In February 2009, a spike in influenza cases was detected in hospitals around Mexico City. Mexican government officials scrambled to estimate the threat to patients from the US Centers for Disease Control (CDC) and the Canadian National Laboratory in Winnipeg, whose scientists found a new version of the H1N1 influenza virus, named for the type of hemagglutinin and neuraminidase molecules on its surface, which enable it to spread within the body. The discovery of what came to be known as "swine flu"—because pigs were the original source of the virus—aroused enormous concern in public health circles. The 1918 flu pandemic that killed tens of millions of people globally was also caused by an apparently new version of H1N1 influenza. Although other H1N1 viruses had been circulating in US populations for more than thirty years, the Mexican virus looked different and at first seemed to be especially aggressive. Soon the World Health Organization (WHO) began raising the alarm. Two billion people—one third of the global population—could contract the disease, the agency warned, and millions might die. World Bank economists suggested that the total cost of such a pandemic—counting lost business and increased health spending—could reach 4.8 percent of global GDP.2

Panic spread throughout the world. In Mexico schools and offices were closed, flights were canceled, and the country lost $2.2 billion within a few weeks.3 In the UK, the government’s swine flu website received 2,600 hits per second and crashed soon after it went live. In New York so many people panicked over any flu-like symptom that hospital emergency rooms were swamped with ten times more patients than normal, worsening care for those who really needed it.4

In China and other countries, border nurses quarantined anyone with a fever seeking to enter the country. Even direct pig-to-human influenza transmission is exceedingly rare. Egypt ordered the slaughter of all the pigs in Cairo, impoverishing thousands of Christian small-scale farmers. And in Afghanistan, the nation’s only pig was quarantined.5 On June 11, 2009, Margaret Chan, the director-general of the WHO, announced that a “pandemic emergency”—or worldwide epidemic—of H1N1 influenza was officially underway. Governments around the world placed immediate orders for anti-flu drugs and vaccines worth hundreds of millions of dollars, as a new stock index, *RXFLU, was created.6 A new “pandemic emergency declaration,” another scramble for the drug was soon underway, and annual Tamiflu sales surged to $2 billion.7 In Korea, rumors of shortages led HSBC and other powerful banks to compete with hospitals for stocks of the drug.8 Countries in Asia, Africa, and Latin America placed urgent Tamiflu orders from WHO’s stockpile, and some governments even took out loans worth tens of millions of dollars from the World Bank’s Avian and Human Influenza Facility to purchase it.9

The predicted dire emergency did not occur. In the 2009–2010 “influenza season” about 18,000 people died from the disease worldwide, fewer than in previous years, and the vast majority of victims had serious underlying conditions such as cancer, lung disease, AIDS, or severe obesity, which can impair breathing.10 Since one influenza strain usually dominates all others during a typical flu season, H1N1 may actually have saved lives by displacing more aggressive viruses. The WHO maintains that its decisions were based on the best available evidence, but last year European governments, stockpiled with hundreds of millions of euros’ worth of unused medicines and vaccines, began asking questions.11

In March 2010, a Council of Europe report concluded that the H1N1 virus was known to be mild well before the WHO issued the pandemic “declaration” and expressed concern about the influence of powerful pharmaceutical companies over decision-making at the agency. A draft of the WHO’s response was released in March 2011.12 It calls for more “transparency” but concludes that “no critic of WHO has produced any direct evidence of commercial influence on decision-making.” Unfortunately, the response does not account for the billions of dollars lost in the panic or for the lives that may have been put at risk by the agency’s hasty medical recommendations.13

Although influenza deaths are relatively rare among those who aren’t otherwise ill, since the 1950s experts have periodically warned that a 1918-like pandemic could recur. They became especially alarmed in 1997, when eighteen people in Hong Kong contracted a new influenza virus known as H5N1 from chickens, and six died. This “avian flu” virus didn’t spread from person to person, but since it was a thousand times more lethal than ordinary influenza, some experts feared that if it mutated into a virus that could spread more easily, it would kill millions in a very short time.14 In 1999, the WHO launched a program to help governments prepare for this terrifying, if unlikely, possibility. The agency produced a document urging governments to draw up plans to alert the public and set up mass vaccination programs in the event that a new “pandemic” virus was found to be spreading. Because such a virus would have been previously unknown, it would take around six months for sufficient quantities of vaccine to be produced. However, the document also contained an annex describing a new class of anti-influenza drugs known as “neuraminidase inhibitors” that might help control the pandemic.15

According to the annex, these drugs, by blocking the action of the neuraminidase protein, prevent the influenza viruses from spreading through the body, reducing the severity of symptoms. The drugs would also protect people who had been exposed to the disease, such as health care workers and relatives of patients, from becoming sick, or so
Tamiflu. Influenza itself can cause de- lirium and death in severe cases and the vast majority of those who took the drug suffered no ill effect. But when Hayashi read the studies, he realized that the neurological symp- toms differed from those sometimes seen in severe influenza cases; rather, they were more like those associated with overdoses of drugs that suppress the central nervous system, such as Valium.28 In response to Hama’s case reports, the Japanese Ministry of Health, Labor, and Welfare commissioned a research team at Yokohama University to study 2,846 pediatric influenza patients, some of whom had taken Tamiflu. The Yokohama researchers reported that hallucinations and other neuropsychiatric symptoms were no more com- mon among children who had taken the drug than among those who had not. When Hama looked closely at this analysis, he concluded there were a number of errors, most having to do with how the study was designed “mis-classification”—such as cases in which children with hallucinations were clas- sified as not having taken Tamiflu when they actually had. Hama reanalyzed the Yokohama data and estimated that Tamiflu re- sulted in a fourfold increase in the frequency of hallucinations and other neuropsychiatric side effects in chil- dren with influenza.29 A journalist later alerted Hama to the fact that Chugai, the Roche subsidiary that markets Tamiflu in Japan, had provided funds for research to two of the scientists who worked on the Yokohama study. While there is no evidence of wrongdoing, such links may raise the possibil- ity of a conflict of interest.30 Shortly after the WHO “pandemic announcement” in June 2009, Keiji Hayashi, a Japanese pediatrician who was aware of Rokuro Hama’s alarming case studies, decided he wanted more information about the risks and ben- efits of Tamiflu. After all, if the drug really worked, it would be worth pre- scripting to his patients, despite the slight risk of severe side effects. But when Hayashi turned to the scientific literature, he found very few articles on Tamiflu. The research had been funded by Roche. The most important paper, whose main author was Laurent Kaiser, a doctor at the Arabi de Genève, appeared in the Archives of Internal Medicine in 2003.31 This paper, based on a summary of ten studies, concluded that if Tamiflu was used to treat all patients in their first week of illness, it would be 50 percent less likely to need hospitaliza- tions—such as pneumonia—and 50 percent less likely to lead to death. When Kaiser and his colleagues24 drew findings from unpromising data.25 According to the documents submitted to the Japanese Ministry of Health, Labor, and Welfare by Chugai, the Japanese Roche subsidiary, the exact same dose of Tamiflu killed more than half of the animals.39 As they died, the rats exhib- ited many of the same central nervous system symptoms that Hama had de- scribed in his case series on the Japa- nese children.40 The Cochrane group found, moreover, that because of the weird accidents have been fairly com- mon reported in Roche’s post- marketing surveillance of Tamiflu.49 An article in the International Journal of Drug Policy concluded that such symptoms were just as common in in- fluenza patients who did not take Tamiflu.50 However, the data on which that observa- tion is based have not been made public. How common are such discrepancies

**While Kaiser’s finding seemed pow- erful, Hayashi was concerned that the drug’s entire reputation seemed to be based on a very small number of others. He contacted Tom Jefferson, a British influenza expert with the Cochrane Collaboration, a British government-funded network of epidemiologists that conducts inde- pendent reviews of medical research. The Cochrane group had published a favorable review of Tamiflu in 2006, based on the same articles that Hayashi had read.23 When Jefferson and his colleagues read Hayashi’s letter, they too began looking into any studies—such as those of Kaiser’s—that had reported to have been caused by influenza itself, raising the possibility that the patients had been selected for some reason that wasn’t made clear in the article.27 All pharmaceutical drugs are tested by randomly assigning one group of pa- tients (in this case flu sufferers) to take a test drug (in this case Tamiflu) and another to take a placebo that looks the same. It is crucial that neither the patients nor their doctors know who is getting which, because if they did, they might be more inclined—consciously or not—to overrate any improvements in the group receiving the test medicine. But according to documents released in 2009, the Tamiflu trials were conducted, up to and including the main author was Laurent Kaiser, a doctor at the Arabi de Genève, appeared in the Archives of Internal Medicine in 2003. This paper, based on a summary of ten studies, concluded that if Tamiflu was used to treat all patients in their first week of illness, it would be 50 percent less likely to need hospitaliza- tions—such as pneumonia—and 50 percent less likely to lead to death. When Kaiser and his colleagues24 drew findings from unpromising data.25 According to the documents submitted to the Japanese Ministry of Health, Labor, and Welfare by Chugai, the Japanese Roche subsidiary, the exact same dose of Tamiflu killed more than half of the animals.39 As they died, the rats exhib- ited many of the same central nervous system symptoms that Hama had de- scribed in his case series on the Japa- nese children.40 The Cochrane group found, moreover, that because of the weird accidents have been fairly com- mon reported in Roche’s post- marketing surveillance of Tamiflu.49 An article in the International Journal of Drug Policy concluded that such symptoms were just as common in in- fluenza patients who did not take Tamiflu.50 However, the data on which that observa- tion is based have not been made public. How common are such discrepancies
in the published medical literature? Six years ago, John Ioannidis, a professor of epidemiology at the University of Ioannina School of Medicine in Greece, found that nearly all published articles in scientific journals contained findings that were false, in the sense that independent researchers couldn’t replicate them. This bias is particularly widespread in medical research, where peer-reviewed articles in medical journals can be crucial in influencing multimillion-dollar spending decisions. It would be surprising if conflicts of interest did not sometimes compromise editorial neutrality, and in the case of medical research, the sources of bias are obvious. Most medical journals receive half or more of their income from pharmaceutical company advertising and reprint orders, and dozens of others are owned by companies like Wolters Kluwer, a medical publisher that also provides marketing services to the pharmaceutical industry.

Some of the Tamiflu articles were composed by “ghostwriters” associated with Adis, a Wolters Kluwer subsidiary that specializes in producing brochures and professional-looking articles for pharmaceutical company clients. This may help explain why some of the authors of the Tamiflu articles told Jefferson that they didn’t have the original clinical trial data upon which those articles were based: some of them may never have seen it. The Tamiflu ghostwriters told Deborah Cohen, a BMJ reporter, that neither they nor the named authors on the articles had handled the Tamiflu data themselves—they had just been given the tables and figures by Roche officials and instructed to emphasize both the dangers of influenza complications and the benefits of Tamiflu in the articles.

Eventually the Cochrane researchers realized that although there was much interest in the documents Roche had sent them, they were still unable to draw any conclusions about whether or not Tamiflu was safe against influenza complications such as pneumonia. Detailed descriptions of the original methods used in the trials were missing from the files they had received, making it impossible to reconstruct how the research had been planned from the start, and whether that plan had been modified along the way. Nor did the company provide them with any of the detailed case histories of patients who had experienced adverse events in the trials. Throughout 2010 and early 2011, Jefferson and his colleagues wrote to Roche on numerous occasions requesting the missing information. Despite the company’s promise to make “full study reports” available to independent researchers, this request was never granted, so the Cochrane group continued to publish articles that were critical of Tamiflu.

All Roche had to say was that Tamiflu skeptics was to release the information they requested. I began to wonder why Roche didn’t do this, and so I wrote to the company directly in February 2011. A Roche representative replied that Jefferson’s Cochrane group had all the material it needed to do a proper analysis of Tamiflu’s effectiveness. Since I knew from previous discussions with Jefferson and his colleagues that they did not consider this to be true, I tried a different approach. Among the documents the Cochrane group received from Roche was a table of contents listing four or five chapters or “modules” for each of the Kaiser studies. Module 1 was a summary of the trial results. But according to the table of contents, Modules 2 through 5 contained the information Jefferson and his colleagues had been seeking, including the randomization protocol and its modifications, detailed patient histories, and reports of adverse events. But while Roche had sent them Module 1, it had not sent the other modules.

“Do the full study reports containing all five modules exist?” I asked my correspondent at Roche. “A simple ‘yes’ or ‘no’ answer will do.” In reply, she did not say “yes” or “no,” but repeated her claim that the Cochrane group had all the information it needed to analyze the Tamiflu studies.

The many contradictions in the evidence concerning Tamiflu and Relenza raise questions about the WHO’s decision to declare an influenza “pandemic emergency” in 2009 and promote these drugs to fight it. In May 2009, a month before the pandemic declaration was issued, Roy Anderson, a prominent British epidemiologist and adviser to both the WHO and the UK government, gravely warned a BBC radio audience that only Relenza and Tamiflu would prevent a catastrophe on the scale of the 1918 influenza pandemic. At the time, Anderson was receiving £161,000 per year from GlaxoSmithKline, manufacturer of Relenza. Calls for Anderson to resign from the UK government’s Scientific Advisory Group for Emergencies soon followed. A few months later, Anderson, citing a desire to concentrate on research, stepped down from his post as rector of Imperial College London, but he remains an adviser to both the UK government and the WHO.

During the ten years leading up to the pandemic declaration of 2009, scientists associated with the companies that were to profit from the WHO’s pandemic preparedness programs, including Roche and GlaxoSmithKline, were involved at virtually every stage of the development of those programs. The companies funded the documents giving guidance on pandemic preparedness for the influenza pandemic, in which the WHO recommended the stockpiling of Tamiflu and Relenza. Consultants drafted parts of these documents and joined WHO officials in fund-raising for the Tamiflu stockpile. Industry-supported scientists were also on the committee that issued the “pandemic emergency declaration.” That announcement caused developing countries to request assistance from the WHO’s Tamiflu stockpile fund, and these requests contributed to a tripling of that fund’s size in 2009. By declaring a pandemic and linking the response to Tamiflu stockpiling, the WHO could not have done a better job of promoting Roche’s interests. Until Roche shares more information on Tamiflu with independent researchers, we won’t know whether the agency did so at the expense of the rest of us.

Conflicts of interest plague American public health agencies too. One member of the WHO’s Emergency Committee was Nancy Cox, head of the Influenza Division at the US Centers for Disease Control, whose lab receives grants from the International Federation of Pharmaceutical Manufacturers’ Association, of which Roche and GSK are members. I was surprised to learn that a US government agency, which issues policy recommendations to state, federal, and international health authorities, could receive money from an organization supported by industries that stood to profit from those recommendations. A recent CDC guidance document issued by the Influenza Division, listing Cox as director on the first page, ignores the Cochrane group’s concerns, claiming that clinical trials show Tamiflu is effective against severe influenza complications and is not associated with neuropsychiatric side effects.

The FDA also relies increasingly upon fees and other payments from the pharmaceutical companies whose products the agency is supposed to regulate. This could contribute to the growing number of scandals in which the dangers of widely prescribed drugs have been discovered too late. Last year, GlaxoSmithKline’s diabetes drug Avandia was linked to thousands of heart attacks, and earlier in the decade, the company’s antidepressant Paxil was discovered to exacerbate the risk of suicide in young people. Merck’s painkiller Vioxx was also linked to thousands of heart disease deaths. In each case, the scientific literature gave little hint of these dangers. The companies have agreed to pay settlements in class action lawsuits amounting to far less than the profits the drugs earned on the market. These precedents could be creating incentives for reduced vigilance concerning the side effects of prescription drugs in general.

The billions wasted on the H1N1 pandemic by the US government alone exceed the entire $3.2 billion annual budget of the FDA. Strengthening this agency, and creating new laws to ensure its independence from the drug industry, could potentially save our cash-strapped government money, and it could also save lives. Forcing drug companies to make all their original data available to all independent researchers would achieve much the same thing, and cost absolutely nothing. Legislators and the public should demand both of these reforms without delay.

—April 14, 2001
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See, for example, Rokuro Hama, “Fatal Neuropsychiatric Adverse Events in Influenza Patients Treated with Oseltamivir;” British Medical Journal, December 8, 2009.

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See Jefferson et al., “Ensuring Safe and Effective Drugs: Who Can Do What It Takes?”


See Tom Jefferson, Cochrane Acute Respiratory Infections Group, Cochrane Collaboration, Rome, Italy; Mark A. Jones, Queensland Health/University of Queensland, Centre for Health Care Related Infection Surveillance and Prevention/School of Population Health, Brisbane, Australia; Peter Doshi, Program in History, Anthropology, Science, Technology and Society, E51-070, Massachusetts Institute of Technology, Cambridge, Massachusetts; USA; Chris B. Del Mar, Faculty of Health Sciences and Medicine, Bond University, Gold Coast, Australia; Carl J. Heneghan, Department of Primary Health Care, University of Oxford, Oxford, UK; Rokuro Hama, Japan Institute of Pharmacovigilance, Osaka, Japan; Matthew J. Thompson, Department of Primary Health Care, University of Oxford, Oxford, UK.

See Jefferson et al., “Ensuring Safe and Effective Drugs: Who Can Do What It Takes?”


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