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Influenza Vaccine Shortages and Implications

Updated December 27, 2004

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Summary

On October 5, 2004, Chiron (pronounced Ki'-ron), a California-based biotechnology company, notified U.S. health officials that British regulatory authorities had suspended production of influenza ("flu") vaccine in its plant in Liverpool, England, due to vaccine safety concerns. The plant was slated to provide between 46 million and 48 million doses of flu vaccine for the U.S. market for the imminent 2004-2005 flu season, almost half the expected nationwide supply.

The announcement of Chiron's suspension prompted the Centers for Disease Control and Prevention (CDC) and its Advisory Committee on Immunization Practices (ACIP) to re-define the groups most at risk, to be given priority for the available vaccine doses. CDC coordinated nationwide tracking of available vaccine, high-priority individuals who might need it, and infections signaling the start of the winter flu season. The Food and Drug Administration (FDA) sent a team to the Liverpool plant to determine whether any of the Chiron vaccine lots could be salvaged (they later determined that they could not) and sought additional sources of vaccine from other manufacturers, domestically and abroad. States launched plans to locate and re-distribute or ration vaccine, and responded to reports of price-gouging. The response of local, state, and federal agencies was limited because most of the U.S. flu vaccine market is in private hands.

Several bills were introduced in response to the shortage, and proposals introduced earlier in the 108th Congress, in response to flu vaccine supply problems during the 2003-2004 season, received renewed attention. Two hearings on influenza vaccine were held immediately prior to announcement of the shortage, indicating Congress's ongoing interest in this issue. Additional hearings were held after the shortage was announced. Congress also passed (in P.L. 108-357, the American Jobs Creation Act of 2004) a provision adding flu vaccine to the National Vaccine Injury Compensation Program (VICP), and provided \$100 million in FY2005 funding for influenza preparedness, which could be used to purchase flu vaccine.

The shortage illustrates the challenges that the federal government faces in responding to public health threats. Much of the responsibility for preventing or managing the shortage rests with the states or with the private sector, and the threshold over which the federal government would wrest control from either appears high. As a result, the federal government may appear disorganized or unresponsive. The shortage also raises questions about the role and effectiveness of government in rationing a scarce health resource.

As communities across the country saw long lines of sick and elderly citizens waiting in vain for flu vaccine, and concerns about the supply for the 2005-2006 season emerged as well, policymakers asked why the system to provide this potentially life-saving product was so unreliable, and what could be done about it. Some have expressed concern that this situation bodes ill for preparedness for an influenza pandemic or a large-scale bioterrorism event. This report will describe the system of flu vaccine production and delivery, the causes of supply problems, and options for improvement. It will be updated as circumstances warrant.

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Influenza Vaccine Shortages and Implications

Introduction

The Centers for Disease Control and Prevention (CDC) estimates that influenza (“flu”), a viral respiratory illness, causes 36,000 deaths and more than 200,000 hospitalizations in the United States each year. For many years, vaccination has been urged for those at highest risk of serious illness from flu, such as older persons and those with chronic illnesses. Peculiarities of flu vaccine production, especially its finite shelf life (it is good only for the one season for which it is produced), have led to supply and demand imbalances in recent years. Overall demand for flu vaccine has grown over the past decade. But CDC reports that there have been vaccine surpluses each of the past five winters, and unused vaccine has been discarded. (See **Table 1.**) Within a season, maldistribution of vaccine may lead to shortages at particular times and places, despite an overall surplus. Gauging demand from year to year in what is mostly a private-sector market is a matter of both art and science, an exercise fraught with difficulty.

The shortage of flu vaccine in the fall of 2004 renewed discussion of the fragility of the nation’s system for providing this potentially life-saving product. Some have expressed concern that this situation bodes ill for national preparedness for an influenza pandemic or a large-scale bioterrorism event. This report will describe the current system of flu vaccine production and delivery, the causes of supply problems, and options for improvement.

Flu Vaccine Shortage in the 2004-2005 Season

Government and Corporate Actions

On October 5, 2004, Chiron (pronounced Kī’ron), a California-based biotechnology company, notified U.S. health officials that British regulatory authorities had suspended production of influenza (“flu”) vaccine in its plant in Liverpool, England, due to vaccine safety concerns. The plant was slated to provide between 46 million and 48 million doses of injectable flu vaccine (Fluvirin®) for the U.S. market for the imminent 2004-2005 flu season, almost half the planned nationwide supply of 100 million doses. Aventis-Pasteur (Aventis), a French-based company with a plant in Swiftwater, Pennsylvania, was slated to produce 52 million doses of its injectable flu vaccine (Fluzone®).

After the Chiron suspension was announced, Aventis announced that its production for this season was on target, and could be augmented somewhat to a total

of 58 million doses by continuing production through January 2005. An additional manufacturer, MedImmune, based in Maryland, produces a flu vaccine made of live virus for intra-nasal administration (FluMist,™ also referred to as live attenuated influenza vaccine, or LAIV). MedImmune was slated to produce 2 million doses for the 2004-2005 season after the product was poorly received the prior year. The company announced that it could ramp up production somewhat, but because LAIV is a live virus product, it is not licensed for use in some of the high-risk priority groups identified by CDC. The Defense Department sought to obtain doses of LAIV for its healthy recruits slated for overseas deployment, in order to assure force protection without consuming the limited civilian supply of injectable vaccine.

The announcement of Chiron's suspension prompted CDC and its Advisory Committee on Immunization Practices (ACIP) to re-define the groups most at risk (enumerated in **Table 2**), to be given priority for the available vaccine doses. CDC also activated its Emergency Operations Center to coordinate nationwide tracking of available vaccine doses, high-priority individuals who might need them, and infections signaling the beginning of the winter flu season. Officials from the Department of Health and Human Services (HHS) and CDC repeated in public statements that vaccine doses from Aventis would continue to roll off production lines for several months, and urged those at risk not to stand in long lines because they believed that there will not be future opportunities to be vaccinated. On November 9, 2004, CDC announced an allocation plan to distribute the remaining vaccine doses to state health departments based on states' unmet needs.¹ The allocation plan would apply to Aventis doses that became available each week through December 2004 and January 2005.

In addition, CDC developed clinician recommendations for the use of *antiviral drugs*. These are drugs that can be given before infection occurs as a preventive measure, or during illness to minimize serious complications. HHS estimated that 40 million doses of antiviral drugs would be available, including 7 million doses purchased by HHS to treat low-income individuals, and the remainder within the private sector.

The Food and Drug Administration (FDA) sent a team to the Liverpool plant to determine if any of the affected Chiron vaccine lots could be salvaged, but announced on October 15, 2004 that none of the vaccine was safe for use. The FDA also sought to identify additional sources of vaccine from other manufacturers, domestically and abroad. (Both British and U.S. regulatory agencies are required to assure the safety and efficacy of the Chiron product, for export and import respectively.) On December 7, 2004, HHS announced that the FDA had authorized the use of a GlaxoSmithKline influenza vaccine, Fluarix® (manufactured in Germany), in the United States under an Investigational New Drug (IND) application, and had reached an agreement with the company to purchase 1.2 million doses for distribution to areas

¹ Centers for Disease Control and Prevention, "CDC and States Announce Plan to Distribute 10.3 Million Flu Shots Nationwide; Public Health Officials Call Allocation Fair and Aimed at Most Vulnerable Americans," press release, Nov. 9, 2004.

most in need.² Because the vaccine is not licensed in the United States, the IND allowed it to be used as an investigational drug. Those receiving it would be required to sign a release form noting informed consent for use of the investigational product, and the company would be required to conduct enhanced monitoring of the product's use.

In response to the shortage, the House Committee on Government Reform launched an investigation of the FDA to determine whether it knew or should have known of the impending production failure, as its British counterpart did, since FDA is required to assure the safety and efficacy of this product for importation. The House Committee on Energy and Commerce launched an investigation of the activities of HHS and Chiron leading up to the shortage.

Also following announcement of the Chiron suspension, the Securities and Exchange Commission (SEC) and the Justice Department launched inquiries into whether the company knew of the imminent failure of its annual production before its public announcement. In addition, several class-action stockholder lawsuits were filed against Chiron on the premise that the company had not fulfilled its disclosure obligations.

States responded to the shortage by launching plans to locate and re-distribute or ration doses of vaccine, and by pursuing widespread reports of price-gouging. Some states exercised authority to prohibit administration of vaccine to non-priority individuals. Some localities held lotteries to apportion limited vaccine to those in priority groups. By early December 2004, some states were reporting that all those in priority groups who sought vaccine had received it, and that they had doses remaining. In order to prevent possible wastage of vaccine, CDC sent an update to states on December 8, 2004, suggesting that they consider expanding vaccination recommendations to those outside the priority groups, if circumstances warranted. A number of states that had earlier placed restrictions on providers relaxed them in response.

Shortage to Surplus?

It is not uncommon for there to be a patchwork of vaccine shortages and surpluses at different times and places in the course of a flu season, or for there to be early shortages that resolve into an eventual surplus at seasons' end. The causes of this paradoxical imbalance include the timing and severity of the flu season, (which affect demand), the overall supply for the season, and the supply at times of peak demand.³

In early December 2004, CDC officials were reporting that the influenza season was off to a slow start, and a number of states were reporting a drop-off in demand

² Department of Health and Human Services, "HHS Purchases 1.2 Million Doses of Flu Vaccine," press release, Dec. 7, 2004.

³ A discussion of this problem in the 2000-2001 flu season is found in GAO, *Flu Vaccine: Supply Problems Heighten Need to Ensure Access for High-Risk People*, GAO-01-624, May 15, 2001.

for flu vaccine. In mid-December 2004, the CDC published the results of two surveys. One found that as of November 30, 2004, only about one-third of individuals in high-priority groups had been vaccinated, below the coverage rate for the prior season.⁴ The other survey of demand for vaccine, conducted by the Harvard School of Public Health, found that slightly less than two-thirds of seniors who sought to be vaccinated were successful, and that more than half of high-risk adults did not attempt to be vaccinated, some because they felt they would not be successful.⁵ After the surveys were published, the ACIP reviewed the status of flu vaccine supply and issued revised guidelines for groups that should receive vaccine, essentially restoring its pre-shortage recommendations.⁶ The challenge for public health officials was to maintain demand among unvaccinated high-risk individuals as vaccine continued to be produced each week, while avoiding a surplus at year's end.

Historically, manufacturers, distributors and providers have absorbed the cost of unused vaccine. The cost of additional vaccine in 2004, when it was specifically requested by the U.S. government, would have to be borne by the U.S. government in this special circumstance. Some vaccine policy experts voiced concern about the possibility of a surplus, and discussion ensued about financial responsibility for vaccine doses that had not yet been delivered. A news report suggested that HHS would use federal funds designated for state immunization programs to purchase the investigational flu vaccine doses from Germany, thereby reducing the amounts available to support childhood immunization programs in states.⁷ The CDC Director subsequently confirmed the use of the state account but noted that it could potentially be reimbursed from other accounts. She also noted that FY2005 appropriations had not yet been signed by the President and therefore were not available at the time the purchase was arranged.⁸ In FY2005 appropriations, Congress provided HHS with \$100 million to ensure year-round influenza vaccine production capacity, stating that the Secretary could use the funds for flu vaccine purchase if deemed necessary.⁹

⁴ CDC, "Estimated Influenza Vaccination Coverage Among Adults and Children — United States, September 1–November 30, 2004," *MMWR*, vol. 53, no. 49, Dec. 17, 2004, pp. 1147–1153.

⁵ CDC, "Experiences with Obtaining Influenza Vaccination Among Persons in Priority Groups During a Vaccine Shortage — United States, October–November 2004," *MMWR*, vol. 53, no. 49, Dec. 17, 2004, pp. 1153–1155.

⁶ CDC, "CDC's Advisory Committee on Immunization Practices Expands Priority Groups for Inactivated Influenza Vaccination," press release, Dec. 17, 2004.

⁷ One of the sources of funds for state immunization programs is the CDC Immunization Grant Program, also called "Section 317" for its authorization in the Public Health Service Act. The proposal for use of Section 317 funds is discussed by Gardiner Harris in "Money for Vaccinating Children Is Diverted, Officials Say," *New York Times*, Dec. 16, 2004. More information on the Section 317 program is at [<http://www.cdc.gov/programs/immun04.htm>].

⁸ CDC, remarks of Director Julie L. Gerberding, "Update on Current Influenza Season and Vaccine Supply in the United States," transcript of telebriefing, Dec. 16, 2004.

⁹ The FY2005 Consolidated Appropriations Act, P.L. 108-447, section on Labor, Health and Human Services, and Education, Public Health and Social Services Emergency Fund, *Congressional Record*, Nov. 19, 2004, p. H10324.

Implications for the 2005-2006 Season

The flu vaccine supply for the 2005-2006 season became a matter of serious concern when, in early December 2004, British regulators extended their suspension of Chiron's Liverpool plant through March 2005.¹⁰ While the action was intended to allow more time for Chiron's remediation efforts at the plant, many were concerned that the company might not succeed in its efforts to return as a licensed U.S. supplier for the upcoming season. It was reported that Aventis would be able to expand its production. In addition, HHS launched an unprecedented effort to license the GlaxoSmithKline vaccine in less than one year, with the company saying it could supply 10 to 20 million doses for the U.S. market for 2005-2006. The process typically takes several years. Another manufacturer, ID Biomedical of Canada, sought FDA licensure for its flu vaccine but did not anticipate its availability in the U.S. before 2007.

Scientific and Technical Issues

Annual Strain Selection and Vaccine Production

In general, vaccines, which are regulated as *biologics* by the FDA Center for Biologics Evaluation and Research (CBER), are more tricky to produce than are drugs. Manufacturers must successfully grow the particular virus or other organism of interest while avoiding the growth of other organisms that might contaminate the final product. Several peculiarities of the influenza virus itself and its production process make flu vaccine production especially complicated. There are numerous points at which the process could fail, and has failed in recent years.

The influenza virus changes over time. From year to year, the dominant strains of virus in circulation change, which is why we may get sick every year from flu, in contrast with having lifelong immunity to more stable viruses such as measles. Each year in late winter, the FDA, with input from the National Vaccine Advisory Committee and using surveillance information from the World Health Organization (WHO) and CDC, reviews virus strains in global circulation and selects three that are most likely to cause serious illness in the United States during the subsequent winter season (i.e., one year hence). The chosen strains are incorporated into that next winter's *trivalent* flu vaccine, which typically contains at least one new strain each year. Strain selection may be based on both the dominance and severity of strains in circulation, but may be limited by certain obstacles. For example, an especially virulent strain called *Fujian* was an obvious choice for the 2003-2004 flu vaccine, but it could not be successfully grown in eggs in time to include it in the vaccine. This problem was eventually surmounted, and based on its continuing circulation, the Fujian strain was included in the 2004-2005 flu vaccine.

¹⁰ Chiron Corporation, "[Britain's Medicines and Healthcare Products Regulatory Agency] Notifies Chiron of Continuing Suspension of Liverpool License for Influenza Vaccines; Suspension May Be Lifted If Compliance with License Demonstrated," press release, Dec. 7, 2004, at [<http://www.chiron.com>].

To make large amounts of virus for vaccine production, the virus must be grown in fertilized eggs. Large numbers of fertilized eggs are required each year to support vaccine production. They must be specially produced, assuring the health of the laying hens, appropriate sanitation, care in transport, incubation, and other actions as required by the FDA to assure vaccine safety and efficacy. This endeavor is far more complicated than the production of unfertilized eggs for food. Reliance on eggs and is a rate-limiting step in flu vaccine production, requiring many weeks for growing the virus and extracting it from the eggs, and introducing contamination risks.

Each year the current flu vaccine production system is a race against the clock. Strains must be selected by February in order that they can be grown, purified, processed and made into vaccine. Under optimal conditions vaccine is made in batches from August through November, barely making it to market ahead of the annual influenza epidemic. Breakdowns in the process, especially one occurring in the fall as with the Chiron vaccine, can subvert the entire production volume. It is difficult, if not impossible, to start over within a given season, so as with the Chiron situation, a large-scale process failure can lead to complete loss of the entire season's vaccine production from that supplier.

Opportunities to Streamline Vaccine Production

The flu vaccine production process can be optimized in a number of ways. A promising option is replacement of the cumbersome egg-growth step with *cell culture* methods, in which the virus is grown in tubes or vats of certain cells. With this technique, growth is faster, more controlled, takes up less space, and introduces fewer contamination problems than using eggs. Cell culture techniques could make the annual flu vaccine production cycle less prone to failures and more amenable to re-starting production within a season if problems do arise. In other words, cell culture techniques can provide *surge capacity* within existing infrastructure. This technique is not currently FDA-approved for flu vaccine production, but is in early stages of clinical trials, funded by the National Institutes of Health (NIH). Potential problems must be evaluated, such as the risk of cell components and genes getting into the vaccine or the virus. Also, for existing flu vaccine manufacturers to use this method they would have to renovate existing facilities or construct new ones, and would have to develop consistency in meeting *good manufacturing practices* (GMPs) and other standards if they are to reliably produce vaccine each year.

Flu vaccine production can also be optimized by using *reverse genetics* to produce “vaccine strains,” strains of influenza virus with the right combination of traits to stimulate immunity, and to grow well in eggs. Currently, obtaining strains with the right characteristics for vaccine production is a trial-and-error process; strains are grown together in batches and sampled in a search for those with the desired traits. With reverse genetics, the desired parts of the viral genome are cloned and combined to create the needed traits more quickly and reliably. Reverse genetics is not currently approved for vaccine production, but NIH-funded clinical trials are currently underway using the technique to produce vaccine for the strain of avian influenza (“bird flu”) now circulating in Asia, in the event that it becomes a serious human pathogen. The safety and efficacy of flu vaccine produced using this technique remains to be evaluated. In addition, there are potential consumer

acceptance concerns, especially in Europe, because the vaccine virus produced is a genetically modified organism.

Another opportunity to optimize annual flu vaccine production rests with steady enhancement of global influenza surveillance, which could improve the speed and accuracy of strain selection.

Ultimately, the influenza virus holds two trump cards for which science does not offer solutions on the near horizon. First, there is a limited ability to predict how the virus will modify itself into each year's dominant circulating strains. Once these strains emerge, there is a race against time to produce vaccine while the strains are actually causing illness somewhere on the planet. Second, the regular *drifts* of the viral genome (and the more cataclysmic *shifts* that define a pandemic) are inherent in its genes, and the resulting evasion of the human immune response is inherent in our genes. This relationship has existed for eons, and no near-term scientific breakthrough is likely to change it. Those seeking to prevent influenza infection are stuck with the prospect of annual flu vaccines for the foreseeable future.

Legal and Policy Issues

Overview

The flu vaccine shortage announced on October 5, 2004, unfolded within a complex interaction of government and private sector actions, leading many to question whether the federal government's authority is adequate to prevent these types of crises. States and the federal government have different roles and authorities with respect to this event. In general, public health authority rests with the states as an exercise of their police powers. As a result, states took the lead in restricting vaccine distribution to high-risk individuals and in prosecuting price-gouging. The federal government, under the *Commerce Clause* in the Constitution, may regulate the safety and efficacy of vaccines in commerce in the United States, but this authority does not extend to controlling the distribution or administration of the product. In a public health emergency, the Public Health Service Act grants the Secretary of HHS broad authority to take such actions as necessary to control infectious diseases. Traditionally, the federal government has supported states in exercising their public health authorities rather than subsuming them. HHS Secretary Tommy G. Thompson said that he did not intend to declare the flu vaccine shortage a public health emergency.¹¹

Flu vaccination is a medical procedure, and many people voluntarily choose to be vaccinated in settings that are primarily non-governmental, such as a physician's office, a workplace, or a local grocery store. While federal, state and local governments do not control these activities directly, they play an important role in studying the use and impacts of flu vaccination, making recommendations and providing guidance on the use of flu vaccine, and educating providers and the public

¹¹ U.S. Department of Health and Human Services, "Flu Vaccines and Antivirals," transcript of news conference, Oct. 19, 2004.

about their findings and recommendations. Examples of relevant public health research include studying the effectiveness of vaccination in preventing illness in different risk groups, and the economic impacts of vaccination such as reduced absenteeism in the workplace. Government-supported education efforts include educational materials for providers outlining the use of different types of flu vaccines in specific populations, and flyers and public service announcements encouraging vaccination.

Federal policies and recommendations also drive private-sector flu vaccine demand. This is discussed further in an upcoming section on “Determining Annual Flu Vaccine Production.”

Government Responsibility for Vaccines

Most federal activities related to flu vaccine are conducted by HHS. The National Vaccine Program Office in HHS serves to coordinate vaccine-related activities in several agencies, and is the hub for federal pandemic influenza preparedness activities. The FDA is responsible for assuring the safety and efficacy of vaccines.¹² The NIH conducts intramural vaccine research and development and funds research in universities. The Health Resources and Services Administration (HRSA) administers the National Vaccine Injury Compensation Program (VICP), which provides compensation for injuries judged to have been caused by certain listed vaccines. The CDC houses the National Immunization Program, which coordinates research projects, state grant programs (including funding for purchase of vaccines), and other immunization activities and supports the Advisory Committee on Immunization Practices (ACIP). CDC also administers the Vaccines for Children (VFC) program, authorized in Medicaid law to provide immunizations for children who are uninsured, Medicaid recipients, Native Americans, and Alaska Natives at physicians’ offices and Federally Qualified Health Centers.

Vaccine responsibilities lie outside of HHS as well. The Department of Defense (DOD) maintains research and development programs for vaccines against both naturally occurring infectious diseases and bioweapons agents. DOD administers routine and deployment-related vaccines to military personnel and some civilian employees and contractors. As a primary healthcare provider, DOD also administers vaccines to its retirees and to current personnel and their families. The Department of Veterans Affairs administers vaccines to veterans within its healthcare system.

Veterinary biologics are regulated by the U.S. Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS), under authority of the Virus, Serum and Toxin Act. These products must meet similar standards of safety, efficacy, purity, and potency as do human products. APHIS currently licenses influenza vaccines for horses and swine.

¹² 21 CFR Parts 600-680 describe regulatory requirements for biologics products. Additional requirements for new drug application, the conduct of clinical trials, good manufacturing practices, and other considerations are found in other parts of 21CFR.

State and local governments carry out relevant activities within their public health authority, such as conducting vaccine clinics, maintaining immunization registries, and establishing immunization requirements for school attendance. (These requirements apply to vaccine-preventable childhood diseases such as measles and whooping cough, but not influenza at this time.) In response to the current flu vaccine shortage, many states have taken action to prohibit administration of vaccine to non-priority individuals and to track available vaccine, among other activities.

For more information on the production, safety and availability of all types of vaccines, see CRS Report RL31793, *Vaccine Policy Issues for the 108th Congress*, by Susan Thaul.

Determining Annual Flu Vaccine Production

Based on historical demand and on the new pediatric recommendation from the ACIP, the two manufacturers licensed for the 2004-2005 season, Aventis and Chiron, planned to make around 100 million doses, about evenly split between them. The failure of all annual production by Chiron cut the supply in half. Gauging demand from year to year in what is mostly a private-sector market is a matter of both art and science, an exercise fraught with difficulty.

In the winter of 2003-2004 Americans received 83 million doses of flu vaccine; 87 million were produced. According to the CDC, doses of unused flu vaccine have remained in each of the last five seasons. (See **Table 1.**) Vaccine manufacturers bear the loss from surpluses, and they attempt to carefully gauge demand each year to avoid these losses. Demand has grown in the past ten years, though, as a result of growing ranks of high-risk groups such as the elderly, increasing use of vaccine by other high-risk groups, and growing interest from low-risk groups, such as employers seeking to decrease absenteeism by offering the vaccine to workers at no cost.

Table 1. Surplus Flu Vaccine, 1999-2003
(doses in millions)

	1999-2000	2000-2001	2001-2002	2002-2003	2003-2004
Doses produced	77.2	77.9	87.7	95.0	86.9
Doses used	76.8	70.4	77.7	83.0	83.1
Surplus	0.4	7.5	10.0	12.0	3.8 ^a

Source: Communication from CDC, Oct. 20, 2004.

Note: Target production for the 2004-2005 season was approximately 100 million doses.

a. Most of this surplus was live attenuated (intra-nasal) influenza vaccine.

Flu vaccine demand is also driven by federal policies and recommendations. In the spring of 2004, for the upcoming flu season, the Advisory Committee on Immunization Practices (ACIP) added healthy young children aged 6 to 23 months to the list of groups that should receive the vaccine. To encourage beneficiaries to be vaccinated, Medicare began covering the full cost of flu vaccine and administration

in 1993. The *Healthy People 2010* project, a public-private national goal-setting agenda for health, set a goal of 90% for influenza vaccine coverage for certain high-risk groups. Recently there has been greater emphasis on the prevention of influenza in institutionalized populations. In 2000 CDC published guidance encouraging *standing orders* programs to increase flu vaccination coverage in long-term care facilities and other settings. These programs give nurses “standing orders” to administer annual flu vaccines to residents without a physician’s explicit authorization. To support this recommendation, in 2002 the Centers for Medicare and Medicaid Services (CMS) removed the physician signature requirement for flu vaccine for Medicare and Medicaid participating hospitals, long-term care facilities, and home health agencies. The ACIP also recommends that healthcare workers receive flu vaccine, following studies showing that vaccination of workers reduces mortality in elderly residents in long-term care facilities.

Flu Vaccine Distribution

The path of flu vaccine from assembly line to injection is complex and largely outside of government control. Manufacturers sell the product to distributors, or may also sell it directly to pharmacy chains, health maintenance organizations, hospitals, state health departments, and others. Vaccine may be transferred through multiple distributors along the way.

The CDC, as a purchaser, would have access to distribution information for the product it has purchased even if the product does not physically pass through CDC’s direct control. But almost 90% of the product is circulated outside of government control, and has not been tracked. The Government Accountability Office (GAO) has noted the lack of a means to redirect flu vaccine during a shortage, a system that would depend on centralized tracking.¹³ In the face of the 2004 shortage, HHS Secretary Thompson announced that CDC had set up a secure website for state health officials to use to identify available vaccine in their jurisdictions. Aventis and many of its downstream distributors provided information for the site, information which the Secretary stressed was proprietary and which state health officials must protect as such. This marked the first time such a system was used to track flu vaccine. Also, when the shortage was announced the FDA waived its prohibition against the transfer of vaccine among hospitals and other healthcare entities, to facilitate their own reallocation efforts. These downstream reallocations, while clearly helpful under the circumstances, might not have been captured in the new CDC tracking system.

Re-Prioritizing Groups in Response to the Shortage

In the afternoon of October 5, 2004, the day Chiron advised U.S. officials of its failed production for 2004-2005, CDC and the ACIP issued interim vaccine recommendations, designating “priority groups” for vaccine coverage following the shortage. The groups previously recommended to receive vaccine and the narrowed recommendations announced after the shortage are listed in **Table 2**. CDC

¹³ Government Accountability Office, GAO-04-1100T, *Infectious Disease Preparedness: Federal Challenges in Responding to Influenza Outbreaks*, testimony, Sept. 28, 2004.

subsequently estimated that the pre-shortage target population of roughly 185 million people (about 2/3 of the population) would be reduced to about 98 million priority recipients. Based on historical vaccine usage by these groups (which ranges from 12.4% for pregnant women to 66.2% for those over age 64), CDC estimated that only about 43 million doses would be needed to vaccinate those in priority groups.¹⁴ CDC acknowledged that some vaccine was administered to non-priority groups before the shortage was announced, and that despite best efforts, reallocation of remaining vaccine to priority groups would be imperfect.

On December 17, 2004, CDC announced that the ACIP had reviewed the current status of flu vaccine demand, and issued revised guidelines, essentially restoring the pre-shortage recommendation that individuals aged 50-64 and out-of-home caregivers and household contacts of persons in high-risk groups be vaccinated. The ACIP suggested that health departments and health care providers consider delaying the implementation of the expanded recommendations until January 3, 2005, to provide more time for unvaccinated persons in high-priority groups to seek vaccination.¹⁵

It is worth noting that the expansion of federal recommendations over time, and the growing recognition of the health benefits of flu vaccination even in healthy individuals, drives demand and serves as a market incentive to increase supply. In the face of a severe shortage, public and private actions to encourage flu vaccination in lower-risk groups have had to be abandoned for the 2004-2005 flu season.

¹⁴ Centers for Disease Control and Prevention, *Interim Estimates of Populations Targeted for Influenza Vaccination*, fact sheet, Oct. 11, 2004.

¹⁵ Centers for Disease Control and Prevention, "CDC's Advisory Committee on Immunization Practices Expands Priority Groups for Inactivated Influenza Vaccination," press release, Dec. 17, 2004.

Table 2. Federal Recommendations for Flu Vaccine, Before and After the Vaccine Shortage

Group	Pre-shortage recommendation	Post-shortage recommendation
Children	All children aged 6-23 months, or older than 23 months with other risk factor	All children aged 6-23 months, or older than 23 months with other risk factor
Children and adolescents on aspirin therapy	All such persons	All such persons
Pregnant women	All women who will be pregnant during the flu season	All women who will be pregnant during the flu season
Adults and children aged 2-64 years with certain chronic conditions, including cardiovascular or respiratory conditions such as asthma	All such persons	All such persons
Persons institutionalized in chronic care facilities	All residents of such facilities	All residents of such facilities
Persons aged 50-64 years	All such persons	Only those with other risk factors
Persons aged 65 or older	All such persons	All such persons
Persons who can transmit influenza to those at high risk	All healthcare personnel in all inpatient, outpatient and home-care settings, and household contacts of high-risk persons	Healthcare workers involved in direct patient care and out-of-home caregivers and household contacts of children younger than six months

Sources: Pre-shortage recommendations: Prevention and Control of Influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP), MMWR Recommendations and Reports, May 28, 2004.

Post-shortage recommendations: Interim Influenza Vaccination Recommendations, 2004-05 Influenza Season: Guidance from CDC, in coordination with the ACIP, Oct. 5, 2004.

Note: In a typical year, in addition to the high-risk groups noted above, many healthy persons without risk factors would also seek and receive vaccine.

Vaccine Rationing

Actions During the 2004 Vaccine Shortage. While the federal government has broad authority to take actions necessary to control infectious diseases in an emergency, traditionally the exercise of public health authority in this respect has rested with states. As a consequence, when the flu vaccine shortage was announced and CDC recommended that vaccine be prioritized to certain groups, several states, counties and the District of Columbia issued orders requiring healthcare providers to comply, and established fines for the administration of scarce vaccine to non-priority individuals. Some of the states declared the situation a public health emergency, while others used narrower authorities to support their orders. A number of states and localities relaxed these restrictions beginning in December 2004, when they had vaccine doses remaining after priority individuals were no longer seeking vaccine. A listing of state actions is maintained by the Association of State and Territorial Health Officials (ASTHO) at [<http://www.astho.org>].

While CDC facilitated states' efforts by gathering information about supplies and unmet needs during the shortage, the agency lacks authority to compel manufacturers or distributors to provide this information. CDC reported good voluntary cooperation with the effort, but the GAO has repeatedly noted the absence of a coordinated national system to assure that those most in need receive flu vaccine when supplies are limited.¹⁶ Outgoing HHS Secretary Tommy G. Thompson said shortly after the shortage was announced that he did not intend to declare the situation a public health emergency, and the federal government would not exercise authority to control vaccine distribution or administration.¹⁷

CDC's plan to identify vaccine doses in distribution and coordinate a three-part information exchange — unmet need, available vaccine, and circulating flu virus — had not been done before and may serve as a useful exercise in preparedness for a variety of public health emergencies. Since it was a new effort, its utility in the face of the vaccine shortage has yet to be demonstrated.

Strategies for Rationing. Rationing of scarce resources is not a new concept in health-related services. Prioritization decisions have been made in many health-related areas including, for example, organ donation and dialysis. Not all attempts at rationing have been met with enthusiasm. One notorious example occurred in the 1960s, when a hospital committee attempted to ration life-saving dialysis based on a notion of "social worth."¹⁸ This rationing mechanism led to heavy criticism of the committee, subsequently deemed the "God Committee" for its valuation of some human lives over others.

¹⁶ Government Accountability Office, GAO-04-1100T, *Infectious Disease Preparedness: Federal Challenges in Responding to Influenza Outbreaks*, testimony, Sept. 28, 2004.

¹⁷ U.S. Department of Health and Human Services, "Flu Vaccines and Antivirals," transcript of news conference, Oct. 19, 2004.

¹⁸ Gregory Pence, *Classic Cases in Medical Ethics* (New York: McGraw Hill, Inc., 1995) pp. 297-299.

In the late 1980s, Oregon developed a rationing system for its entire Medicaid program, allocating various types of services rather than distributing one scarce resource. The rationing system was designed to provide coverage to all Oregonians living below the federal poverty line, not just those who met more selective financial eligibility standards, by ranking condition-treatment pairs in order to determine on an annual basis what services would be covered for which ailments. The system was based upon a combination of cost-effectiveness, available funding, and a prioritization of medical services “from most to least important to the entire population.”¹⁹ Oregon’s rationing plan caused some controversy when it was first enacted because it explicitly involved a concept of rationing in providing access to care, and because it created difficulty in determining which services would be covered; however the system is still in place today.

Despite the moral difficulties involved with rationing, allocation of scarce medical resources must still occur when the supply is not sufficient to meet the demand. Allocation decisions can be made with a range of rationing mechanisms, each with its own benefits and drawbacks. Potential mechanisms are discussed below. Not all of these options were considered in response to the 2004 flu vaccine shortage, but a number of them may come into play during an influenza pandemic or large-scale bioterrorism event, when governments will face more dire circumstances. The mechanisms are discussed in the context of vaccine rationing, but may also be applied to the rationing of antivirals or other medications as well.

Most Likely to Suffer Health Consequences. In a selection system that gives a preference to those most likely to suffer health consequences, vaccine is given first to those most likely to catch the flu, suffer serious consequences such as hospitalization, and/or die from infection (e.g., the elderly, young children, pregnant women, and those with suppressed immune systems).

- **Recommended by:** WHO,²⁰ CDC.²¹
- **Benefit(s):** Those most vulnerable to death or serious health effects from flu infection are protected from the virus.
- **Drawback(s):** This selection method does not address impact of epidemic on the continuation of essential services, nor does it focus on how to stop the spread of the flu. This method also fails to address the state’s obligation to those within its control or custody, except to the extent that those in custody are at an increased risk of suffering serious health effects from infection.²²

¹⁹ “The Prioritized List — An Overview,” *Oregon Department of Health Services website* at [<http://www.dhs.state.or.us/healthplan/priorlist/main.html>], visited Dec. 27, 2004.

²⁰ WHO, Department of Communicable Diseases, Surveillance, and Response, “WHO Guidelines on the Use of Vaccines and Antivirals during Influenza Pandemics” (2004), p. 4, at [<http://www.who.int/csr/resources/publications/csrpublications/en/index7.html>].

²¹ CDC, “CDC Guidelines for Large-Scale Influenza Vaccination Clinic Planning 2004-05,” at [<http://www.cdc.gov/flu/professionals/vaccination/pdf/vaxclinicplanning0405.pdf>].

²² “Institutions like prisons are notorious as places where infectious diseases spread.”
(continued...)

Key Personnel. With a preference for key personnel, vaccine is given first to persons whose health is necessary to limit social disruption (e.g., health care workers, government employees and military personnel).

- **Recommended by:** WHO, CDC.
- **Benefit(s):** This method limits social disruption, maintains human infrastructure for essential services.
- **Drawback(s):** A preference for key personnel may favor vaccinating those empowered to make decisions about who is vaccinated, creating an appearance of conflict. The method does not address issues of how to stop the spread of the flu, or the morbidity and mortality rates of flu on various populations. In addition, it does not address the state's obligation to those within its control or custody.

Special Relationships. In a selection system based on special relationships, vaccine is given first to those people whose health care is the responsibility of the state or federal government (e.g., prisoners, and military personnel).

- **Recommended by:** American Civil Liberties Union, for at-risk prisoners.²³
- **Benefit(s):** Governing bodies meet their obligations to protect the health and safety of persons within their sole control.
- **Drawback(s):** Selection based on special relationships does not address issues of contagion, or the morbidity and mortality rates of flu on various populations, except to the extent that those within the state's control are more likely to suffer serious health effects and/or spread the virus. It also does not address impact of epidemic on the continuation of essential services.

Most Likely to Spread Disease. In a selection system based upon those most likely to spread disease, populations known for rapidly transmitting infection are vaccinated first (e.g., children and prisoners).

- **Recommended by:** Some scientific studies.²⁴
- **Benefit(s):** The spread of disease is curbed across the population.

²² (...continued)

Elizabeth Alexander, executive director of the ACLU's Prison Rights Project in Washington, *quoted in* Mark Pitsch, "Few Kentucky Inmates Will Get Flu Shots," *The Courier Journal* (Louisville, KY), Oct. 28, 2004, at [<http://www.courier-journal.com/localnews/2004/10/28ky/A1-prisonflu1028-6253.html>].

²³ Elizabeth Alexander, executive director of the ACLU's Prison Rights Project in Washington, *quoted in* Mark Pitsch, "Few Kentucky Inmates Will Get Flu Shots," *The Courier Journal* (Louisville, KY), Oct. 28, 2004, at [<http://www.courier-journal.com/localnews/2004/10/28ky/A1-prisonflu1028-6253.html>].

²⁴ "A pilot scheme to vaccinate thousands of children in Texas found that when just a quarter of them were given the vaccine it led to a drop of up to 18 per cent in flu cases among unvaccinated adults." "Children, Not the Elderly, Should Get Flu Vaccines," *Independent Newspapers*, Nov. 22, 2004, at [<http://www2.netdoctor.co.uk/news/index.asp?id=116485&D=22&M=11&Y=2004>].

- **Drawback(s):** This selection method does not address impact of epidemic on the continuation of essential services, or state's obligation to those within its control or custody, except to the extent that those in custody are at an increased risk of spreading disease. This method also fails to address the morbidity and mortality rates of flu on various populations.

Lottery. With a lottery system, vaccine is given to people who are selected randomly.

- **Recommended by:** Used in some places in the United States to allocate flu vaccine.²⁵
- **Benefit(s):** The system does not require people to choose any one person or population over others.
- **Drawback(s):** Registration and communication with lottery winners could prove cumbersome. Lottery selection does not address impact of an epidemic on the continuation of social services and infrastructure. This method does not address the state's obligation to those within its control or custody. Lottery selection also fails to address issues of how to stop the spread of the flu, or the morbidity and mortality rates of flu on various populations. (Note: some of these drawbacks could be averted if lottery selection were used in conjunction with other selection criteria.)

First come-first served. With a first come-first served selection system, vaccine is given to those who arrive first at a designated time and place.

- **Recommended by:** Used in some places in the United States to allocate flu vaccine.²⁶
- **Benefit(s):** This method is easy to coordinate, requires only basic advertising, and does not require people to choose any one person or population over others.
- **Drawback(s):** A first come-first served method favors those with flexible schedules, transportation to vaccination site, and does not address impact of epidemic on the continuation of social services and infrastructure. This method does not address the state's obligation to those within its control or custody, issues of contagion, or the morbidity and mortality rates of flu on various populations. (Note: some of these drawbacks could be averted if first come-first served were used in conjunction with other selection criteria.)

²⁵ See, for example, "Portland to Hold Flu Vaccine Lottery," *Kennebec Journal online*, Oct. 21, 2004, at [<http://kennebecjournal.maintoday.com/news/local/1080656.shtml>]; "Flu Vaccine Lottery in One NJ Town," *Eyewitness News 7 Online*, Oct. 19, 2004, at [http://abclocal.go.com/wabc/news/wabc_101804_bloomfieldflushots.html].

²⁶ See, for example, "Lines for Flu Vaccine Clinics Get Longer as Supply Dwindles," *ABC 7 News*, Oct. 13, 2004, at [<http://www.wjla.com/news/stories/1004/180203.html>]; "Imminent Flu Epidemic Lengthens Vaccine Lines," *CNN.com*, Dec. 13, 2003, at [<http://www.cnn.com/2003/HEALTH/12/13/sprj.flu03.flu/>].

Some recent scientific studies suggest that there may be two additional methods of rationing vaccine. The first study indicates that vaccine is more effective in some populations than in others.²⁷ Based upon this finding, vaccine doses could be withheld from those populations in which it is least effective. The problem is that the group in whom the vaccine is least effective is also one that is most likely to suffer health consequences from the flu: the elderly. For this reason, the vaccine's effectiveness in a population is unlikely to be used as a tool for rationing.

The second study indicates that less than a full dose of some types of flu vaccine may create a serum antibody response (indicating that the vaccine may be effective) in healthy individuals.²⁸ This finding could lead to a system of rationing that increases the number vaccine doses by giving certain populations less than a full dose. However, this strategy has not been fully evaluated to test its effectiveness, and it was not implemented during the 2004 vaccine shortage.

One confounding issue is that studies suggest that particular populations, including some minority groups, are less likely to participate in vaccination programs.²⁹ The rationing system of choice might have some mechanisms designed to encourage participation by targeted populations that historically have low rates of vaccination.

When designing a rationing policy, many of the aforementioned rationing methods may be used alone, or in conjunction with one another. For example, priority could be given to both key personnel and those most likely to suffer serious health effects. In addition, if the number of eligible people were larger than the number of available doses, a lottery could be used to determine which of the prioritized people would receive vaccine.

During the 2004 flu season, states and localities employed a variety of rationing methods, many of which were derived from federal guidelines presented in Table 2. The guidelines call for the vaccination of some individuals who are most likely to suffer health consequences (some categories of elderly, sick, and children), as well as some who are most likely to spread the virus (some categories of children, health care workers, and institutionalized persons), and certain key personnel (some categories of health care workers).

²⁷ Sandy Kleffman, "Flu-vaccine Shortage Leaves Seniors at Risk; but Effectiveness Wanes with Age," *Seattle Times*, Nov. 27, 2004, p. A4.

²⁸ See, for example, J. Treanor et al., "Evaluation of a Single Dose of Half Strength Activated Influenza Vaccine in Healthy Adults," *Vaccine* (Jan. 15, 2002) vol. 20, nos. 7-8, p. 1099.

²⁹ See, for example, Victoria Stagg Elliott, "Creativity Needed to Reach Minority Elderly," *AMA News*, Apr. 14, 2003, at [<http://www.ama-assn.org/amednews/2003/04/14/hlsc0414.htm>].

Price Gouging

Media reports of price gouging were widespread following the announcement of the vaccine shortage, with reports that distributors were seeking more than 10 times the original price. The Attorneys General of Connecticut, Florida, Kansas, and Texas responded with lawsuits. In addition, most state attorneys general issued consumer alerts, urging consumers to report price gouging violators. According to a chart compiled by the National Association of Attorneys General, more than half of the states have statutes prohibiting price-gouging, though there are a variety of definitions and triggering events, not all of which would apply to this situation. However, the Association also provided information showing that most if not all states could bring action under broader, more flexible authorities that prohibit “unfair and deceptive acts and practices.”

On October 14, 2004, HHS issued a press release urging states to aggressively prosecute flu vaccine price-gouging.³⁰ State action would require not only the requisite authority, but also the decision to act and the resources to do so. Some in Congress, concerned that states may not always be able to respond effectively, have asked about relevant federal authorities. Neither CDC nor FDA has authority to act in this matter, though CDC (which activated its Emergency Operations Center when the shortage was announced) gathered reports of price-gouging and referred them to state attorneys general. On October 22, 2004, HHS announced that it had filed (along with the Department of Justice) a friend of the court brief in support of Florida’s price-gouging lawsuit against a distributor.³¹ HHS reported that the brief lays out the public health threat posed by price gouging, namely that price gouging leads to allocation of scarce flu vaccine based on who has the most money and not on who has the most need, that it risks the health of Medicare and Medicaid eligible patients, who are vulnerable and most in need of the vaccine, and that it may also lead to violations of the Federal Food, Drug, and Cosmetic Act such as tampering with, and counterfeiting of, flu vaccine.

On October 15, 2004, the House Committee on Government Reform called on the Federal Trade Commission (FTC) to launch a nationwide investigation of flu vaccine price-gouging, and to report on enforcement actions it is taking or plans to take.³² It is not clear under what specific authority the FTC would act, as there is no federal price gouging statute. However, as noted above for states, the Commission could possibly bring an action under its general authority to prohibit unfair or deceptive acts or practices under the Federal Trade Commission Act.

³⁰ Department of Health and Human Services, “HHS Secretary Urges States to Aggressively Prosecute Flu Vaccine Price Gouging” press release, Oct. 14, 2004.

³¹ Department of Health and Human Services, “HHS Files Brief in Support of Florida Price Gouging Lawsuit,” press release, Oct. 22, 2004.

³² House Committee on Government Reform, “Davis and Waxman Ask FTC to Launch Inquiry on Flu Vaccine Price Gouging,” press release, Oct. 15, 2004.

Economic Issues

Overview

Vaccines for the U.S. market are made by private, for-profit firms, and most of the supply is privately controlled. For the 2004-2005 season, CDC purchased 11.4 million doses of flu vaccine, or about 11% of total production. (See **Table 3** for a breakdown of CDC purchases.) The public purchase price ranged from \$6.80 to \$10.00 per dose, depending on the formulation, which is generally lower than private sector prices.

Table 3. CDC Purchases of Flu Vaccine for 2004-2005

Program	Doses from supplier (thousands)		Total
	Aventis	Chiron	
Vaccines for Children (VFC)	4,752	255	5,007
Section 317 (purchases for states)	900	377	1,277
Purchases to stockpile	2,500	2,000	4,500
Purchases using state funds	461	179	640
Total	8,613	2,811	11,424

Source: Communication from CDC on Oct. 10, 2004.

Note: Table reflects purchasing contracts prior to announcement of shortage.

Manufacturers point to a number of disincentives that deter them from the flu vaccine market, such as poor profitability, risk of a production failure, and injury liability.³³ Policymakers point to a number of problems in assuring adequate supply, including too few manufacturers, low vaccination rates among groups who are advised to be vaccinated, unpredictable timing and severity of annual flu seasons, and reluctance of manufacturers to overshoot demand estimates. The 2004 flu vaccine shortage resulted from failure of production by a company that held almost 50% of the market share, because there were only two companies producing injectable flu vaccine for the U.S. market. During the 2001-2002 season, when there were three manufacturers supplying the U.S. market, one sustained significant losses from unused surplus vaccine, which led to its decision to drop out of the market

Many have noted that expanded public purchase of vaccine would have helped this situation only if such purchases had increased overall production by shifting some of the risk of over-production from the manufacturer to the government. Then, if a product were to fail, the other supplier would have produced relatively more and a shortage would not have been as severe. Long term, many feel that it is essential

³³ Christine Gorman, "The Flu Snafu: A Vaccine Shortfall Grows into a Political Headache," *Time*, Nov. 1, 2004.

to have more manufacturers involved, so the consequences of a failure of one would have less impact on supply. But absent a substantial increase in demand, diversification would likely cut into the market for existing manufacturers, potentially reducing their incentives for remaining engaged.

A number of these issues have been discussed in the context of Project BioShield, a program to promote research and development of countermeasures for bioterrorism. In some ways Project BioShield is an imperfect model for flu vaccine shortages, because BioShield is designed to create production incentives for products that lack a commercial market. Nonetheless, there are enough similar issues at play that flu vaccine supply may be added to the agenda in ongoing discussions of the BioShield program. For example, the Project BioShield Act of 2004, P.L. 108-276, contains a provision which allows the Secretary of HHS to temporarily authorize the emergency use of non-licensed drugs and vaccines. Some in Congress called on the Secretary of HHS to exercise this new authority in response to the flu vaccine shortage, by locating available flu vaccine in other countries and making it available to Americans as quickly as possible. As Congress considers follow-on legislation to address remaining concerns, additional issues such as ways to expand vaccine production capacity may also be relevant for flu vaccine.³⁴

The next section will explore several disincentives to flu vaccine manufacture, and several proposals for removing these barriers or otherwise stabilizing the annual flu vaccine market.

Economic Risk

The Problem. It is often suggested that making flu vaccine is not a good business proposition. The product is not highly profitable. Furthermore, production of vaccines is technically difficult, and lot failures resulting from sterility breaks or other causes are not uncommon. Flu vaccine is especially tricky because of the time constraints inherent in using eggs, and because vaccine does not have a shelf life beyond the year it is produced. It is difficult to start from scratch if a problem crops up mid-way in production. If annual demand is overestimated, unused vaccine is discarded at a loss to the manufacturer.

Manufacturers have an obligation to investors to make sound business decisions, and to adhere to standards of transparency in their business conduct. Following Chiron's announcement of its failed flu vaccine production for 2004-2005, the company became the subject of Securities and Exchange Commission (SEC) and Justice Department inquiries, reportedly to determine whether Chiron knew of the

³⁴ For more information, see CRS Report RS21507, *Project BioShield*, by Frank Gottron, and CRS Report RL32549, *Project BioShield: Legislative History and Side-by-Side Comparison of H.R. 2122, S. 15, and S. 1504*, by Frank Gottron and Eric Fischer. The Biological, Chemical, and Radiological Weapons Countermeasures Research Act, S. 666, was introduced in the 108th Congress to address issues remaining after passage of the BioShield Act.

imminent failure of its product before its public announcement.³⁵ Several class-action shareholder lawsuits were filed on the premise that the company had not fulfilled its disclosure obligations.³⁶ In early December 2004, British regulators extended their suspension of Chiron's Liverpool plant through March 2005. The company has tried to balance its obligations to shareholders and its interests in remaining a U.S. supplier, saying that it seeks to produce vaccine for the 2005-2006 season, but not stating with assurance that it could overcome regulatory hurdles by March 2005, when production for the upcoming season would have to begin in earnest. This situation also poses a challenge for CDC as it attempts, in its discussions with other suppliers, to set production targets without knowing Chiron's status with certainty.

Proposals to Mitigate Economic Risk. Some in Congress and others have proposed a number of incentives to vaccine manufacturers to encourage entry into the market and to guarantee demand for vaccine, which would in turn promote diversity of manufacturers and increase annual supply.

Government Buy-Back of Surplus. Under this proposal the federal government would purchase vaccine that remained unused at the end of a season. This would work, in theory, by encouraging manufacturers to produce more than they believed they could sell, thereby providing a cushion if annual supply were to fall short for any reason. However, if manufacturing problems or other supply disruptions did not occur, wastage of unused doses would become a government expense rather than a private one.

In FY2005 appropriations, Congress provided HHS with \$100 million to ensure year-round influenza vaccine production capacity, stating that the Secretary could use the funds for flu vaccine purchase if deemed necessary. Some have considered these funds appropriate for the purchase of any surplus vaccine from the 2004-2005 season, while others have argued that it was intended to back-stop the 2005-2006 season if necessary (though if a surplus resulted in that season, it would occur in FY2006). Still others have argued that the original intent of the funds was to support pandemic influenza preparedness. Neither statutory language nor committee report language clarifies the intended use of these funds.

Government Purchase for Stockpiling. Under this proposal, the federal government would purchase doses of vaccine at the beginning of the season, to serve as a cushion if needed. However, because of its one-season shelf life, flu vaccine is not an attractive candidate for stockpiling. Products such as smallpox vaccine have a long shelf life, and stockpile purchases can be considered one-time expenditures for which a high cost is acceptable. CDC purchased 4.5 million doses of flu vaccine to stockpile for the 2004-2005 season, at a cost of \$40 million. Two and a half million of these doses were produced by Aventis and would be used to ameliorate the shortage, but it was a small amount in the face of a shortfall of 46 million doses. A

³⁵ Paul Elias, "Grand Jury Investigating Chiron's Flu Vaccine Failure," *Associated Press*, Oct. 13, 2004.

³⁶ Bernadette Tansey, "Chiron Shows a Profit: Battered Flu Vaccine Company Circling the Wagons," *San Francisco Chronicle*, Oct. 21, 2004.

federal flu vaccine purchase of sufficient magnitude to cushion a two-supplier market in the event that one failed would be costly, considering that in each of the past five seasons there were surpluses of flu vaccine, and that the 2004 shortage may be the exception. But by expanding annual demand, stockpile purchasing could encourage additional manufacturers to enter the market.

Incentives for Construction of New Facilities. Since the shortage was announced, several vaccine manufacturers expressed interest in entering the flu vaccine market. For new manufacturers to be licensed in the United States, they must apply years in advance for FDA approval, and pay for plant construction or renovation, clinical trials and other regulatory obligations before any profit can be realized. Given the high capital cost for entry into this market, some have proposed offering tax credits or other incentives to offset these costs and encourage new manufacturers to join the U.S. flu vaccine market.

Injury Liability

An Aventis executive, when asked about the impact of injury liability on flu vaccine producers, commented that it is a burden, that it is absorbed as a cost of doing business, and that his company is committed to remaining in the flu vaccine business.³⁷ The chair of an Institute of Medicine (IOM) panel examining vaccine financing testified that when the panel attempted to determine how serious this problem is, as far as its potential deterrent effect on manufacturers and therefore on vaccine availability, the panel had difficulty obtaining pertinent information.³⁸

Vaccine manufacturers have two potential avenues for protection against injury liability claims. They can purchase insurance to cover the costs of defending against or paying out claims, and incorporate costs into the price of vaccine. Also, certain vaccines are covered under the National Vaccine Injury Compensation Program (VICP). Congress added flu vaccine to the VICP list in October 2004, in the American Jobs Creation Act of 2004 (P.L.108-357). Under VICP, an excise tax applied to vaccine sales pays for a public compensation fund. Congress enacted the program in 1986 as a no-fault alternative to the tort system for resolving claims resulting from adverse reactions to mandated childhood vaccines. Individuals of any age alleging injury from any covered vaccine must seek compensation through the program first, though they may decline a proposed award and then seek a remedy in court. The program is administered by the Office of Special Programs in the Health Resources and Services Administration (HRSA).³⁹ HRSA says that the program has been successful in providing compensation to those injured by vaccine-associated adverse events, in reducing liability for vaccine manufacturers and healthcare

³⁷ U.S. Department of Health and Human Services, "Flu Vaccines and Antivirals," transcript of news conference, Oct. 19, 2004.

³⁸ Testimony of Frank Sloan before the Senate Special Aging Committee, hearing on *Liability, Licensing and the Flu Vaccine Market: Making Decisions Today to Prevent a Crisis Tomorrow*, 108th Cong., 2nd sess., Nov. 16, 2004.

³⁹ See HRSA National Vaccine Injury Compensation Program Home Page at [<http://www.hrsa.gov/osp/vicp/INDEX.HTM>].

workers who administer vaccines, and in achieving vaccine market stabilization. Others have reported problems in program administration and performance.⁴⁰

Vaccine Pricing

A number of vaccines in the U.S. market are purchased by federal agencies at prices that are discounted or capped through various mechanisms. Some have argued that this depresses overall prices and contributes to the lack of attractiveness of vaccines as business ventures. Examples of such public purchases include CDC purchases of pediatric vaccines for uninsured children, and purchases by the Veterans Administration for its patient population. HHS notes that the Centers for Medicare & Medicaid Services (CMS) has more than doubled the Medicare payment rates for the flu vaccine, from \$8.92 in 2000 to \$18.30 in 2004.⁴¹ According to HHS, this increase will help assure that beneficiaries can get the vaccine from their physicians' offices, and help cover the costs of vaccine and administration for the providers.

An Institute of Medicine (IOM) panel examining vaccine financing and its effects on availability has recommended a different approach to financing, based on the premise that vaccines confer benefit not just to the individuals who receive them, but to society as a whole.⁴² The panel recommended replacing a government purchase price with a federal subsidy to maintain affordable vaccine coverage for target groups, and mandating that private insurers cover federally-recommended vaccines. The recommendations have not been universally embraced and their implementation has not gone forward, though they have stimulated further discussions of vaccine financing and availability among interested parties.

Implications for Pandemic Preparedness

Influenza circulates around the globe every year, changing slightly each year so that healthy adults have partial immunity to new strains. The virus, its genome in constant flux, typically makes healthy people sick, but not too sick, each year. Now and then, usually several times in a century, the virus changes enough that there is no partial immunity. This event, called an influenza *pandemic*, results in severe illness and death, even in healthy people. The CDC estimates that in the United States, while an annual flu season results in 36,000 deaths, on average, a pandemic could cause more than 200,000. The extent and severity of illness, and the disabling impact on healthy young people, could cause serious disruptions in services and social order.

⁴⁰ See, for example, Stanley A. Plotkin and Walter A. Orenstein, *Vaccines*, 4th ed. (Philadelphia: W.B. Saunders, 2004), chapter 63, pp. 1591 ff.; and Myron Levin, "Vaccine Injures Claims Face Grueling Fight," *Los Angeles Times*, Nov. 29, 2004.

⁴¹ Department of Health and Human Services, "HHS Says Supply of Flu Vaccines, Medicines Will Help Keep People Safe During Coming Flu Season," press release, Oct. 19, 2004.

⁴² Institute of Medicine, *Financing Vaccines in the 21st Century: Assuring Access and Availability*, Aug. 4, 2003, at [<http://www.iom.edu/report.asp?id=14451>].

Some have expressed concern that the 2004 flu vaccine shortage presages problems for a national response to an influenza pandemic. The shortage was in some ways a relevant drill for pandemic preparedness, but in other ways was different. In the face of the shortage, many were concerned with the logistics of finding available vaccine and vaccinating high-risk individuals. Others were concerned about fairness in the way that companies and federal, state and local agencies handled the situation.

Many of these concerns about limited resources and equity in their allocation will be writ large during a flu pandemic. Potentially, a vaccine could not be produced until a pandemic virus strain is actually circulating. For this and other reasons, severe vaccine shortages are expected during an influenza pandemic. The WHO and HHS each have published plans for influenza pandemic preparedness.⁴³ Both stress the role of basic infection control practices and have expanded guidance for handling large numbers of victims, such as expanding capacity for isolation and enacting plans to keep people at home.

The WHO says that with current technology, worldwide production capacity for influenza vaccine would cover only 5% of the world's population. Countries are advised to consider how they would apportion this scarce resource. WHO notes that because healthy individuals may become severely ill, or may even die from infection with a pandemic flu strain, consideration should be given to maintaining essential services by prioritizing vaccine delivery to critical service providers such as healthcare, public health and public safety workers. Americans are accustomed to deferring to those who are most vulnerable in situations where risk of death is low, as they have been asked to do for the current flu vaccine shortage, but a pandemic may require a different message. (See the previous section on "Vaccine Rationing" for further discussion.)

Some in Congress have expressed concern that a portion of the U.S. flu vaccine supply is produced in a foreign facility. The concern is that during a flu pandemic or other emergency, foreign governments may seize vaccines and production facilities within their borders. The International Federation of Pharmaceutical Manufacturers Associations reports that in 2003, more than 95% of the world's flu vaccine was produced in nine countries: Australia, Canada, France, Germany, Italy, Japan, Netherlands, the United Kingdom, and the United States.⁴⁴ The global flu vaccine market is a confusing patchwork of companies and subsidiaries that may be based in one country, producing vaccine in another, and marketing in multiple other countries. Aventis and Chiron are the only companies currently licensed by the FDA to produce injectable flu vaccine for the U.S. market, though other companies have expressed interest in having their products licensed in the future.

⁴³ World Health Organization, "Influenza Pandemic Preparedness Plan: The Role of WHO and Guidelines for National or Regional Planning," Geneva, Switzerland, Apr. 1999; and U.S. Department of Health and Human Services, "Pandemic Influenza Preparedness and Response Plan," Aug. 26, 2004.

⁴⁴ World Health Organization, "Global Distribution of Influenza Vaccines, 2000-2003," *Weekly Epidemiological Record*, vol. 79:(40), pp. 357-368, Oct. 1, 2004.

While both the WHO and HHS plans also stress the use of antiviral drugs during a pandemic, these are likely to be in very short supply as well. A similar problem may arise with access to healthcare facilities and providers. A flu pandemic could result in mass casualty situations, and while these may be isolated in time and place, they may force what is referred to as *degradation of care*, the circumstance in which a standard of care is lowered in the face of overwhelming resource constraints in order to maximize overall survival. Providers are concerned about the ramifications on social order and liability, and have sought federal guidance on this matter.

The 2004 flu vaccine shortage demonstrates the concept of *dual use* in public health preparedness, in which plans, systems and protocols for one event are applicable to others as well. CDC's flu vaccine reallocation plan, which coordinated information about vaccine availability, unmet need, and circulating virus, is a useful model for any number of natural or intentional public health emergencies, including pandemic influenza. In addition, efforts to bolster bioterrorism preparedness have yielded bonuses for pandemic preparedness, such as the development of community mass-vaccination plans. Generally, advancements in the development of vaccines for pandemic influenza will benefit annual flu vaccine production, and vice versa.

The response of the public to government recommendations during the 2004 shortage is illustrative. According to CDC surveys (discussed in an earlier section "Shortage to Surplus?"), persons not in designated priority groups mostly deferred vaccination, while a small number of them reported that they sought vaccination but were unsuccessful. Of particular concern were findings that significant numbers of high-risk individuals did not seek vaccination because they doubted they could get it, and that willingness to be vaccinated dropped off when the vaccine was investigational and required signing a consent form. These findings remind public officials of an important premise for public health preparedness: that imperfect compliance with recommendations is expected and should be taken into account in planning.

Serious questions remain about the exercise of federal authority during an influenza pandemic. Many of these questions were raised in the face of the 2004 flu vaccine shortage. Should the federal government have, or exercise, authority to identify and control doses of scarce flu vaccine? Should the federal government have, or exercise, authority to control administration of vaccine by healthcare providers? Is the current model, which leverages state authorities with federal assistance, adequate for the current shortage, or for pandemic influenza or other public health emergencies? Given that the federal government has overarching emergency authorities but has not used them, will federal officials know how to conduct themselves if such authorities were invoked in an emergency? The flu vaccine shortage presents a small study of these important questions.

Conclusion

It is intuitively appealing to think that federal officials, when faced with a public health emergency, could take charge of information and assets, and assure that remedies and burdens were equitably and efficiently distributed. Actually, the

shortage of flu vaccine illustrates two serious challenges that the federal government faces in a public health emergency. Law and tradition place much of the responsibility for preventing or managing the shortage either with the states, or with the private sector, and the threshold over which the federal government would wrest control from either appears high. The federal government does not dictate the practice of medicine or compel companies to do business. As a result, in situations like this one, free market forces operate, the public health system responds in a decentralized fashion, efforts may seem disorganized, and the federal government may appear unresponsive.

Since the terror attacks of 2001, some barriers have been overcome without substantial changes in the legal landscape. An example is state preparedness planning with uniform guidance, so that states aim for the same targets in planning for mass drug distribution, or in overhauling their emergency public health authorities. Decentralization of public health authority to states is less of a problem if all of them can respond capably and in a consistent fashion. Another example is the government use of proprietary information, such as drug store sales, to conduct surveillance for unusual health events. The flu vaccine shortage has prompted further examination of the coordination of these partners in response to a national challenge, posed another opportunity to explore creative solutions, and offered another chance for lessons learned.

Appendix A. Congressional Action in the 108th Congress

Legislation

Selected legislative proposals aimed at addressing flu vaccine production or shortages are listed. A number of bills were introduced before the 2004-2005 shortage was announced, some in response to flu vaccine problems during the 2003-2004 season. Several proposals would subject flu vaccine to an excise tax, in order to add it to the Vaccine Injury Compensation Program table. A version of this provision was passed in P.L. 108-357, the American Jobs Creation Act of 2004, which was signed by the President on October 22, 2004. Other proposals in authorizing legislation listed below have not been considered in either chamber as of this writing.

H.R. 3758 (Emanuel)

The Flu Protection Act of 2004, to amend the Public Health Service Act to provide for an influenza vaccine awareness campaign, ensure a sufficient influenza vaccine supply, and prepare for an influenza pandemic or epidemic, to amend the Internal Revenue Code of 1986 to encourage vaccine production capacity, and for other purposes.

Introduced February 3, 2004.

Related bill S. 2038.

H.R. 4520 / S. 1637 (Thomas, Grassley)

The American Jobs Creation Act of 2004, includes a provision to add any trivalent influenza vaccine as a taxable vaccine for purposes of the excise tax on certain vaccines.

Became P.L. 108-357 on October 22, 2004.

H.R. 5243 (DeFazio)

The Influenza Vaccine Emergency Act, to amend the Public Health Service Act to provide for emergency distributions of influenza vaccine.

Introduced October 7, 2004.

H.R. 5404 (Kucinich)

The Fair Vaccine Price Act of 2004, to prohibit price-gouging during a shortage of a covered vaccine.

Introduced November 19, 2004.

H.R. 5409 (Lowey)

The Emergency Flu Response Act of 2004, to amend the Public Health Service Act to address the shortage of influenza vaccine, and for other purposes.

Introduced November 19, 2004.

S. 15 (Gregg)

Project BioShield Act of 2004, to amend the Public Health Service Act to provide protections and countermeasures against chemical, radiological, or nuclear agents by giving the National Institutes of Health contracting flexibility, infrastructure

improvements, and expediting the scientific peer review process, and streamlining the Food and Drug Administration approval process of countermeasures. Introduced March 11, 2003.

Became P.L. 108-276 on July 21, 2004.

S. 666 (Lieberman)

The Biological, Chemical, and Radiological Weapons Countermeasures Research Act, to provide incentives to increase research by private sector entities to develop antivirals, antibiotics, vaccines and other products to prevent and treat illnesses associated with a biological, chemical, or radiological weapons attack.

Introduced March 19, 2003.

S. 754 (Frist)

The Improved Vaccine Affordability and Availability Act, to amend the Public Health Service Act to improve immunization rates by increasing the distribution of vaccines (including flu vaccine) and improving and clarifying the vaccine injury compensation program.

Introduced April 1, 2003.

S. 1817 (Santorum)

To amend the Internal Revenue Code of 1986 to include influenza vaccines in the Vaccine Injury Compensation Program.

Introduced November 4, 2003.

S. 1896 (Grassley)

To add to the definition of taxable vaccines any vaccine against hepatitis A and any trivalent vaccine against influenza.

Introduced November 19, 2003.

S. 2038 (Bayh)

The Flu Protection Act of 2004, to amend the Public Health Service Act to provide for an influenza vaccine awareness campaign, ensure a sufficient influenza vaccine supply, and prepare for an influenza pandemic or epidemic, to amend the Internal Revenue Code of 1986 to encourage vaccine production capacity, and for other purposes.

Introduced January 28, 2004.

Related bill H.R. 3758.

S. 2959 (Dayton)

The Influenza Preparation and Vaccination Act, to amend the Public Health Service Act to ensure an adequate supply and distribution of influenza vaccine.

Introduced October 8, 2004.

S. 2968 (Reed)

The Emergency Flu Response Act of 2004, to amend the Public Health Service Act to address the shortage of influenza vaccine, and for other purposes.

Introduced October 8, 2004.

S. 2997 (Inhofe)

The Flu Vaccine Incentive Act of 2004, to amend the Social Security Act to encourage the production of influenza vaccines by eliminating the price cap applicable to the purchase of such vaccines by HHS, to amend the Internal Revenue Code of 1986 to establish a tax credit to encourage vaccine production capacity, and for other purposes.

Introduced November 18, 2004.

H.R. 2660 / S. 1356 (Regula / Specter)

Making appropriations for Labor, Health and Human Services, Education and Related Agencies for FY2004, includes funding for influenza vaccine research and stockpile purchase.

Became Public Law No. 108-199, the Consolidated Appropriations Act, 2004, on January 23, 2004.

H.R. 5006 / S. 2810 (Regula / Specter)

Making appropriations for Labor, Health and Human Services, Education and Related Agencies for FY2005, includes funding for influenza vaccine research and vaccine purchase.

Became Public Law No. 108-447, the FY2005 Consolidated Appropriations Act, on December 8, 2004.

Hearings

House Committee on Energy and Commerce, Subcommittee on Health and Subcommittee on Investigations, joint hearing on *Flu Vaccine: Protecting High-Risk Individuals and Strengthening the Market*, November 18, 2004.

House Committee on Government Reform, full committee hearing on *The Nation's Flu Shot Shortage*, November 17, 2004.

Senate Special Aging Committee, hearing on *Liability, Licensing and the Flu Vaccine Market: Making Decisions Today to Prevent a Crisis Tomorrow*, November 16, 2004.

House Committee on Government Reform, full committee hearing on *The Nation's Flu Shot Shortage*, October 8, 2004.

Senate Committees on the Judiciary and Health, Education, Labor and Pensions, joint hearing on *BioShield Legislation*, October 6, 2004.

House Appropriations Committee, Subcommittee on Labor, Health and Human Services and Education, hearing on *Influenza Vaccine*, October 5, 2004.

Senate Special Aging Committee, hearing on *Influenza and the Elderly*, September 28, 2004.

House Committee on Government Reform, Subcommittee on Human Rights and Wellness, hearing on *Mercury and Autism*, September 8, 2004.

House Appropriations Committee, Subcommittee on Labor, Health and Human Services and Education, hearing on *Global Diseases Programs Appropriations*, April 28, 2004.

House Committee on Government Reform, hearing on *Health System Preparedness to Handle Health Threats*, focused on the 2003-2004 influenza season, February 12, 2004.

Investigations

The House Committee on Energy and Commerce is conducting an investigation into the federal role in the flu vaccine shortage. The Committee Chairman and Ranking Member sent letters to the Chiron Corporation, the Acting FDA Commissioner and the Secretary of HHS, requesting information, on November 18, 2004, available at [http://energycommerce.house.gov/108/News/11182004_1408.htm].

The House Committee on Government Reform is conducting an investigation into FDA's role in the shutdown of the Chiron plant. The Committee Chairman and Ranking Member sent a letter to the Acting FDA Commissioner, requesting information, on October 13, 2004, available at [<http://reform.house.gov/UploadedFiles/101304fdaletterrelease.pdf>].

Appendix B. Information Resources

CRS Products

CRS Report RL31793, *Vaccine Policy Issues for the 108th Congress*, by Susan Thaul.

CRS Report RS21507, *Project BioShield*, by Frank Gottron.

CRS Report RL32549, *Project BioShield: Legislative History and Side-by-Side Comparison of H.R. 2122, S. 15, and S. 1504*, by Frank Gottron and Eric Fischer.

CRS Report RS21747, *Avian Influenza: Multiple Strains Cause Different Effects Worldwide*, by Jim Monke.

CRS Report RL31333, *Federal and State Isolation and Quarantine Authority*, by Angie A. Welborn, (discusses state and federal authority for public health emergencies).

CRS Report RL31719, *An Overview of the U.S. Public Health System in the Context of Bioterrorism*, by Holly Harvey and Sarah Lister.

Government Accountability Office (GAO) Products

GAO-05-177T, *Flu Vaccine: Recent Supply Shortages Underscore Ongoing Challenges*, testimony, November 18, 2004.

GAO-04-1100T, *Infectious Disease Preparedness: Federal Challenges in Responding to Influenza Outbreaks*, testimony, September 28, 2004.

GAO-04-458T, *Public Health Preparedness: Response Capacity Improving, but Much Remains to Be Accomplished*, testimony, February 12, 2004.

GAO-02-987, *Childhood Vaccines: Ensuring an Adequate Supply Poses Continuing Challenges*, report, September 13, 2002.

GAO-01-786T, *Flu Vaccine: Steps Are Needed to Better Prepare for Possible Future Shortages*, testimony, May 30, 2001.

GAO-01-624, *Flu Vaccine: Supply Problems Heighten Need to Ensure Access for High-Risk People*, report, May 15, 2001.

Institute of Medicine (IOM) Reports

IOM, *The Threat of Pandemic Influenza: Are We Ready? A Workshop Summary* November 16, 2004, at [<http://www.iom.edu/report.asp?id=23639>].

IOM, *Immunization Safety Review: Influenza Vaccines and Neurological Complications*, October 6, 2003, at [<http://www.iom.edu/report.asp?id=15625>].

IOM, *Financing Vaccines in the 21st Century: Assuring Access and Availability*, August 4, 2003, at [<http://www.iom.edu/report.asp?id=14451>].

IOM, Board on Health Care Services, *Calling the Shots: Immunization Finance Policies and Practices*, June 16, 2000, at [<http://www.iom.edu/report.asp?id=5508>].

Health and Human Services (HHS) Resources

HHS National Vaccine Program Office Home Page: general information on vaccines, and the Draft Pandemic Influenza Preparedness and Response Plan. [<http://www.hhs.gov/nvpo/>].

Centers for Disease Control and Prevention (CDC) Resources

CDC Influenza Home Page: information for health professionals and the general public, including guidelines related to the current vaccine shortage, [<http://www.cdc.gov/flu/>].

CDC, Prevention and Control of Influenza, Recommendations of the Advisory Committee on Immunization Practices (ACIP), *MMWR Recommendations and Reports*, May 28, 2004, recommendations prior to announcement of the vaccine shortage for 2004-2005.

CDC National Immunization Program Home Page: information about CDC-funded vaccine purchases and related information, [<http://www.cdc.gov/nip/>].

CDC Public Health Law Program Home Page: information on state authorities and actions taken to assure priority distribution of flu vaccine, [<http://www.phppo.cdc.gov/od/phlp/Influenza.asp>].

Food and Drug Administration (FDA) Resources

FDA Center for Biologics Evaluation and Research, Influenza Virus Vaccine 2004-2005 Home Page: information about Chiron, Aventis, and MedImmune vaccine production, [<http://www.fda.gov/cber/flu/flu2004.htm>].

Health Resources and Services Administration (HRSA) Resources

HRSA National Vaccine Injury Compensation Program (VICP) Home Page, [<http://www.hrsa.gov/osp/vicp/INDEX.HTM>].

National Institutes of Health (NIH) Resources

NIH National Institute of Allergy and Infectious Diseases influenza Home Page:
[<http://www.niaid.nih.gov/dmid/influenza/>].

World Health Organization (WHO) Resources

WHO Influenza Home Page at [<http://www.who.int/csr/disease/influenza/en/>].

Other Key Resources

F.A. Sloan et al., “The Fragility of the U.S. Vaccine Supply,” *New England Journal of Medicine*, 351:2443-2447, Dec. 2, 2004.

J. Treanor, “Weathering the Influenza Vaccine Crisis,” *New England Journal of Medicine*, 351:2037-2040, Nov. 11, 2004.

R. Giffin et al., “Childhood Vaccine Finance and Safety Issues,” *Health Affairs*, 23(5): 98-111, Sept./Oct. 2004 (despite the title, a general overview of federal/state/private vaccine financing and distribution issues).

National Vaccine Advisory Committee, “Strengthening the Supply of Routinely Recommended Vaccines in the United States: Recommendations from the National Vaccine Advisory Committee,” *JAMA* 290(23), Dec. 17, 2003, pp. 3122-3128