In February 2009, a spike in influenza cases was detected in hospitals around Mexico City. Mexican government officials soon emphasized the threat from patients to 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 that 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,1 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 even reach 4.8 percent of global GDP.2

Pandemic 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 though direct pig-to-human 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*, tracked the surge. According to J.P. Morgan, up to $10 billion was spent globally on “influenza preparedness” in 2009, including over $4 billion by the US alone.6

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.7 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, stuck with hundreds of millions of euros’ worth of unused medicines and vaccines, began asking questions.

In March 2010, a Council of Europe report8 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 2011.9 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.

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 H5N1.10 Ten 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.

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.11

According to the annex, these drugs, by blocking the action of the neuraminidase protein, prevent the influenza virus 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 
very vast majority of those who took the 
drug suffered no ill effect. But when 
Hayashi turned to the scientific 
machine, he realized that the neurological 
symptoms differed from those sometimes 
seen in severe influenza cases; rather, 
they seemed to resemble the symptoms 
associated with overdoses of drugs that 
suppress the central nervous system, 
such as Valium.25
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, 
something that Kaiser’s Roche subsid- 
ary had done in Yokohama. The 
Yokohama researchers reported that 
 hallucinations and other neuropsychi- 
atric 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 
what he called “misclassification”—such cases in which 
children with hallucinations were clas- 
sified as not having taken Tamiflu when 
they 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.26 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 funding always raises the possibil- 
it of a conflict of interest.27
Shortly after the WHO “pandemic 
announcement” in June 2009, Keiji 
Hayashi, a Japanese pediatrician who 
was aware of Rokuro Hama’s alarming 
findings, left his job to work on the 
Yokohama study. He became increas- 
ingly aware that even after 
the patient data has been collected, the 
statistical analysis of that data can be 
sensitive to the wishful thinking. For 
example, since most trials are con- 
ducted at several clinics, a statistician 
might select for analysis only those 
clinics, or subgroups of patients, in 
which the drug seems to have worked. 
In fact, it might be the case that the 
statistics might select for analysis only 
those trials showing that the 
test drug had a positive effect, while 
suppressing the findings of the others. 
Moreover, companies even use “data-mining” 
computer programs to extract positive 
findings from unpromising data.28
While Kaiser’s finding seemed pow- 
erful, Hayashi was concerned that 
the drug’s entire reputation seemed 
to hinge on the case of one 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, 
and then updated it with the same articles 
that Hayashi had read.29
When Jefferson and his colleagues 
read Hayashi’s letter, they too began 
scouring the literature. The Cochrane 
group already contained many of the 
same articles that were 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.30
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 override any improvements 
in the group receiving the test medicine. 
Jefferson was in the middle of publish- 
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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 25% of published articles in scientific journals contained findings that were false, in the sense that independent researchers couldn’t replicate them. This problem 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, these conflicts of interest are obvious. Most medical journals receive half or more of their income from pharmaceutical company advertising and reprint orders, and dozens of other papers 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 and effective 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 do to silence these criticisms was point to the FDA report 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