shaking (NMR performed was normal).
When he was 6 months old, about 5 days after vaccination with Infanrix Hexa and Prevenar, he had an episode of diplopia (described as strabismus) and ataxia.
The ataxia remained until the age of 9 months.
The shaking moves have repeated in some occasions. Metabolic status was normal.
Since the patient started with neurological profile a month before, it seemed possible that he could have a previous problem more than a vaccine reaction.

The reporter assessed this case as clinically significant.
He reported that the patient was hospitalized at the time of reporting but it is not confirmed.

Further information is expected.

Follow up information received on 9 July 2010:

Previous vaccination included combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (GlaxoSmithKline); meningococcal b c vaccine (non-GSK manufacturer); pneumococcal vaccines (non-GSK manufacturer) given on an unspecified date at the age of 2 months and 4 months.

On 25 March 2010, 5 days after vaccination with Infanrix hexa and Prevenar, the subject experienced certain trunk instability when sitting, although he could maintain the position without support. No shivering on limbs was noted.

Relevant test results included: EEG normal, previous magnetic resonance normal.
Catecholamines and muscular biopsy results were still pending.

The subject underwent EEG in July 2010 and showed 3 lesions compatibles with metabolic disorder.

The final diagnosis was a possible metabolic disease.

He was hospitalized in the pediatric intensive care due to a possible aspiration from 16 to 24 June 2010.

At the time of reporting, the subject was stable at home with very few clinic.

Follow up information received on 19 August 2010:

The subject died in July 2010 due to a possible metabolic disorder of a mitochondrial origin.
The events seemed to be unrelated to vaccination.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL

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Biopsy muscle	pending
Catecholamines	pending
Electrocardiogram	normal
Electroencephalogram	normal
Laboratory test	normal
NMR	see text
NMR	normal
Nonspecific abnormal findings in cerebrospinal fluid	negative

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
SHAKING OF HEAD, ARMS AND LEGS	Unknown	Unknown	No

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Germany	23Oct2005		M	20Jan2006

7. & 13. DESCRIBE EVENT(S)

Death,

This case was reported by a German regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2009022528) and described the occurrence of death - at present cause unknown in a 12-week-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis.
The case was reported by a physician who has heard about this case.

Co-suspect vaccinations included pneumococcal vaccine (non-GSK) (Prevenar, Wyeth).

Familial risk factor included epilepsy of the mother. The subject's mother was treated with levetiracetam (Keppra).
The subject's medical history included drug exposure in utero to levetiracetam during about the first three months of pregnancy.
The rest of pregnancy and birth have been inconspicuous, except for

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA094A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 09Jan2006-09Jan2006

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar Injection 15619 (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 09Jan2006-09Jan2006

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

Levetiracetam Unknown

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

D0063296A

24c. DATE RECEIVED: 15FEB2010

DATE OF REPORT: 16FEB2010

24d. REPORT SOURCE: [ ] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

fracture of a clavicle.
Concurrent medical conditions included agitation and crying abnormal (whiny baby).

On 09 January 2006 the subject received an unspecified dose of Infanrix hexa (0.5 ml, intramuscular, unknown) and an unspecified dose of Prevenar (0.5 ml, intramuscular, unknown).

Approximately 11 days post vaccination with Infanrix hexa and Prevenar, on 20 January 2006, the subject experienced died. The cause of death was not further specified.

It was unknown whether an autopsy was performed.

On 15 February 2010 the German regulatory authority (DE-Paul-Ehrlich-Institut) informed that despite of repeated requests no further information could be obtained.

No further information will be available.

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
FRACTURED CLAVICLE	Unknown	Unknown	Unknown
CRYING ABNORMAL	Unknown	Unknown	Yes
AGITATION	Unknown	Unknown	Yes
FAMILIAL RISK FACTOR	Unknown	Unknown	Yes
DRUG EXPOSURE IN UTERO	Unknown	Unknown	Unknown

CONFIDENTIAL

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Germany	24Jun2009		M	02Oct2009

7. & 13. DESCRIBE EVENT(S)

Cardiac arrest, Sudden infant death syndrome, Sepsis, Viral infection, Resuscitation, Pyrexia, Loss of consciousness, Cyanosis,

This case was reported by a German regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2009025095) and described the occurrence of cardiovascular arrest in a 3-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis.

Co-suspect vaccinations included pneumococcal vaccine (non-GSK) (Prevenar, Wyeth).

On 29 September 2009 the subject received an unspecified dose of Infanrix hexa (0.5 ml, unknown) and an unspecified dose of Prevenar (0.5 ml, unknown).

Approximately three days post vaccination with Infanrix hexa and

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [x] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [x] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA576A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 29Sep2009-29Sep2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar Injection D94951 (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 29Sep2009-29Sep2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

D0064259A

24c. DATE RECEIVED: 18DEC2009

DATE OF REPORT: 23DEC2009

24d. REPORT SOURCE: [ ] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

Prevenar, on 02 October 2009, the subject died from an unknown cause. An autopsy was performed. An autopsy report was not provided.

Post-mortem showed uncharacteristic findings, nevertheless according to the emergency physician the subject showed high fever of 39.4 degC.

The subject experienced no consecutive symptoms in the time between date of vaccination with Infanrix hexa and Prevenar and date of death from an unknown cause. Therefore the reporter considered that death from an unknown cause occurred coincidentally and most likely only by chance to vaccination with Infanrix hexa.

Follow-up information was received on 18 December 2009 from the German regulatory authority (DE-Paul-Ehrlich-Institut).

The subject’s parents have separated about two weeks prior to the events. The subject was cared for by the father with help of sister in law and mother in law.

On 29 September 2009 the subject received the first dose of Infanrix hexa (0.5 ml, intramuscular, left thigh) and the first dose of Prevenar (0.5 ml, intramuscular, right thigh), contralaterally.

Approximately three days post vaccination with Infanrix hexa and Prevenar, on 02 October 2009, the subject experienced cardiovascular arrest.

The subject was hospitalised for cardiopulmonary resuscitation.
The events were reported to be life threatening.

In the morning of 02 October 2009 at around 07:30 the subject appeared normal. About half an hour later, on 02 October 2009 at around 08:00, the subject was supposed to be fed with a bottle. The subject was found unconscious and the subject’s body got blue (cyanosis). Upon arrival of an emergency physician the pupils were medium wide, no pulse could be determined and oxygen saturation could not be measured. The subject was intubated and cardiopulmonary resuscitation was started. Under ongoing resuscitation the subject was transferred to a hospital. In hospital the subject was treated with adrenaline (Suprarenin) and atropine (Atropin), which were intraosseously administered. Nevertheless the pupils showed no reaction to light. Transthoracic echocardiography and electrocardiogram (ECG) both showed no detectable heart reaction. Body temperature, taken in the ear, was 39.4 degC. Resuscitation was without success and was stopped on 02 October 2009 at 09:14. Natural cause of death was not unambiguously clear. Therefore the police was informed for further investigations.

The subject died on 02 October 2009 from cardiovascular arrest. By differential diagnosis possible sudden infant death syndrome (SIDS) or possible fulminant sepsis were considered.

An autopsy was performed. The results of autopsy were not conclusive. According to autopsy both sudden infant death syndrome (SIDS) and viral infection were possible causes of death. External force and shaken impact syndrome (shaken baby syndrome) were excluded by autopsy.

No further information will be available.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Body temperature	02Oct2009	39.4degC		

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Germany	23Jul2009		M	13Nov2009

7. & 13. DESCRIBE EVENT(S)

Sudden infant death syndrome,

This case was reported by a German regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2009026024) and described the occurrence of sudden infant death syndrome (SIDS) in 3-month-old male subject who was vaccinated with 10 valent pneumococcal conjugate vaccine (Synflorix, GlaxoSmithKline) and combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis.

The subject has no underlying or concurrent medical conditions or other risk factors.
The subject has received previous vaccination with Synflorix and Infanrix hexa. It was unknown whether or not the subject has tolerated previous vaccinations well.

On 04 November 2009 the subject received an unspecified dose of Synflorix (0.5 ml, unknown, unknown thigh) and an unspecified dose

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [x] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Synflorix Injection ASPNA007AE (10 Valent Pneumococcal Co) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 04Nov2009-04Nov2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA609A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 04Nov2009-04Nov2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

D0064689A

24c. DATE RECEIVED: 05MAR2010

DATE OF REPORT: 09MAR2010

24d. REPORT SOURCE: [ ] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

of Infanrix hexa (0.5 ml, unknown, unknown thigh).

Approximately nine days post vaccination with Synflorix and Infanrix hexa, on 13 November 2009, the subject died from sudden infant death syndrome (SIDS). The event was also reported as life threatening.

It was not specified whether an autopsy was performed.

One vaccine was reported as a lot number only, but was identified as 10 valent pneumococcal conjugate vaccine (Synflorix, GlaxoSmithKline) according to lot number. The other vaccine was reported as diphtheria and tetanus toxoids and acellular pertussis vaccine (Infanrix, GlaxoSmithKline), but according to lot number the subject was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline).

On 21 January 2010 the German regulatory authority (DE-Paul-Ehrlich-Institut) informed that despite of repeated requests no further information could be obtained up to now.

Follow-up information including autopsy report was received on 05 March 2010 from the German regulatory authority (DE-Paul-Ehrlich-Institut).

The subject was found lifeless on 13 November 2009 at 11:40 in bed in supine position covered by a cushion / pillow. An emergency physician was only able to certify death. The subject has had no underlying medical conditions. According to a police report the children’s room was severely overheated and in the whole apartment people had been smoking (passive smoking).

Autopsy was performed on 20 November 2009 and showed age-corresponding state of development and very good state of care. Both height and weight was 50 percentile. Multiple punctual haemorrhages up to the size of a pinhead were found under the thymus capsule, subepicardial and on the surface of the lungs. Distinct disorder of blood distribution was seen in the lungs as well as increased fluid and blood content in the lungs and foam in the respiratory tract (pulmonary edema). Neither signs of external force by a third party nor signs of shaken baby syndrome have been detected. No signs of organic malformation have been detected.

The cause of death could not be unambiguously determined. Punctual haemorrhages under the thymus capsule, subepicardial and on the surface of the lungs were normally seen within the scope of sudden infant death syndrome (SIDS) and therefore the autopsy performing physicians considered SIDS. Possible risk factors associated with SIDS included coverage with a pillow, severely overheating of the surrounding, not feeding with breast milk and nicotine abuse of the parents. Furthermore autopsy showed increased water retention of the lungs as well as distinct disorder of blood distribution within the lungs. These findings could be signs of a beginning pulmonary infection. Therefore histological and microbiological examinations will be performed. Additionally chemical toxicological examinations will be performed to exclude intoxication. Shaken baby syndrome has been excluded by preparation of the bridging veins.

Microbiological examinations, performed on 20 November 2009, showed solitary Staphylococcus aureus in both pulmonary swabs and a single Staphylococcus aureus colony in the spleen swab as potential infectious agent, but this bacterium was also known as normal bacterial flora of the upper respiratory tract. All other bacteria found belong either to physiological intestinal flora or were normal parts of the throat and skin flora.
Microscopically no signs of inflammation could be detected. Therefore infectious events could be excluded with some probability. Final conclusions could from microscopic examinations can only been made including histopathologic results.

No further information will be available.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Head circumference		38cm		

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
PASSIVE SMOKING	Unknown	Unknown	Yes

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Germany	08Sep2009		F	10Dec2009

7. & 13. DESCRIBE EVENT(S)

Sudden infant death syndrome,

This case was reported by a physician and described the occurrence of sudden infant death syndrome (SIDS) in a 3-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis.

Co-suspect vaccinations included pneumococcal vaccine (non-GSK) (Prevenar, Wyeth).

On an unknown date in 2009 the subject received an unspecified dose of Infanrix hexa (0.5 ml, unknown) and an unspecified dose of Prevenar (0.5 ml, unknown).

Approximately one day post vaccination with Infanrix hexa and Prevenar, on an unknown date in 2009, the subject died from an unknown cause.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA619A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 09Dec2009-09Dec2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar Injection D78232 (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 09Dec2009-09Dec2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

D0065445A

24c. DATE RECEIVED: 04MAR2010

DATE OF REPORT: 11MAR2010

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

It was unknown whether an autopsy was performed.

Follow-up information was received on 21 December 2009 from the reporting physician. Additional information was received by fax on the same day from the reporting physician.

On 09 December 2009 the subject received the first dose of Infanrix hexa (0.5 ml, intramuscular, right deltoid) and the first dose of Prevenar (0.5 ml, intramuscular, left deltoid), contralaterally.

Approximately one day post vaccination with Infanrix hexa and Prevenar, on 10 December 2009, the subject died from sudden infant death syndrome (SIDS). It was unknown whether an autopsy was performed.

The reporting physician also provided the answers to a GSK questionnaire asking for additional information in cases of sudden infant death syndrome (SIDS):

The mother was married.
No information was provided concerning employment of father and mother, age of father and mother and the number of brothers and sisters.

None of the following diseases were known in family history: metabolic disorders or inborn errors of metabolism, cardiac problems, non-accidental injury in child and non-accidental injury in siblings.
It was unknown, whether or not family history included, SIDS or SUD, near miss, infant death due to other reason or epilepsy or convulsions.
It was unknown whether or not either mother or father was smoking.
No information was provided whether or not mother or father were abusing alcohol and drugs.
The subject’s family was living in a rural region.

The mother had been pregnant for an unknown number of times with 2 deliveries.
It was unknown whether or not conditions during present pregnancy included maternal illness or complication during pregnancy, maternal smoking or maternal medication.
It was unknown whether or not the mother took any medication during breast feeding.
It was unknown whether or not there was any fetal distress.

The subject was born by normal delivery at 39 weeks with a birth weight of 2800 g, unspecified length, unspecified head circumference and unspecified APGAR score.
There were no birth defects.
The subject was breast-fed for three months.
The subject’s development and weight gain were normal.

The subject had none of the following pre-existing diseases: allergies, inborn errors of metabolism or enzymatic abnormalities, episodes of cyanosis, stop breathing or apnea, gastroesophageal reflux, convulsions, sleep disorder, past surgery or known mistreatment.
The subject had none of the following conditions in the past two weeks: emergency room visit, exposure to contagious disease, infection, fever, excessive sweating during sleep, loud breathing or snoring during sleep, vomiting, appetite changes, diarrhea or stool changes, dyspnea, abnormal crying or lethargy.
There were no recent changes of the way of life..

The subject had received the last meal, consisting of mother’s breast milk on 10 December 2009.
Afterwards the subject was brought to bed. About one hour later when looking for the subject everything was normal. About two hour later the subject was found dead in bed in supine position.

On an unspecified time on 10 December 2009 the subject was found dead in the bed.
The subject was found by chance.
It was unknown whether the subject was sleeping alone.
The subject was sleeping in the bed.
When placed, the position of body was face up.
When found, the position of body was face up.
Sleeping or supporting surface, items in contact with infant or in immediate environment included, the number of blankets covering the subject, body temperature of the subject at the time when found dead and room temperature at the time when found dead were unknown.
The subject was looked after by the mother.

The subject has received no previous vaccinations.

Follow-up information of the same case was received on 04 January 2010 from the German regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2009030789).

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Co-suspect vaccinations included 7 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar, Wyeth).

The subject was a healthy infant and received breast feeding.
No concomitant medication has been reported.

On 09 December 2009 at approximately 09:45 the subject received the first dose of Infanrix hexa (0.5 ml, intramuscular, unknown) and the first dose of Prevenar (0.5 ml, intramuscular, unknown).

Post vaccination with Infanrix hexa and Prevenar the subject experienced no adverse reaction like fever. On the next morning, on 10 December 2009, the subject was normally drinking and was put to bed. Approximately two to three hours later, on 10 December 2009, the subject was found lifeless in bed in supine position.

The cause of death was reported as sudden infant death syndrome (SIDS). An autopsy was performed, but results were not provided.

No additional information was available at the time of this report but additional information has been requested.

On 28 January 2010 the reporting physician confirmed the reported date of birth of the subject to be 08 September 2009.

Follow-up information was received on 04 March 2010 from the German regulatory authority (DE-Paul-Ehrlich-Institut).

The German regulatory authority (DE-Paul-Ehrlich-Institut) informed that case D0066295A was identified to be a duplicate of case D0065445A. All future correspondence of case D0066295A will be submitted to this case.
Additionally, the German regulatory authority (DE-Paul-Ehrlich-Institut) identified a third case received to be also a duplicate of this case of record (case D0065445A). The new only active PEI number for all PEI cases was now DE-PEI-PEI2009029991. The PEI cases with the numbers DE-PEI-PEI2009030789 and DE-PEI-PEI2010002277 will been nullified.

The duplicate case D0066295A was initially received on 28 January 2010 from the German regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2010002277).

At the time of vaccination the subject was healthy.
Co-suspect vaccination included pneumococcal vaccine (non-GSK) (Prevenar, Wyeth).

On 09 December 2009 at 09:30 or 09:45 the subject received an unspecified dose of Infanrix hexa (intramuscular, unknown thigh) and an unspecified dose of Prevenar (intramuscular, unknown thigh), contralaterally.

On 09 December 2009 and in the morning of the next day, on 10 December 2009, the subject was normal and showed no adverse effect. The subject was breast fed in the morning of 10 December 2009. The subject was drinking normal. After breast feeding the subject was put to bed.

Approximately two to three hours later, on 10 December 2009, the subject was found dead in bed in supine position. An emergency physician was called.

The subject died on 10 December 2009 from sudden infant death syndrome (SIDS). An autopsy was performed, but no results were available at the time of reporting.

At the moment no further information will be available.

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
BREAST FEEDING	Unknown	Unknown	Yes

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Germany	28Sep2009		M	29Dec2009

7. & 13. DESCRIBE EVENT(S)

Sudden infant death syndrome,

This case was reported by a physician via a sales representative and described the occurrence of possible sudden infant death syndrome (SIDS) in a 3-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis.

Co-suspect vaccinations included pneumococcal vaccine (non-GSK) (Prevenar, Wyeth).

On 29 December 2009 the subject received an unspecified dose of Infanrix hexa (0.5 ml, unknown) and an unspecified dose of Prevenar (0.5 ml, unknown).

Less than one day post vaccination with Infanrix hexa and Prevenar, on 29 December 2009, the subject was falling asleep and did not wake up again. The subject died (death - at present cause unknown).

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [x] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA633A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/~~CUMULATIVE~~ DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 29Dec2009-29Dec2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar Injection D80552 (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/~~CUMULATIVE~~ DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 29Dec2009-29Dec2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

D0066068A

24c. DATE RECEIVED: 02FEB2010

DATE OF REPORT: 09FEB2010

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

It was not reported whether an autopsy was performed.

Follow-up information was received on 15 January 2010 by phone from the reporting physician.

The subject has three healthy siblings.
The subject was healthy.
The subject was beast fed.
The subject's mother did not smoke.

On 29 December 2009 the fourth preventive medical examination for infants (U4) was performed.

On 29 December 2009 at around 10:00 the subject received the first dose of Infanrix hexa (0.5 ml, unknown) and the first dose of Prevenar (0.5 ml, unknown) at the reporting physician's practice.

According to the subject's mother, after leaving the practice on the way home, the subject has fallen asleep and did not wake up again. It was not quite clear at which time the subject was found dead. The subject must have died in the evening of 29 December 2009 or in the night between 29 December 2009 and 30 December 2009.

An autopsy was performed on an unknown date. According to verbal information to the reporter autopsy showed no pathologic findings. Sudden infant death syndrome (SIDS) was considered. According to verbal information to the reporter no causal relationship of possible sudden infant death syndrome (SIDS) to vaccination with Infanrix hexa and Prevenar was considered.

On 18 January 2010 the same case was received from a German regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2010000799).

The subject's past medical condition was not provided.

On 29 December 2009 the subject received a dose of Infanrix hexa (0.5 ml, intramuscular, unknown) and a dose of Prevenar (0.5 ml, intramuscular, unknown).

In the night post day of vaccination the subject was found dead in bed.

The German regulatory authority (DE-Paul-Ehrlich-Institut) reported date of death to be 30 December 2009 and cause of death to be possible sudden infant death syndrome (SIDS).

The case was reported to be life threatening.

An autopsy was performed, but the German regulatory authority (DE-Paul-Ehrlich-Institut) has not received the autopsy report up to now.

On 21 January 2010 the German regulatory authority (DE-Paul-Ehrlich-Institut) informed that despite of repeated requests no further information could be obtained up to now.

Follow-up information was received on 02 February 2010 from the reporting physician.

The subject has no underlying or concurrent medical conditions or other risk factors.
The subject received no concomitant medication.

On 29 December 2009 the subject received the first dose of Infanrix hexa (0.5 ml, intramuscular, right thigh) and the first dose of Prevenar (0.5 ml, intramuscular, left thigh), contralaterally.

Less than one day post vaccination with Infanrix hexa and Prevenar, on 29 December 2009, the subject died. The subject received no treatment. An autopsy was performed. The results of autopsy were inconclusive and showed no obvious cause of death. Therefore cause of death was considered to be sudden infant death syndrome (SIDS).

The reporting physician also provided the answers to a GSK questionnaire asking for additional information in cases of sudden infant death syndrome (SIDS):

The mother was married and cohabiting with her husband.
The mother was not employed and the father's state of employment was unknown.
The ages of the mother and the father were not reported.
The subject had two brothers and one sister.

None of the following diseases were known in family history: metabolic disorders or inborn errors of metabolism, cardiac problems, SIDS or SUD, near miss, infant death due

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to other reason, epilepsy or convulsions, non-accidental injury in child, non-accidental injury in siblings.
The mother or and father did not smoke, abuse alcohol and drugs.
The subject’s family was living in a rural region.

The mother had been pregnant for four times with four deliveries.

During present pregnancy there was no maternal illness or complication, maternal smoking or maternal medication.
There was no maternal medication during breast feeding.
There was no fetal distress.

The subject was born by normal delivery at unknown week of pregnancy as mature newborn with a birth weight of 3760 g, an unknown length, an unknown head circumference and an APGAR score of 10/10.
There were no birth defects.
The subject was breast-fed until death.
The subject development well and weight gain was normal.

The subject had none of the following pre-existing diseases: allergies, inborn errors of metabolism or enzymatic abnormalities, episodes of cyanosis, stop breathing or apnea, gastroesophageal reflux, convulsions, sleep disorder, past surgery, mistreatment prior to contact with social worker or other relevant medical conditions.
The subject had none of the following conditions in the past two weeks: emergency room visit, exposure to contagious disease, infection, fever, excessive sweating during sleep, loud breathing or snoring during sleep, vomiting, appetite changes, diarrhea or stool changes, dyspnea, abnormal crying, lethargy or other relevant medical conditions.
There were no recent changes of the way of life..

The subject had received the last meal, consisting of mother’s milk on 29 December 2009 in the evening

On 29 December 2009 in the evening the subject was found dead under unknown circumstances in the bed.
The subject was found by chance.
It was unknown whether or not the subject was sleeping alone in the bed.
When placed, the position of body was unknown.
When found, the position of body was unknown.
The type of sleeping or supporting surface was unknown.
Whether there were items in contact with infant or in immediate environment was unknown.
Whether the subject was covered by one or more blankets was unknown.
Body temperature when found was unknown.
Room temperature when found was unknown. The type of heating was unknown.
The subject was looked after by the mother.

There were no adverse events following the last vaccination because vaccination with Infanrix hexa and Prevenar was the first course of vaccination received ever.

No further information will be available.

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Germany	27Jan2010		M	03Apr2010

7. & 13. DESCRIBE EVENT(S)

Sudden infant death syndrome, Death, Apnoea, Cardiac arrest, Loss of consciousness, Resuscitation,

This case was reported by a German regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2010014329) and described the occurrence of sudden infant death syndrome (SIDS) in a 9-week-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis.
Follow-up information was received on 10 June 2010 and 11 June 2010 from the German regulatory authority (DE-Paul-Ehrlich-Institut). Due to initial mix up in source documentation the case has to be completely rewritten. Initially the outcome had been reported as recovered.

Co-suspect vaccinations included 13 valent pneumococcal conjugate vaccine (non-GSK) (Prevenar 13, Wyeth).

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [x] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA704G (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 31Mar2010-31Mar2010

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar 13 Injection E19519 (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 31Mar2010-31Mar2010

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

Colecalciferol	Unknown
Iron (Iron salt)	Unknown

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

D0067790A

24c. DATE RECEIVED: 16SEP2010

DATE OF REPORT: 20SEP2010

24d. REPORT SOURCE: [ ] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

Past medical history was not provided.
It was unknown whether or not the subject has received any previous vaccinations and how these vaccinations may have been tolerated.

On 31 March 2010 the subject received an unspecified dose of Infanrix hexa (0.5 ml, unknown) and an unspecified dose of Prevenar 13 (0.5 ml, unknown)

Approximately three days post vaccination with Infanrix hexa and Prevenar 13, on 03 April 2010, the subject experienced sudden infant death syndrome (SIDS).

The event was reported to be life threatening.

The subject died on 03 April 2010 from sudden infant death syndrome (SIDS) according to diagnosis by an emergency physician.

An autopsy was performed but autopsy revealed no obvious cause of death and therefore the cause of death could not be determined (death due to unknown cause).

Follow-up information including protocol from the emergency physician was received in 14 June 2010 from the German regulatory authority (DE-Paul-Ehrlich-Institut).

Concurrent medical conditions included old contusion and hematoma on right side of chest.

On 03 April 2010 in the morning the subject experienced apnea. On 03 April 2010 at 09:42 an emergency physician was called and arrived about five minutes later on 03 April 2010 at 09:47. When the emergency care team arrived the subject was unconscious. Cardiac arrest with apnea and asystole was diagnosed. Resuscitation was unsuccessful. Sudden infant death syndrome (SIDS) was suspected. The subject was declared dead on 03 April 2010 at 10:03.

Follow-up information, received on 17 June 2010 from the German regulatory authority (DE-Paul-Ehrlich-Institut), contained no new information.

Follow-up information including preliminary autopsy report was received in 18 June 2010 from the German regulatory authority (DE-Paul-Ehrlich-Institut).

Complication during pregnancy included cranial hemorrhage of the mother due to cerebral artery aneurysm in the 19th week of gestation.
The subject was born in the 33rd week of pregnancy by Caesarean section.
The subject’s medical history was uneventful. The subject seemed to be healthy.
During last scheduled prophylactic medical examination of infants, on 31 March 2010, the subject showed no conspicuous findings.
On the same date the subject was vaccinated with Infanrix hexa.

Approximately three days post vaccination with Infanrix hexa, on 03 April 2010, the subject was brought to bed by the father. About one hour later, the subject was found lifeless. The subject was in the crib in prone position. An emergency physician was called immediately. Resuscitation by the emergency physician was unsuccessful.

Autopsy was performed on 06 April 2010 from 09:30 to 10:30.

According to percentile curve of the WHO the subject was in reduced nutritional condition with a weight of 3700 g and a height 55cm.
Autopsy showed multiple punctual, in parts confluent hemorrhage under the serous membranes of thymus gland and heart, bloated lungs (pulmonary emphysema) both sides and signs of shock kidneys both sides, tiny fissures of skin at the left corner of the mouth, extensive ecchymoses in the area of the central chest wall and the upper epigastric region, two small round ecchymoses in the line of the left mamilla, hemorrhage in the connective tissue like capsule of the right adrenal gland and right kidney.
Macroscopically, autopsy revealed no unambiguous cause of death. All autopsy findings were known to occur in cases of sudden infant death syndrome (SIDS). The findings not consistent with SIDS (skin fissures in the corner of mouth, ecchymoses in area of central chest wall, hemorrhage in capsule of adrenal gland and kidney) can be explained with plausibility by long and continuous resuscitation.
Final diagnosis of SIDS has not been made because SIDS is a diagnosis based on exclusion of other diagnoses and additional examinations, including histology and toxicology, have not been performed. Furthermore, death due to causes which provide little traces or medical findings, like e.g. soft covering, might stay undetected by autopsy.
The cause of death was unknown. The manner of death was unsolved.

Follow-up information concerning medical history was received in 09 July 2010 from the German regulatory authority (DE-Paul-Ehrlich-Institut).

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The subject’s mother experienced severe cerebral hemorrhage in October 2009 in the 19th week of pregnancy. The subject’s mother was cared for at a neurosurgery department followed by rehabilitation measures.

The subject was born premature in the 33 + 2 week of pregnancy by caesarean section. At that time the subject was immature with a birth weight of 1805 g /(20th percentile), length of 43 cm (25th percentile), head circumference of 32 cm, Apgar score of 8/9/9, umbilical blood ph of 7.35 and mild respiratory distress syndrome with 23 % oxygen demand. The subject was hospitalised from 27 January 2010 to 18 February 2010. Postnatal the subject showed good adaptation, but chest X-ray, performed on 28 January 2010, showed mixed picture of mild neonatal respiratory distress syndrome and wet lung. Repeated central nervous system (CNS) sonography, performed on 28 January 2010, 29 January 2010 and 08 February 2010, as well as neonatal screening, performed on 29 January 2010 and 15 February 2010, were normal. The subject developed normal without complications. On 18 February 2010 the subject was discharged from hospital in stable general condition.

Concurrent medications included colecalciferol (Vitamin D3) and iron salt (Iron).

In third child heath check, performed on 04 March 2010, the subject showed normal development concerning weight, length and head circumference. The subject showed no pathologic findings except mild hydrocele.

In fourth child heath check, performed on 31 March 2010, the subject showed no pathologic findings. The subject received the first dose of Infanrix hexa and the first dose of Prevenar 13.

Approximately three days later, on 03 April 2010, the subject died from possible sudden infant death syndrome (SIDS).

Follow-up information was received via the regulatory authority on 16 September 2010. Reports on toxicologic and histologic examinations, performed on 18 August 2010, were provided. Findings were summarized by the regulatory authority as follows: "Unexplained death (no definite cause of death), probably sudden infant death syndrome, according to the autopsy report as well as to the toxicologic and histologic examinations. No further information was available at the date of this report."

According to the report on the toxicologic examination, there were no findings which could identify the cause of death. Any examination had resulted negatively / normally. Urine analysis revealed detectable concentrations of paracetamol and lidocaine. Lidocaine might possibly be due to the reanimation procedures. Paracetamol might be due to a possible treatment of febrile infection during the last days prior to the subject’s death. As the subject’s blood was free of paracetamol, the finding was considered not contributory.

According to the report on the histologic examination, results largely confirmed the findings of the autopsy. Results included hemostasis of inner organs, cerebral edema, haemorrhage of the organs’ connective tissue coatings and acute pulmonary emphysema. Besides unspecific signs of death, punctuate haemorrhage of the organs’ connective tissue coatings and pulmonary emphysema were considered the essential findings. Acute emphysema could be interpreted as evidence of suffocation.

It was concluded that a definite cause of death could not be identified, neither in histologic examinations nor in toxicologic tests. It was discussed that the toxicologic tests covered a certain spectrum of substances only and would miss some rare and exceptional substances. Histology could not identify a definite cause of death either. Because of the combination of pulmonary emphysema and the fissures at the left corner of the mouth, which had been observed during the autopsy, death due to suffocation following violent obstruction of respiratory orifices could not be excluded. Likewise it could not be excluded that these findings were caused during the reanimation procedures.

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
COMPLICATION OF PREGNANCY	Oct2009	Oct2009	No
HOSPITALIZATION	27Jan2010	18Feb2010	No
NEONATAL RESPIRATORY DISTRESS SYNDR	28Jan2010	18Feb2010	No
HYDROCELE	04Mar2010	Unknown	Yes
HEMATOMA ON SIDE OF CHEST	Unknown	Unknown	Yes
CONTUSION TO SIDE OF CHEST	Unknown	Unknown	Yes
EXTREME IMMATURITY, 1,750-1,999 GRA	Unknown	Unknown	No
PREMATURE BABY 33 TO 36 WEEKS	Unknown	Unknown	No

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INTERNATIONAL EVENT REPORT

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I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Germany		Unknown	Unknown	Unknown

7. & 13. DESCRIBE EVENT(S)

Death,

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [ ] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [x] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) DTPa-HBV-IPV-HIB Injection (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax)

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: Unknown

18. THERAPY DATES (From / To): Unknown

19. THERAPY DURATION: Unknown

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADMINISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [ ] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [ ] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

D0069211A

24c. DATE RECEIVED: 21OCT2010

DATE OF REPORT: 25OCT2010

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [ ] FOLLOW-UP

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APPENDIX 5B : NARRATIVES OF FOLLOW-UP OF FATAL CASES RECEIVED IN A PREVIOUS PERIOD

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Netherlands	18Apr2009		F	Jun2009

7. & 13. DESCRIBE EVENT(S)

Death, Depressed level of consciousness, Hypotonia, Pallor,

This case was reported by a healthcare professional and described the occurrence of death nos in a 2-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-gsk) (Prevenar) for prophylaxis.

On an unspecified date, the subject received 1st dose of Infanrix hexa (unknown route), 1st dose of Prevenar (unknown route). No lot number available.

1 day after vaccination with Infanrix hexa and Prevenar, the subject experienced death nos.

The subject died, cause of death is not specified. It was unknown whether an autopsy was performed.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA487A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 16Jun2009-16Jun2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar Injection (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 16Jun2009-16Jun2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0580597A NL2009/01225

24c. DATE RECEIVED: 23MAR2010

DATE OF REPORT: 23MAR2010

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

This was all the available information. The reporter will send additional details in a proactive way.

Follow up information received on 2 July 2009 from regulatory authority:
The subject had no medical history and no concomitant medication.
On 16 June 2009 the subject received 1st dose of Infanrix hexa (unknown route), 1st dose of Prevenar (unknown route).

1 day after vaccination with Infanrix hexa and Prevenar, the subject was found in bed nonresponsive, floppy and pale.

The subject died on 17 June 2009, cause of death was not reported.

Despite several attempts, no further information could be obtained; therefore the case has been closed.

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Netherlands		11 M	F	25Aug2009

7. & 13. DESCRIBE EVENT(S)

Cardiac arrest, Vomiting, Constipation,

This case was reported by a regulatory authority (NL-College ter Beoordeling van Geneesmiddelen # NL-LRB-90943) and described the occurrence of asystolia in a 11-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline), pneumococcal vaccines (non-GSK, Prevenar) for prophylaxis.

In August 2009, the subject received 1st dose of Infanrix hexa (unknown route), 1st dose of Prevenar (unknown route).

In August 2009, 1 day after vaccination with Infanrix hexa and Prevenar, the subject experienced death nos.

The subject died, cause of death is not specified.

Normally children receive 4th dose of vaccination in schedule at age

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA487A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/~~CUMULATIVE~~ DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 24Aug2009-24Aug2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar Injection 37369 (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/~~CUMULATIVE~~ DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Unknown

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 24Aug2009-24Aug2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

Co-careldopa	Unknown
Calcium folinate	Unknown
Oxitriptan	Unknown

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0590738A NL2009/01850

24c. DATE RECEIVED: 28DEC2009

DATE OF REPORT: 05JAN2010

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

11 months.

Further information will follow when available.

Follow up information received on 8 September 2009:

Concurrent medical conditions included malignant phenylketonuria.

On 24 August 2009 the subject received 1st dose of Infanrix hexa and 1st dose of Prevenar.

On 25 August 2009, 1 day after vaccination with Infanrix hexa and Prevenar, the subject experienced adverse drug reaction unspecified.

The subject died on 25 August 2009, cause of death was not reported. It was unknown whether an autopsy was performed.

Follow up information received on 5 November 2009:
Lot numbers were provided.

Follow up information received on 28 December 2009:
Comment and conclusion from regulatory authority received.
The parents were Armenian.
Concurrent medical conditions included developmental motor delay (tested by AIMS: 4 months), phenylketonuria and dihydropteridin reductase deficiency.

Concurrent medications included Co-careldopa (Carbidopa + levodopa), Calcium folinate (Leucovorine), Oxitriptan and BH4 (tetrahydrobiopterine).

3 days before vaccination, the subject was seen by a physiotherapist who observed low-pressure mood, crying and tiredness.
Vaccinations were started at age of 11 months (instead of 2 months age normally) due to miscommunication between physicians.

The subject received Infanrix-hexa and Prevenar at 10:30 on 24 August 2009.

The subject was not ill, no fever was observed. The baby experienced vomiting a few times that day and difficulties with defecation. She slept well and played normally the next morning.

On 25 August 2009, the subject went to bed for a nap and her mother found her blue colored and not breathing at 13:00 in bed.

On 25 August 2009, 1 day after vaccination with Infanrix hexa and Prevenar, the subject experienced asystolia.

The subject died on 25 August 2009, cause of death was unknown.

Pediatrician suggested (according forensic physician report) the possibility that the subtle balance on neurotransmitter level which is part of the underlying metabolic disorder has been disturbed.

The unknown cause and the rare underlying disease make it difficult to assess the causality of vaccinations and death. The interval between vaccinations and death was longer than 24 hours and girl did not have fever, both make causality less likely. Most probably this is a coincidence and not an adverse reaction.

No further information has been requested, the case has been closed.

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
PHENYLKETONURIA	Unknown	Unknown	Unknown
DEVELOPMENTAL MOTOR DELAY	Unknown	Unknown	Unknown
TIREDNESS	Unknown	Unknown	Unknown
CRYING	Unknown	Unknown	Unknown

CONFIDENTIAL

INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Taiwan, ROC		6 M	M	24Aug2009

7. & 13. DESCRIBE EVENT(S)

Acute respiratory failure, Hypoxia, Altered state of consciousness, Pyrexia, Cough, Decreased appetite, Discomfort,

This case was reported in a newspaper article and described the occurrence of acute respiratory failure in a 6-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis.

On 22 August 2009, the subject received 3rd dose of Infanrix hexa (intramuscular, unknown injection site). Lot number not provided.

After vaccination, the subject experienced discomfort.

On 24 August 2009, 2 days after vaccination with Infanrix hexa, the subject experienced fever, cough and poor appetite.
The subject was hospitalised for 2 days.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [x] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 22Aug2009-22Aug2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADMINISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [ ] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [ ] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0591078A TW2009/00150

24c. DATE RECEIVED: 04MAR2010

DATE OF REPORT: 04MAR2010

24d. REPORT SOURCE: [ ] HEALTH PROFESSIONAL [ ] STUDY [x] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

The subject died on 31 August 2009, cause of death was not reported. It was unknown whether an autopsy was performed.

On 30 August 2009, 8 days after vaccination with Infanrix hexa, the subject was hospitalized for acute respiratory failure, hypoxemia, and conscious disturbance.

The subject was transferred to ICU and intubated for 3 hours, but it failed.

The subject died on 31 August 2009, cause of death was not reported. It was unknown whether an autopsy was performed.

Follow up on 4 March 2010:

Despite several attempts, no further information could be obtained.
The case has been closed.

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Austria		2 M	F	06Oct2009

7. & 13. DESCRIBE EVENT(S)

Sudden infant death syndrome, Product quality issue,

This case was reported by a regulatory authority (AT-Bundesministerium fur Gesundheit und Frauen # AT-BASGAGES-091755) and described the occurrence of sudden infant death syndrome in a 2-month-old female subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine. (Infanrix hexa, GlaxoSmithKline), 10 valent pneumococcal conjugate vaccine (Synflorix) and rotavirus vaccine (non-gsk) (RotaTeq) for prophylaxis.

Subject's medical condition showed nothing suspicious, no basic disease.
No concomitant medication.

On 6 October 2009 at about 11:00 am the subject received 1st dose of Infanrix hexa (intramuscular), 1st dose of Synflorix (intramuscular), 2nd dose of RotaTeq (oral).

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) 1) Infanrix hexa Injection A21CA561A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 06Oct2009-06Oct2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) 2) Synflorix Injection ASPNA007AG (Pneumoc.polysac S.Type 1 + Pneumoc.polysac S.Type 4 + Pneumoc.polysac S.Type 5 + Pneumoc.polysac S.Type 6B + Pneumoc.polysac S.Type 7F + Pneumoc.polysac S.Type 9V + Pneumoc.polysac S.Type 14 +

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 06Oct2009-06Oct2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

B0598135A AT2009/00162

24c. DATE RECEIVED: 29JUN2010

DATE OF REPORT: 29JUN2010

24d. REPORT SOURCE: [ ] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

CONFIDENTIAL

INTERNATIONAL EVENT REPORT

DESK COPY (Page 2 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Austria		2 M	F	06Oct2009

7. & 13. DESCRIBE EVENT(S)

On 6 October 2009, 12 hours at around 23:00 pm after vaccination with Infanrix hexa, RotaTeq and Synflorix, the subject experienced sudden unexpected death in infancy. The child was reanimated in hospital unsuccessfully.

The subject died on 6 October 2009, cause of death was not reported.

Follow up received on 19 October 2009 from the physician, head of the national vaccination board, not the treating physician: Results of the autopsy included cerebral swelling, congestion-hemorrhage; both might be leaded back to the reanimation for half an hour. The subject was found in abdominal position, therefore the physician supposed a sudden infant death syndrome. The virological investigation did not show anything relevant.

Follow up received on 22 October 2009 including the QA statement: A complete review of the batch Synflorix has been performed. No

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- ☐ PATIENT DIED AS OUTCOME OF EVENT
- ☐ RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING
- ☐ CONGENITAL ANOMALY
- ☐ CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- ☐ OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) 3) RotaTeq Lyophilized 0255Y (Rotavirus vaccine Non-GSK) Sanofi Pasteur MSD

15. DAILY/CUMULATIVE DOSE: 2 ml

16. ROUTE OF ADMINISTRATION: Oral

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 06Oct2009-06Oct2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

14. IDENTIFIED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADMINISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☐ N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

B0598135A AT2009/00162

24c. DATE RECEIVED: 29JUN2010

DATE OF REPORT: 29JUN2010

24d. REPORT SOURCE: ☐ HEALTH PROFESSIONAL ☐ STUDY ☐ LITERATURE

25a. REPORT TYPE: ☐ INITIAL ☐ FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

deviation that could be linked to the complaint has been highlighted.

Follow up received on 29 October 2009 from the regulatory authority:
On 12 October 2009 the autopsy was performed, no macroscopic findings detectable at this time.
The child was admitted to hospital under reanimation. Autopsy report was not available at the moment.
Follow up was received from national vaccination board on 30 October 2009 and SIDS was confirmed.

Follow up received on 27 April 2010 (protocol autopsy):
Relevant test performed on 12 October 2009 included parechovirus test which was not detectable in the intestinal fluid, VZV, CMV, HHV6, HHV7, entero virus, parvo virus, norovirus genotype I and II, rotavirus, astrovirus, norwalk like virus, influenza A and B and RSV test, all were negative.

In the follow up received on 29 June 2010 it was mentioned that no further information was received. Therefore this case has been closed.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Adenovirus test	12Oct2009	negative		
Cytomegalovirus test	12Oct2009	negative		
Enterovirus test negative	12Oct2009	negative		
Human herpes virus 6 serology	12Oct2009	negative		
Influenza serology	12Oct2009	negative		
Parvovirus B19 test negative	12Oct2009	negative		
RSV serology	12Oct2009	negative		
Rotavirus test negative	12Oct2009	negative		
Varicella zoster serology nega tive	12Oct2009	negative		

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
PRIVACY	Germany	20Dec2001		F	17Apr2002

7. & 13. DESCRIBE EVENT(S)

Respiratory arrest; Anaphylactic reaction;.
Pyrexia,

A physician reported the occurrence of death possibly due to anaphylaxis in a 4 month old female who was vaccinated with DTPa-HBV-Polio/Hib vaccine (Infanrix Hexa) for prophylaxis.

The pregnancy was normal, but after birth the subject had mild respiratory problems and was hospitalised for three days. There were no severe illnesses since birth. No hereditary diseases were known within the subject's family. The subject's brother, born on 01 January 1999, had epilepsy of unknown cause since the age of two years. The reporting physician also stated, that the grandparents of the subject had several deaths among their children, but no detailed information about this was available.

On 16 April 2002 at 11:00 the subject received the first dose of DTPa-HBV-Polio/Hib vaccine, lot number 21H0027, intramuscularly right gluteal. There was no injection site reaction. In the evening

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [X] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection 21H0027, HIB416A47 (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GSK

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 16Apr2002-16Apr2002

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [X] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [X] N/A

14. IDENTIFIED DRUG(S)

15. DAILY/CUMULATIVE DOSE

16. ROUTE OF ADMINISTRATION

17. INDICATION(S) FOR USE

18. THERAPY DATES (From / To)

19. THERAPY DURATION

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [ ] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [ ] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

(See attached page)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

D0038393A

24c. DATE RECEIVED: 07JAN2010

DATE OF REPORT: 12JAN2010

24d. REPORT SOURCE: [X] HEALTH PROFESSIONAL [ ] STUDY [X] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [X] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

of the same day the subject developed mild fever up to 38.7 degC, which was treated by a paracetamol suppository at 20:30. The subject was fed normally and brought to bed in lateral position. On 17 April 2002 at 8:30 the mother found the subject dead in bed, in prone position. An emergency physician was called but could only testify the subject's death. The cause of death was unknown, but a respiratory arrest was suspected. An autopsy was performed. According to verbal information from forensic medicine via the regulatory authority, the subject died from possible anaphylaxis.

According to information received on 03 June 2002 the reporting physician considered that the possible respiratory arrest was not related to vaccination with Infanrix Hexa, while the forensic physician did not specify the causality of possible anaphylaxis.

The autopsy was performed on 18 April 2002 and received on 03 March 2003 via the regulatory authority (PEI, case number 2680-2002). The possible anaphylaxis was not mentioned in the autopsy report. There was no indication for mechanic force or infection of the airways. The brain was very compact with severe congestion. The physician doing the autopsy suggested that this could possibly be due to hypoxia. The right side of the heart was dilated and the subject had arteria lusoria. There were several local bleedings in the region of the thymus, which was considered to be an indication for sudden infant death syndrome (SIDS). But the arterial vessels were dilated and thin with changes of the wall structure, which the physician could not assign to a concrete syndrome. For this reason he was not able to do a final evaluation. No signs were found for a relationship of the death to vaccination, but the physician also stated that it would probably need special examinations to clarify this. In the cover letter the physician stated that it was not possible to quantify the probability of a causal relationship between the death and the vaccination.

An expert report received on 02 April 2003 stated the following: The autopsy findings and the general causes of cerebral oedema were reviewed with a Belgian opinion leader in Neuropathology. He concluded that the large thymus, with multiple bleedings under the capsule and on the surface of the cut were suggestive for SIDS. He actually identified that the signs for an oedema were very limited in this autopsy report. The presence of cerebral edema could only be suspected based on the decreased volume of the ventricles. The weight of the brain was within normal ranges. It would only be possible to conclude for the presence of oedema when additional histological analyses will be performed. If confirmed, the oedema present would most probably be of the "cytotoxic" type due to hypoxia, which may have many different causes at this age.
Another expert report concluded that the reports did not produce any argument suggesting that the death was due to the vaccine and that the death was not a coincidental event.

After an expert meeting in March 2003 virological PCR test results were received by the regulatory authority. The test showed negative values for Enterovirus, Adenovirus, Influenza A and Parainfluenza in the lung, for Enterovirus, Adenovirus, Influenza A, Parainfluenza and Parvovirus B19 in the heart and for Enterovirus, Adenovirus and Herpes simplex virus in cerebrospinal fluid. A low value for human Herpes virus 6 was found in cerebrospinal fluid, indicating an old but not acute infection.

According to information received from the EMEA on 29 March 2004, the subject was a premature baby with very low birth weight (821 g) and possibly cardiac problems. The EMEA stated that it is not possible to conclude a causal relationship between the death and the immunisation with Infanrix Hexa.

This case was mentioned without any case details in literature in 2009 within a general discussion on hexavalent vaccines and SIDS.

Knuf M., Sutter U. Padiatr. Prax. 2009 74:2 (379-382)

Autopsy on 18 April 2002:
Result:
no indication for mechanic force or infection of the airways
brain very compact with severe congestion, possibly be due to hypoxia
right side of the heart dilated
arteria lusoria
several local bleedings in the region of the thymus
arterial vessels dilated and thin with changes of the wall structure

Virological testing (PCR):
Cerebrospinal fluid (CSF): negative for Enterovirus, Adenovirus and Herpes simplex virus, low value for human Herpes virus 6, indicating an old but not acute infection
Lung: negative for Enterovirus, Adenovirus, Influenza A and Parainfluenza
Heart: negative for Enterovirus, Adenovirus, Influenza A, Parainfluenza and Parvovirus B19

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL

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Body temperature 16Apr2002 38.7degC

MEDICAL CONDITION	START DATE	END DATE	CONTINUING
NEONATAL DISORDER	Unknown	Unknown	No
POSSIBLE CARDIAC DISORDER	Unknown	Unknown	Unknown

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Germany	06Sep2008		M	16Feb2009

7. & 13. DESCRIBE EVENT(S)

Sudden infant death syndrome,

This case was reported by a German regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2009007377) and described the occurrence of sudden infant death syndrome (SIDS) in a 5-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis.

Co-suspect vaccinations included pneumococcal vaccine (non-GSK) (Prevenar, Wyeth).

Previous vaccinations with the first two doses of combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) in combination with the first two doses pneumococcal vaccine (non-GSK) (Prevenar, Wyeth), given on 19 December 2008 and 16 January 2009, have been well tolerated.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [x] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA482A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 13Feb2009-13Feb2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar Injection 34874 (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/CUMULATIVE DOSE: .5 ml

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 13Feb2009-13Feb2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

Infanrix hexa (GlaxoSmithKline) 19Dec2008 - 19Dec2008
(Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax)

Infanrix hexa (GlaxoSmithKline) 16Jan2009 - 16Jan2009
(Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax)

Prevenar (Wyeth Labs) 19Dec2008 - 19Dec2008
(Pneumococcal vac NonGSK)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

D0061280A

24c. DATE RECEIVED: 06APR2010

DATE OF REPORT: 09APR2010

24d. REPORT SOURCE: [ ] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

On 13 February 2009 the subject received the third dose of Infanrix hexa (0.5 ml, intramuscular, right thigh) and the third dose of Prevenar (0.5 ml, intramuscular, left thigh), contralaterally.

Approximately three days post vaccination with Infanrix hexa and Prevenar, on 16 February 2009, the subject dies from sudden infant death syndrome (SIDS). An autopsy was performed. The results of autopsy confirmed SIDS. At the time of reporting the autopsy report was not at hand.

Follow-up information, including a preliminary autopsy protocol, was received on 27 April 2009 from the German regulatory authority (DE-Paul-Ehrlich-Institut).

Autopsy was performed on an unspecified date in 2009. Superficial examination by eye showed no findings. Autopsy showed no external or internal malformations. Internal organs showed no pathologic findings on closer inspection. Thymus gland was very pronounced. Above the anterior cardiac wall the pericardial heart sac showed several punctual haemorrhages. The results of chemical - toxicological examinations were still pending. Considering anamnesis (subject found dead in bed) and assuming negative results of chemical - toxicological examinations the findings were basically consistent with diagnosis of sudden infant death syndrome (SIDS). Final assessment cannot be made until results of all pending examinations have been received. The subject’s body was released for burial.

Follow-up information, including a final autopsy protocol, was received on 06 April 2010 from the German regulatory authority (DE-Paul-Ehrlich-Institut).

Histology of five samples of lung tissue showed mild chronic bronchitis and blood congestion but the lung tissue was otherwise normal. Histology of four samples of heart tissue showed blood congestion but was otherwise age-corresponding with normal heart muscle tissue. Histology of one sample each of brain tissue, liver tissue, renal tissue and spleen tissue were all normal and showed no relevant pathologic changes of the organs.
No bacteriological examinations have been performed because all samples had been fixed in formaline.
Overall histology showed no signs of inflammatory processes and no pathologic changes in tissue samples of the organs which could have caused the death of the subject. Therefore, assuming negative results of chemical and toxicological examinations, no reasons for a refusal of diagnosis of sudden infant death syndrome (SIDS) have been found.

No further information will be available.
CONCOMITANT DRUGS AND DATES OF ADMINISTRATION

Prevenar (Wyeth Labs) 16Jan2009 - 16Jan2009
(Pneumococcal vac NonGSK)

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 3)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Germany	18Nov2008		M	30Apr2009

7. & 13. DESCRIBE EVENT(S)

Cardiac failure acute, Pulmonary oedema, Sudden death, Cardiopulmonary failure, Respiration abnormal, Tachypnoea, Myocarditis, Myocardial infarction, Haemostasis,

This case was reported by a physician and described the occurrence of acute cardiac failure in a 5-month-old male subject who was vaccinated with combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis. Co-suspect vaccination included pneumococcal vaccines (non-gsk) (Prevenar, Wyeth).

On 30 April 2009 the subject received 3rd dose of Infanrix hexa and 3rd dose of Prevenar (unknown route and application site). According to subject's mother, the subject developed breathing not normal since the day of vaccination on 30 April 2009. At examination during doctor visit saturation and pulse were normal. At the time of reporting the outcome of the event was unspecified.

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [x] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [x] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA482A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 30Apr2009-30Apr2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Prevenar Injection 36470 (Pneumococcal vac NonGSK) Wyeth Labs

15. DAILY/CUMULATIVE DOSE: Unknown

16. ROUTE OF ADMINISTRATION: Intramuscular

17. INDICATION(S) FOR USE: PROPHYLAXIS

18. THERAPY DATES (From / To): 30Apr2009-30Apr2009

19. THERAPY DURATION: 1 Days

20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A

21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

D0061486A

24c. DATE RECEIVED: 09AUG2010

DATE OF REPORT: 10AUG2010

24d. REPORT SOURCE: [x] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

Follow-up information was received on 14 May 2009 by the physician.
Previous vaccinations with Infanrix hexa and Prevenar were well tolerated.
Subject’s sibling also died suddenly at the age of 5 months without receiving prior vaccinations.

On 30 April 2009 the subject received 3rd dose of Infanrix hexa (intramuscular, unknown application site left sided) and 3rd dose of Prevenar (intramuscular, right upper thigh).

On 30 April 2009, less than one day after vaccination with Infanrix hexa and Prevenar, the subject died. Reanimation was ineffective.

The physician considered death was possibly related to vaccination with Infanrix hexa and Prevenar.
The subject died on 30 April 2009 from death NOS. An autopsy was performed on 7 May 2009.

Follow-up information was received on 3 June 2009 by the physician.
A targeted follow-up questionnaire was provided but not filled in.
According to the physician it was not a sudden infant death. The subject died in hospital.
Autopsy results were not available for the reporter.

Follow-up information was received on 10 June 2009 by the physician via telephone call.
Subject’s brother showed same symptoms of abnormal breathing on 22 February 2007 after unspecified vaccination on 30 November 2006. The sibling died from cardiomegaly on 24 February 2007 in hospital. The physician did not see a relation to vaccination. Subject’s parents consulted genetic advice, but a cause was not found.

The subject was vaccinated at nine o’clock in the morning at a wide-awake general condition. Three hours after vaccination subject’s mother had a doctor call and came for a doctor visit. There, the subject suffered from breathing not normal (tachypnea). Otherwise the subject was bright and awake.
The subject was hospitalised for security due to anamnesis. At hospital subject’s condition was normal except tachypnea.
Approximately 40 minutes later tachypnea worsened significantly, the subject experienced cardiopulmonal failure and died of an unknown cause.
The physician only considered vaccination as a trigger at an unknown genetic or familiar predisposition.

Follow-up information was received on 22 April 2010 from German regulatory authority Paul-Ehrlich-Institut (# DE-PEI-PEI2009009966).
Following information was provided:
Case narrative including clinical course, therapeutic measures, outcome and additional relevant information:
A 5-month-old male patient was vaccinated with Prevenar, batch-no.: 36470 and with Infanrix hexa, batch-no.: A21CA482 for Prophylactic vaccination. Past medical history were not provided. 8 hours after vaccination the patient presented with Sudden infant death. An autopsy was performed. Further information is requested.
Phone information of the pediatrician on 12.05. 2009:
The baby was vaccinated in the morning in good status of health with Infanrix hexa and Prevenar.
At about 12:oo am the parents presented again in the practice claming that the baby was tachypnoic. The pediatrician found the baby in good staus of health and sent them home.
at 15:00 p.m the parent presented again in the practice and the baby was found a little bit tachypnoic but in good conditions of health.
Due to the fact that the couple had lost another baby boy at the same age due to cardiopolmonary disfuction (probably myocarditis) the physician admitted the baby to a hospital. At 15:30 p.m the baby was found in reduced status of health and tachpnoic.
After 45 min and repeated reanimation intents the baby died.
Intensified diagnostics (post-mortem diagnostics in the hospital) as well as pathological diagnostics have be initiated.

Additional information was received regarding the events, patient’s demographics, dose details, medical history and outcome.
Information regarding Prevenar (pneumococcal 7-valent conjugate vaccine (diphtheria crm197 protein) syringe pre-filled) was received from a healthcare professional regarding a 5-month-old male patient who experienced tachypnoea and who died of sudden death. The patient received the third dose on 30-Apr-2009.
MEDICAL HISTORY:
Past vaccinations included the first two doses of Prevenar (pneumococcal 7-valent conjugate vaccine (diphtheria crm197 protein) syringe pre-filled) and Infanrix hexa (diphtheria vaccine/tetanus vaccine/acellular pertussis vaccine/polio virus inactivated/haemophilus influenzae b/hepatitis b vaccine). One of the patient’s siblings died of fulminant cardiomyopathy at the same age. The sibling has received the last

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vaccination 2.5 months prior to date of death.
PRODUCT DETAILS:
Indication for Prevenar was immunisation. Product was administered in right thigh at 9.20 am on 30-Apr-2009. Dose regimen was 1 dose 1 time per day (intramuscular).
Additional suspect medication included Infanrix hexa (diphtheria vaccine/tetanus vaccine/acellular pertussis vaccine/polio virus inactivated/haemophilus influenzae b/hepatitis b vaccine) which was administered in left thigh on the same time.
CONCOMITANT THERAPY:
Concomitant medications were not reported.
EVENT DETAILS:
After vaccination the parents went twice to the doctor with the patient on the same morning. The patient experienced mild tachypnoea (tachypnoea). The patient was clinically without severe findings. The second visit to the doctor was approximately three hours after the vaccination and during the visit the doctor decided to hospitalize the patient due to the death of the patient’s sibling. Therefore the patient’s parents took the patient to hospital for monitoring. The way to hospital was without any complications but on arrival at hospital the patient’s condition impaired and the patient received permanent drop infusion for example. 40 minutes after the arrival at hospital the patient’s condition got really worse so that reanimation was performed but without success. The patient died of sudden death on 30-Apr-2009. An autopsy was performed but at the time of report the result was unknown.
The reporting physician’s assessment of relatedness between the adverse events and Prevenar and Infanrix hexa was possible related.
The cause of death was reported as sudden death.
No additional information was available at the time of this report.

Follow-up information was received on 28 July 2009 by the prosecutors’ office:
The cause of death and manner of death were unknown at the date of the autopsy result.
Further results of histological and toxicological examinations are requested.

Follow- up information was received from prosecution on 20 April 2010:
The results of histological and toxicological examinations were not yet available at the date of this report.

Follow-up information was received on 9 August 2010 from regulatory authority.
Results of histological and toxicological examinations included significant findings like heart cell necrosis, lymphocytic myocarditis, and haemorrhagic pulmonary edema as well as acute blood congestion in spleen, liver, adrenal glands and kidneys. Indications of active ingredients were found (probable substances which were administered during emergency treatment at intensive care unit. Cause of death was cardiac failure left side and pulmonary edema cardiac cause.

No further information will be available.

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INTERNATIONAL EVENT REPORT

DESK COPY (Page 1 of 2)

I. EVENT INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH	2a. AGE	3. SEX	4. - 6. EVENT ONSET
Unknown	Germany	31May2009		M	18Aug2009

7. & 13. DESCRIBE EVENT(S)

Respiratory tract inflammation, Pneumonitis, Myocarditis, Bacterial tracheitis,.
Pyrexia,

This case was reported by a German regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2009018995) and described the occurrence of severe infection of respiratory tract in a 12-week-old male subject who was vaccinated with 10 valent pneumococcal conjugate vaccine (Synflorix, GlaxoSmithKline) and combined diphtheria, tetanus-acellular pertussis, hepatitis B, inactivated poliomyelitis and Haemophilus influenzae type b vaccine (Infanrix hexa, GlaxoSmithKline) for prophylaxis.
Initially suspected sudden infant death syndrome (SIDS) was not confirmed.

Up to now the subject has been healthy.

On 17 August 2009 the subject received the first dose of Synflorix (0.5 ml, unknown, right thigh) and the first dose of Infanrix hexa

(See attached page)

8. - 12. CHECK ALL APPROPRIATE TO EVENT

- [x] PATIENT DIED AS OUTCOME OF EVENT
- [ ] RESULTED IN OR PROLONGED INPATIENT HOSPITALISATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] CONGENITAL ANOMALY
- [ ] CLINICALLY SIGNIFICANT / REQUIRED INTERVENTION
- [ ] OTHER

II. DRUG INFORMATION

14. IDENTIFIED DRUG(S) Synflorix Injection ASPNA007AE (Pneumoc.polysac S.Type 1 + Pneumoc.polysac S.Type 4 + Pneumoc.polysac S.Type 5 + Pneumoc.polysac S.Type 6B + Pneumoc.polysac S.Type 7F + Pneumoc.polysac S.Type 9V + Pneumoc.polysac S.Type 14 +

15. DAILY/CUMULATIVE DOSE: .5 ml
16. ROUTE OF ADMINISTRATION: Unknown
17. INDICATION(S) FOR USE: PROPHYLAXIS
18. THERAPY DATES (From / To): 17Aug2009-17Aug2009
19. THERAPY DURATION: 1 Days
20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A
21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

14. IDENTIFIED DRUG(S) Infanrix hexa Injection A21CA596A (Hepatitis B vaccine + Polio.vaccine inactivated + Tetanus vaccine + Diphtheria toxoid + Haemophilus influenzae ty + Acellular pertussis vax) GlaxoSmithKline

15. DAILY/CUMULATIVE DOSE: .5 ml
16. ROUTE OF ADMINISTRATION: Unknown
17. INDICATION(S) FOR USE: PROPHYLAXIS
18. THERAPY DATES (From / To): 17Aug2009-17Aug2009
19. THERAPY DURATION: 1 Days
20. DID EVENT ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [x] N/A
21. DID EVENT REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [x] N/A

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event)

23. OTHER RELEVANT HISTORY

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

GlaxoSmithKline

Rue De L'Institut 89,
Rixensart, B-1330, Belgium

D0062778A

24c. DATE RECEIVED: 15JAN2010
DATE OF REPORT: 22JAN2010

24d. REPORT SOURCE: [ ] HEALTH PROFESSIONAL [ ] STUDY [ ] LITERATURE

25a. REPORT TYPE: [ ] INITIAL [x] FOLLOW-UP

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7. & 13. DESCRIBE EVENT(S)

(0.5 ml, unknown, left thigh), contralaterally.

Less than one week post vaccination with Synflorix and Infanrix hexa, on an unknown date in August 2009, the subject experienced fever. Fever was resolved after one day.

Approximately seven days post vaccination with Synflorix and Infanrix hexa, on 24 August 2009 at around 18:00, the subject died from possible sudden infant death syndrome (SIDS).

An autopsy has been applied for. At the time of reporting, on 25 August 2009, autopsy was performed.

Follow-up information including autopsy report was received on 14 December 2009 from the German regulatory authority (DE-Paul-Ehrlich-Institut # DE-PEI-PEI2009018995).

Medical history included normal course of pregnancy and regular visits of a paediatrician for child health checks.

On 17 August 2009 the subject was vaccinated with Synflorix and Infanrix hexa.

On the next day, on 18 August 2009, the subject experienced mild fever.

The subject died on 24 August 2009 at around 18:30 at home. The nearly 3-month-old male subject was found dead on 24 August 2009 at around 19:00 by the subject’s mother.

An autopsy was performed on 27 August 2009 at 08:30. The autopsy report was dated 17 November 2009.

Macroscopically autopsy showed normal general and nutritional condition, no signs of malformations, bloody foam in respiratory tract, bloody wet lung, no signs of punctual hemorrhage at serous membranes, and no signs of mechanical external force.
Microbiological examinations showed no bacteria in cerebrospinal fluid (CSF) and in blood from heart, Staphylococcus aureus and Escherichia coli in pulmonary swab, as well as Staphylococcus aureus, Moraxella catarrhalis and Escherichia coli in pharyngeal swab.
Histology showed mucous-hemorrhagic inflammation of respiratory tract with mixed cell infiltration of mucous membrane of respiratory tract, in parts acute bloating of lung tissues next to areas with underventilation, activation of bronchus associated lymphatic tissue, acute blood congestion in lungs, focal inflammatory pulmonary infiltrations, in parts with multinuclear giant cells; a singular round-cell infiltration in heart muscle, so called tubular heart muscle change; acute blood congestion in the liver.

Autopsy, as well as subsequent microbiological and histological examinations, showed severe infection of respiratory tract and to a lesser extent of lungs above all with bacteria of the species Staphylococcus aureus. Furthermore, histology showed a single inflammatory focus in the heart muscle. With reservation of outstanding results of chemical-toxicological examinations the findings were consistent with death within the scope of inflammation of respiratory tract with involvement of the lungs and accompanying myocarditis. No signs of external mechanical force have been found, but killing with low evidence, e. g. soft covering of mouth and nose, cannot be excluded.
The subject’s body was released for funeral.

Follow-up information was received on 15 January 2009 from the German regulatory authority (DE-Paul-Ehrlich-Institut).

The case has been reassessed. Initially suspected sudden infant death syndrome (SIDS) was excluded by autopsy and therefore has been deleted as adverse event.

No further information will be available.

LABORATORY TEST NAME	TEST DATE	TEST RESULT	LOW NORMAL	HIGH NORMAL
Head circumference	24Aug2009	41cm		