



CONGRESSIONAL BUDGET OFFICE
U.S. Congress
Washington, DC 20515

Douglas Holtz-Eakin, Director

December 8, 2005; revised July 27, 2006

Honorable William H. Frist, M.D.
Senate Majority Leader
United States Senate
S-230 Capitol
Washington, DC 20515

Dear Senator Frist:

In response to your request, the Congressional Budget Office (CBO) has prepared an assessment of the possible macroeconomic effects of an avian flu pandemic. The assessment concludes that a pandemic involving a highly virulent flu strain (such as the one that caused the pandemic in 1918) could produce a short-run impact on the worldwide economy similar in depth and duration to that of an average postwar recession in the United States. Most of the pandemics of the past involved much milder strains; an outbreak of that kind would have a much smaller economic impact, which might be indistinguishable in the macroeconomic data.

In its assessment, CBO also describes the current state of preparedness for addressing a possible pandemic and options for increasing the nation's preparedness. (However, in accordance with CBO's mandate to provide objective, impartial analysis, this document contains no recommendations.) The billions of dollars spent in recent years preparing for health crises that could arise from possible terrorist attacks would provide some limited benefits in the event of a flu pandemic. Even so, if a pandemic were to occur in the near term, the options for the United States would be limited to attempts to control the spread of the virus and judicious use of limited medical facilities, personnel, and supplies. In the longer term, more tools are potentially available, including an increased treatment capacity, greater use of vaccines and antiviral drug stockpiles, and possible advances in medical technology.

The details of CBO's assessment are in the attachment to this letter. We would be pleased to address any further questions you might have.

Sincerely,

A handwritten signature in dark ink, appearing to read "Douglas Holtz-Eakin".

Douglas Holtz-Eakin

Attachment

cc: Honorable Harry Reid
Minority Leader
United States Senate

Honorable J. Dennis Hastert
Speaker
U.S. House of Representatives

Honorable Nancy Pelosi
Minority Leader
U.S. House of Representatives

A Potential Influenza Pandemic: Possible Macroeconomic Effects and Policy Issues

December 8, 2005; revised July 27, 2006

This revision incorporates corrected estimates of the supply-side impact of a potential pandemic: about 2-1/4 percent in the severe scenario and about 1/2 percent in the mild scenario. The estimated overall impact on gross domestic product is about 4-1/4 percent in the severe scenario and about 1 percent in the mild scenario.

Note

This assessment was written by Robert Arnold, Jeanne De Sa, Tim Gronniger, Allison Percy, and Julie Somers under the supervision of Robert Dennis, Joseph Kile, David Moore, and Robert Sunshine. Outside the Congressional Budget Office (CBO), the following individuals read an early draft and provided technical advice and helpful comments. However, the assistance of external reviewers implies no responsibility for the final product, which rests solely with CBO.

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Introduction and Summary

There is widespread concern among policymakers and public health experts about the possibility of a worldwide epidemic of avian influenza. Such pandemics are not new: there were three in the 20th century, of which one, the 1918–1919 Spanish flu outbreak, is estimated to have killed over 500,000 people in the U.S. and up to 50 million worldwide. Public health concerns arise because of the challenge of creating the public health infrastructure in the United States and other countries that would be adequate to meet the challenges of a severe pandemic.

Although a pandemic could be caused by any of several influenza strains, scientists are particularly worried about H5N1, a strain that has caused repeated epidemics with high mortality among poultry in Asia, has spread from Southeast Asia to flocks in Central Asia and Europe, and has made the jump from birds to humans, causing the deaths of over 60 people. Moreover, viruses of the H5 subtype are not known to have ever circulated among the human population, which means that there would be little immunity to it. To date, close contact with infected poultry is thought to be required for human infection, but the danger exists that the virus will evolve in a way that allows for efficient human-to-human transmission. If the virus does acquire that capability, a worldwide epidemic, or pandemic, could occur. Depending on the virulence of the particular strain of flu, such an outbreak could have substantial consequences for people and economic activity around the world.

Infectious diseases are, however, unpredictable. It is impossible to say for sure whether another pandemic will arise, whether it will involve H5N1, and, if it does, when it will happen or whether it will be mild or severe. The H5N1 virus could mutate in a way that caused a severe pandemic next year or a mild epidemic in a decade or two. Or it could evolve in a way that rendered it harmless, and a pandemic could arise from an entirely different virus subtype.

This paper focuses on the potential for, and possible economic effects of, a pandemic of avian flu—although many of the policy issues that avian flu raises apply also to pandemics of other types of influenza. The paper provides background on the effects of a potential avian flu pandemic, gives very rough estimates of the economic effects of two possible scenarios, and discusses policy options related to the preparedness of the United States for such an outbreak.

Based on an analysis of past pandemics, CBO has devised two scenarios to outline the possible economic effects of a potential avian influenza pandemic. There is a substantial amount of uncertainty associated with these scenarios because there is scant empirical evidence available to inform many of the assumptions that are needed for the calculations underlying the economic effects. The first, and more severe, scenario is roughly similar to the 1918–1919 Spanish flu outbreak. In the severe-pandemic scenario, roughly 90 million people become sick and 2 million people die in the United States, and in CBO's estimation, real GDP would be about 4-1/4 percent lower over the subsequent year than it would have been had the pandemic not taken place. That

estimate of the effect on GDP is comparable to the effect of a typical business-cycle recession in the United States during the period since World War II. In the mild-pandemic scenario, which resembles the 1957 and 1968 pandemics, about 75 million people are infected in the United States and about 100,000 of them die. In that scenario, the pandemic reduces real GDP by a modest amount, about 1 percent relative to what would have happened without a pandemic, but probably would not cause a recession and might not be distinguishable from the normal variation in economic activity.

The Administration and the Congress have proposed to improve preparedness for a potential pandemic. But the uncertainties associated with whether a pandemic flu will occur in the next several months or in the next five years—and if an outbreak does occur, what measures will be effective in reducing its human and economic costs—make finding the best approach a difficult task. Improving the capacity of the health system to care for many people in all parts of the country who are sick at the same time stands out as a priority—but one that the federal government may be less suited to address because of the local delivery of health care services. A promising federal object of attention is support for the efforts of governments of other countries and international organizations to contain avian influenza strains and control their evolution to diseases that are easily transmitted from person to person. Federal policies may also be effective in building stockpiles of vaccines and improving antiviral drugs as well as putting in place new technologies that allow effective vaccines to be produced more rapidly and in large quantities. The challenge for vaccine, drug, and technology policy will be to do enough to provide private producers with incentives to meet national needs without introducing inefficiencies that have sometimes occurred when government is very actively involved in specific decisions about technologies and investments.

Background

Avian influenza (or “bird flu”) is a contagious animal disease that infects birds and some mammals.¹ Scientists believe that all bird species are susceptible to infection but that some are more resistant than others. Wild waterfowl, especially ducks, are a so-called natural reservoir of influenza viruses, including the bird flu. The birds carry the virus without displaying any symptoms of the disease and can spread the virus over great distances while remaining healthy.

Poultry are quite susceptible to avian influenza, which can cause a wide range of symptoms, from mild (reduced egg production) to severe (rapid death). The severe

1. Material for the background section of this paper was drawn from several sources but primarily World Health Organization, *Avian Influenza: Assessing the Pandemic Threat* (Geneva: World Health Organization, January 2005); Howell Pugh, “Pandemic, The Cost of Avian Influenza,” *Contingencies* (September/October 2005), pp. 22-27; and Laurie Garrett, “The Next Pandemic,” *Foreign Affairs* (July/August 2005), pp. 3-23.

form of the disease, which is known as “highly pathogenic avian influenza,” is extremely contagious and has been the source of numerous epidemics among domesticated birds. It is also characterized by very high and rapid mortality, with rates approaching 100 percent and death sometimes occurring on the first day that symptoms appear.

Although frequently deadly for poultry, avian influenza viruses in the past have rarely caused severe disease in humans. However, in 1997, a highly pathogenic strain of bird flu known as H5N1 jumped from birds to humans during an outbreak among poultry in Hong Kong.² The 1997 event was notable for two reasons. First, molecular studies indicated that the genetic makeup of the human and avian viruses were virtually identical, indicating direct transmission from birds to humans.³ Second, the H5N1 virus caused severe illness with extreme mortality among humans: of the 18 persons known to be infected, six died. The outbreak ended after authorities slaughtered Hong Kong’s entire stock of poultry (about 1.5 million birds).

The Hong Kong episode put world health officials on alert because the H5N1 strain had fulfilled two of the three prerequisites for a pandemic. First, the strain was a new virus subtype to which the population would have little or no immunity, and second, the virus had the ability to replicate in humans and cause serious illness. However, the virus still has not developed the ability to be transmitted efficiently from human to human.

The genetic makeup of influenza viruses can change in two different ways. The first type of change, known as antigenic drift, occurs when small errors creep into a virus’s genetic sequence when the virus copies itself. As a result, influenza viruses undergo frequent small changes in structure, or mutations, which allow them to continually find susceptible populations to infect. The second type of change involves a swapping or mixing of genes between two types of virus—such as avian and human forms of influenza—when they are present in the same animal or individual. That change is termed reassortment, or antigenic shift. If either type of genetic change produced an influenza strain with a particular mix of genes—one that caused severe disease and allowed for efficient transmission among humans—it could ignite a pandemic.

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2. Strains of influenza are grouped into subtypes that are identified by the hemagglutinin (HA) and neuraminidase (NA) protein spikes on their surfaces. A population that has been exposed to a strain acquires “herd immunity” when enough individuals have gained immunity to interfere with the transmission of the virus. Of the 15 HA subtypes, H1, H2, and H3 are known to have circulated among humans during the past century. Hence, a virus from the H5 subtype, such as H5N1, would probably be unfamiliar to the immune system of everyone in the world, and there would be no herd immunity.
 3. More commonly, avian influenza’s route from birds to humans involves an infection in a third species, usually thought to be pigs (because they are susceptible to both human and avian influenza), during which genetic material is exchanged.

Since the 1997 episode in Hong Kong, there have been several outbreaks of the H5N1 influenza around the world, leading to tens of millions of infections among poultry and dozens of cases among humans. The first human infection occurred in Hong Kong in February 2003, when a nine-year-old boy and his father became sick after a trip to southern China. The man, who was 33, died, but his son recovered. Then, in 2004, the H5N1 virus spread among poultry populations in Southeast Asia, with outbreaks of influenza reported in two separate waves. The first wave, in January and February, affected Vietnam, Japan, Korea, Thailand, Laos, Cambodia, Indonesia, and China. The second wave, which began in July and continued into 2005, included outbreaks in the same countries and in Malaysia as well. More recently, the virus has shown up in Russia, Kazakhstan, Turkey, and Romania. The scope of the outbreaks is historically unprecedented: a highly pathogenic strain of avian influenza has not been known before to spread so widely and so rapidly.

The number of human cases of the H5N1 virus has also grown. Between January 2004 and August 2005, there were 112 human cases of H5N1 avian flu (in Vietnam, Thailand, Cambodia, and Indonesia) that resulted in 57 deaths. The vast majority of those cases (and deaths) involved children and young adults. However, accurately computing the case fatality rate (the percentage of infected persons who eventually die from the disease or from its complications) is impossible because authorities do not know how many people had milder cases but did not seek medical care or how many received care that was not reported. Nearly all of the human cases resulted from close contact with infected birds. There is evidence, though, of at least one case of probable human-to-human transmission, and some experts suspect that a few other cases of human-to-human spread of the H5N1 virus have occurred.⁴

Events since the beginning of 2004 have heightened concerns among public health officials. Not only has the H5N1 virus spread widely—expanding beyond Southeast Asia and China into Central Asia and Europe—but laboratory results indicate that the virus has evolved in ways that may make a pandemic more likely:

- It has found a permanent ecological niche, becoming entrenched among domestic ducks in rural areas of Asia.
- It has become more robust than the 1997 strain and is able to survive longer under a broad range of environmental conditions.
- It has become increasingly pathogenic in poultry and has increased the range of species it can infect, now including domestic cats (in laboratory experiments) and captive tigers (after being fed infected chicken carcasses in a zoo in Thailand).

4. See World Health Organization, “Avian Influenza Frequently Asked Questions,” available at http://www.who.int/csr/disease/avian_influenza/avian_faqs/en/; and Centers for Disease Control and Prevention, “Information About Avian Influenza (Bird Flu) and Avian Influenza A (H5N1) Virus,” CDC Fact Sheet (May 24, 2005).

- It has become resistant to one of the two classes of antifu drugs.

Experts do not know if an avian influenza pandemic is likely to occur, largely because they cannot predict when, or even if, the H5N1 virus might acquire the ability to pass readily from human to human. But the wider presence of the avian strain raises the probability of a pandemic because it increases the likelihood that an individual will become infected with the human strain and the avian strain at the same time, thus opening up the possibility of a genetic reassortment that could improve transmissibility of the disease. Wider prevalence of the virus also increases the likelihood that a series of mutations will produce a pandemic strain, even without the virus's undergoing reassortment.

Nevertheless, despite the widespread concern, some scientists caution that an H5N1 pandemic is not a forgone conclusion.⁵ Although they agree that a pandemic is possible, those researchers argue that the H5 subtype of the influenza virus has not shown the ability to pass efficiently among mammals. Indeed, one mystery associated with the H5N1 virus is why it has not reassorted, despite ample opportunity to do so. Human and avian strains have circulated concurrently since 1997 (and perhaps earlier), and thousands of workers were exposed to H5N1 during poultry-culling operations in Asia. Luck may have played a role, but another explanation is that H5N1 may not possess the capacity for efficient human transmission.⁶

Although no scientific basis exists to calculate the probability of an influenza pandemic during the next 10 years, history provides a gauge to judge those chances at least roughly. Since 1700, there have been between 10 and 13 influenza pandemics (or probable pandemics) in the world, including the three that have occurred since the beginning of the 20th century.⁷ Those pandemics have taken place at irregular intervals, with as little as two years separating some outbreaks and as many as 55 years separating others. Hence, one could assume that there is a roughly 3 percent to 4 percent probability of a pandemic occurring in any given year. Gauging the severity of a potential pandemic is more difficult. Of the three pandemics that have occurred since the beginning of the 20th century, two were mild and one was severe, suggesting a fairly high probability of a severe event. However, the 1918 pandemic appears to be unique in its severity when compared with the other post-1700 pandemics. For example, although the estimates are very rough, case fatality rates during the pandemics in the 18th and 19th centuries more closely resembled those of the mild pandemics of

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5. See Dennis Normile, "Pandemic Skeptics Warn Against Crying Wolf," *Science*, vol. 310 (November 18, 2005), pp. 1112-1113.
 6. That argument relates solely to H5-subtype viruses. Researchers who believe that an H5N1 pandemic is unlikely allow for the possibility of a pandemic caused by an H1, H2, or H3 subtype.
 7. According to Michael Osterholm ("Preparing for the Next Pandemic," *Foreign Affairs*, July/August 2005), there have been 10 influenza pandemics during the past 300 years, while K. David Patterson (*Pandemic Influenza 1700-1900: A Study in Historical Epidemiology*, Totowa, N.J.: Rowman & Littlefield, 1986) asserts that there have been 13 pandemics since 1700.

1957 and 1968 than those of the 1918 pandemic. Moreover, mortality was generally concentrated among the elderly, and the degree of social disruption was much smaller than during the 1918 episode.⁸ Consequently, based only on historical frequencies, the chances of a severe pandemic's occurring appear to be relatively small, perhaps on the order of 0.3 percent. However, given the evidence of an existing epidemic of H5N1 in fowl, and the possibility that it might mutate to circulate efficiently in humans, the probability of a severe pandemic may exceed the historical frequency.

Possible Pandemic Scenarios

The uncertainty surrounding the occurrence of an influenza pandemic makes it very difficult to forecast the economic effects of such an event. As noted earlier, scientists do not know whether the H5N1 virus will acquire the properties necessary for efficient human-to-human transmission. Moreover, even if the virus acquired those properties, there is no way to predict how virulent the resulting strain would be. Consequently, a substantial amount of uncertainty is associated with any forecast of the effects of an avian flu pandemic. The Congressional Budget Office (CBO) has devised two scenarios based on past pandemics to outline possible outcomes.

The 20th century has seen three influenza pandemics: the 1918-1919 Spanish flu outbreak, the Asian flu pandemic of 1957-1958, and the 1968-1969 outbreak of Hong Kong flu.⁹ Of the three, the 1918-1919 pandemic was the most severe. An estimated 25 percent to 30 percent of the world's population became ill, and the death rate is estimated to have been as high as 11 percent of those stricken. Estimates of deaths as a result of the Spanish flu range from 500,000 to 675,000 in the United States and from 40 million to 50 million worldwide.¹⁰ (However, estimates of the number of persons affected are extremely rough because a clinical test for influenza had not been developed at that time.) The 1918 strain of influenza was not unusual with regard to its transmissibility, but it was unusual in its very high rate of mortality and in the large percentage of deaths among victims between the ages of 15 and 35. Most deaths from influenza are caused by pneumonia resulting from a secondary bacterial infection. Although many of the deaths in 1918 and 1919 followed that pattern, the Spanish flu pandemic was unusual in that a large proportion of the deaths were caused

8. See Patterson, *Pandemic Influenza 1700-1900*, p. 91, who stresses the unique nature of the 1918 outbreak. No other pandemic spread so rapidly, killed as many victims, or caused anything like the mortality seen among young and middle aged people.

9. Why the virus that caused the 1918 pandemic was termed the "Spanish" flu is unclear, given that there is no evidence that it originated in Spain or that it hit that country particularly hard. Possibly, the term arose because of heavy coverage by the Spanish media.

10. Deaths attributed to past pandemics reflect mortality above that expected in a normal flu season. According to the Centers for Disease Control and Prevention, 5 percent to 20 percent of the population catches the flu each year in the United States, and roughly 36,000 people die from the disease.

directly by the virus and the body's immune response to it, which could kill young, otherwise healthy, people in less than 48 hours.¹¹

The pandemics of 1957 and 1968 were much milder than the Spanish flu outbreak. Part of the reason was that the influenza strains in those later pandemics were less virulent, but there were also other contributing factors. Medical technology had progressed, and, in the case of the 1968 episode, some immunity had been conferred by exposure to the 1957 strain. The spread of the viruses in the two events was characteristically rapid, but the lethality of the two strains was much less than that of the 1918 virus. In addition, global surveillance had improved, which allowed public health authorities to quickly isolate the viruses, and manufacturers were able to provide vaccines for the two strains before the pandemics had eased. Also lessening the later pandemics' severity was that doctors were able to use antibiotics and other post-1918 technology to deal with bacterial infections and there were fewer cases of viral pneumonia than in 1918.

Perhaps as a result, the pattern of mortality in the 1957 and 1968 pandemics was more typical of normal seasonal outbreaks (that is, it was concentrated among the very young and very old). The two outbreaks killed far fewer people who previously had been healthy. The 1957 outbreak is estimated to have caused 2 million deaths worldwide and roughly 70,000 in the United States. The 1968 pandemic is thought to have caused 34,000 deaths in the United States. The viruses that caused the pandemics of 1957 and 1968 are known to have been caused by genetic reassortment, or, an exchange of genes between avian and human influenza viruses.¹²

Although the dimensions of a future flu pandemic are unknowable, past outbreaks suggest the following pattern of events:

- The virus would spread widely in a very short time. On the basis of experience with severe acute respiratory syndrome (SARS) in 2003, a pandemic influenza virus would be expected to cross national borders very rapidly.
- A rapid surge in the number of cases in each affected area would occur very quickly, within weeks. The number of cases would vary with the severity of the outbreak, but there would be a sharp increase in demand for medical services.

11. The H5N1 strain of avian influenza has shown a similar ability to cause a fatal form of viral pneumonia in human cases.

12. In contrast, the virus that caused the 1918 pandemic is thought to have evolved from a purely avian strain through a series of mutations ("antigenic drift") that produced a genetic structure that allowed for efficient transmission among humans.

- The pandemic would probably spread across geographic areas and vulnerable populations in waves. In any given geographic region, each wave could last for three to five months, and a second wave could appear anywhere from one to three months after the first disappears.¹³

For this analysis, CBO developed two pandemic scenarios, one mild and one severe, which it based on past experience, applying the infection and case fatality rates from the earlier pandemics to the current U.S. population of just under 300 million. Estimates of the percentage of the population that became ill with influenza during past pandemics (the so-called gross attack rates) are extremely rough. But experts generally agree that the three past outbreaks during the 20th century did not differ markedly with respect to their attack rates and that those rates ranged from about 25 percent to 30 percent. Consequently, CBO applied a 25 percent attack rate in the mild scenario and a 30 percent rate in the severe scenario.

The reason that the 1918 pandemic was so much more severe than the two later outbreaks was that it killed a far greater percentage of those that it infected than did the 1957 or 1968 strains. Like the attack rate, the case fatality rate for a pandemic is extremely difficult to estimate, largely because the total number of infected people, including those who do not seek treatment, is unknown. Nonetheless, using available evidence, experts estimate that the case fatality rate during the 1918 outbreak was about 2.5 percent in the United States, whereas during the 1957 and 1968 episodes, the case fatality rate ranged from just under 0.1 percent to about 0.2 percent.¹⁴ CBO thus assumed a rate of 2.5 percent for the severe scenario and just over 0.1 percent for the mild scenario.

Using those assumptions, the two pandemic scenarios that this paper considers are:

- A severe pandemic, similar to the 1918-1919 episode, that could infect 90 million people in the United States and cause the deaths of more than 2 million of them; and
- A mild pandemic that resembled the 1957 and 1968 outbreaks, which might be expected to infect 75 million people and cause roughly 100,000 deaths in the United States.

13. During the 1918-1919 pandemic, the second wave (which began at the end of August 1918) had a higher case fatality rate than did the first (which had begun the previous spring). During the 1957 pandemic, the first wave primarily affected school-age children, whereas the second had a greater impact among the elderly.

14. For more details on attack and case fatality rates, see Martin Meltzer, Nancy Cox, and Keiji Fukuda, "The Economic Impact of Pandemic Influenza in the United States: Priorities for Intervention," *Emerging Infectious Diseases*, vol. 5, no. 5 (September-October 1999).

Both scenarios presume that effective vaccines are not available in time to significantly alter the pandemic's course. Quarantine and travel restrictions are among the other possible policy responses, but those approaches have been shown to have little effect on overall mortality and only a limited ability to forestall the onset of local epidemics.

Although it is impossible to predict with confidence what the next pandemic will look like, several factors suggest that the worst-case scenario will be less severe than the 1918 pandemic outlined earlier. Medical technology has advanced significantly, providing health care providers with more information and better treatment options, especially for complications associated with bacterial infections. Antiviral drugs are also available and, if provided quickly, offer the prospect of decreasing the severity of infection.¹⁵ In addition, international mechanisms have been put in place that allow for better surveillance and a more rapid response to a new disease. Once the virus had been identified, vaccines would be developed to protect vulnerable populations, an option that was not available in 1918. However, the length of time required to produce sufficient quantities of a vaccine would limit its ability to lessen the effects of the pandemic.

Balanced against those factors are some that might suggest a worse outbreak than the one that occurred in 1918. The world is now more densely populated, and a larger proportion of the population is elderly or has compromised immune systems (as a result of HIV). Moreover, there are interconnections among countries and continents—faster air travel and just-in-time inventory systems, for example—that suggest faster spread of the disease and greater disruption if a pandemic was to occur.

Economic Effects of a Pandemic

Just as it is difficult to forecast the severity of a pandemic, it is hard to predict its economic effects, even if the outbreak's scope and severity are known. Only a few estimates based on past flu epidemics exist, so this paper will rely in part on evidence from the SARS epidemic of 2003. Based on past influenza pandemics and the SARS outbreak, the most important effects would be a sharp decline in demand as people avoided shopping malls, restaurants, and other public spaces, and a shrinking of labor supply as workers became ill or stayed home out of fear or to take care of others who were sick.

An avian flu pandemic could be thought of as a “shock” to the economy, with both demand- and supply-side effects in the short run. In addition, the pandemic would have longer-term supply-side effects. The short-term effects of the pandemic would depend on its scope. Under the conditions in the severe scenario described above, the

15. For evidence on that point, see Neil Ferguson and others, “Strategies for Containing an Emerging Influenza Pandemic in Southeast Asia,” *Nature* (September 8, 2005), pp. 209-214; and Ira Longini and others, “Containing Pandemic Influenza at the Source,” *Science* (August 12, 2005), pp. 1083-1087.

human toll would be devastating, and the economic effects would be greater than in recent recessions and roughly the same size as the average postwar recession. In the long term, however, the economy's response to natural disasters demonstrates that people can adapt to extreme hardship and businesses can find ways to work around obstructions. As a result, economic activity would recover, and the economy would eventually return to its previous trend growth rate.

What follows will be a discussion of the economic effects of an influenza pandemic, with emphasis on the reaction to a severe outbreak. Many of the short-run disruptions to the economy that would come to pass under the conditions of CBO's severe scenario might also occur in the event of a relatively mild outbreak. That is, the public's response to an avian flu pandemic, as to the SARS outbreak, might be disproportionate to the event's clinical severity (or lethality). However, it might not be clear during the outbreak that the public's response was disproportionate because there would be a considerable amount of uncertainty about the pandemic's severity. It might only become obvious in retrospect that the pandemic had been mild.

Short-Term Effects

The most immediate impact of a pandemic would be a surge in demand for medical services. During a severe pandemic, hospitals, clinics, and doctors' offices would probably be overwhelmed, and surveillance (keeping track of where the disease was and where it was going) would be difficult. Health care workers would be exposed to the disease, resulting in further strains on the health care system's capacity, as some workers became sick and others stayed home to care for family members or to avoid becoming ill. Care for nonacute health problems would be sharply curtailed.

As the pandemic progressed, international travel would dramatically decline, as people avoided avian flu "hotspots" and governments restricted travel. It seems unlikely that domestic and international air travel would cease completely, but as a point of reference, at the peak of the SARS outbreak in April 2003, airline passenger arrivals in Hong Kong had declined by nearly two-thirds relative to their levels in March.¹⁶

In all likelihood, people would quarantine themselves and their families by staying at home more. Nonessential activities that required social contact would be sharply cut, which would lead to significant declines in retail trade. People would avoid public places, such as shopping malls, community centers, places of worship, and public transit. Attendance at theaters, sporting events, museums, and restaurants would decline. It seems likely that many schools would close, and even if they did not, attendance would fall dramatically as parents kept their children at home. In either event, large-scale school closings would lead to a spike in workplace absences because parents would stay home to care for their children even if they were not sick.

16. See Alan Siu and Richard Wong, "Economic Impact of SARS: The Case of Hong Kong," *Asian Economic Papers*, vol. 3, no. 1 (Winter 2004), p. 76. The authors note that air travel recovered rapidly as the epidemic subsided, returning to its pre-epidemic level by August 2003.

The general slowdown in economic activity would reduce gross domestic product (GDP). Business confidence would be dented, the supply of labor would be restricted (owing to illness, mortality, and absenteeism spurred by fear of contracting the disease), supply chains would be strained as transportation systems were disrupted, and arrears and default rates on consumer and business debt would probably rise somewhat. It seems quite likely that the stock market would fall initially and then rebound later, as it did in Hong Kong during the SARS episode.

Of course, economic activity would slow, but it would not halt completely. Experience with such catastrophes as natural disasters and terrorist attacks has demonstrated the ability of people to cope with and adapt to extremely difficult circumstances. Moreover, the advances in technology of recent years would allow many companies, especially those in service industries, to conduct business via electronic communications, which would permit their employees to work from home. And to the degree that shipping companies were operating, on-line purchases could offset some of the decline in retail trade.

The actions of governments could influence the effects of a pandemic on the economy. Attempts to quarantine people would probably amplify the reductions in trade, travel, and tourism. However, government actions could also help mitigate economic impacts. Effective global surveillance and prompt identification of the pandemic strain by government agencies—along with quarantine and social isolation—could provide the opportunity for manufacturers to develop a vaccine to lessen the human and economic costs of a pandemic during its latter stages.

Little information is available for estimating the magnitude of the short-term economic impact of a pandemic. CBO was unable to find any estimates of the short-run economic effects of the three flu pandemics during the 20th century. Consequently, it based its estimate on three strands of analysis:

- A rough estimate of the supply-side effects from a large share of the labor force's becoming ill;
- A very rough estimate of a pandemic's effect on demand in individual industries; and
- A comparison with the impact of the SARS epidemic in Southeast Asia and Canada.

Effects Under a Severe Pandemic Scenario. To calculate the supply-side impact of a severe pandemic, CBO combined a rough estimate of the loss of employee work days with an estimate of average productivity per worker. For most sectors of the economy, CBO assumed that, on average, 30 percent of the workers in each sector would become ill and of those workers, 2.5 percent would die. Further, CBO assumed that those who survived would miss three weeks of work, either because they were sick, be-

cause they feared the risk of infection at work, or because they needed to care for family or friends. For the farm sector, where the work generally requires less social interaction, CBO assumed that the impact would be milder: one-tenth of workers would be affected and survivors would miss only a single week of work (the case fatality rate would be the same). CBO used average productivity per worker, by sector, for 2004 to compute the impact on GDP of the employment lost to the pandemic. Under the assumptions detailed above, GDP would be about 2-1/4 percent lower in the year in which the pandemic occurred, CBO estimates, than it would have been had the pandemic not taken place (see the Technical Appendix for a more complete description of these calculations).

In addition to workers' absences, many businesses (such as restaurants and movie theaters) would probably suffer a falloff in demand because people would be afraid to patronize them or because the authorities would close them. To calculate those demand-side effects, CBO examined GDP by industry and assumed different declines in demand for different industries, based loosely on Hong Kong's experience with SARS. Those assumed effects were based on judgments about the degree of social interaction required in different industries and are extremely rough. CBO assumed that a pandemic's effects would be especially severe among industries whose products required that customers congregate; examples include the entertainment, arts, recreation, lodging, and restaurant industries. Other industries, including retail trade, were assumed to suffer a smaller decline in demand, and one industry, health care, was assumed to experience an increase in demand because of the surge in demand for medical care. The estimated demand-side impacts sum to about 2 percent of GDP; combining them with the supply-side impacts implies about a 4-1/4 percent reduction in GDP in the year of the pandemic.¹⁷

That scenario suggests that a severe influenza pandemic would have an impact on the U.S. economy that was slightly larger than the typical recession experienced during the period since World War II. On average, real (inflation-adjusted) GDP declined by 0.6 percent during the four quarters following each of the 10 business cycle peaks between 1947 and 2005. Those declines indicate that the average postwar recession lowered real GDP by about 4.1 percent, relative to a baseline in which output continued to grow according to its long-run trend of 3.5 percent. In addition, the estimated effect on real GDP in the severe scenario exceeds the impact of every postwar recession except the one following the 1981 peak, which pushed real GDP more than 7 percent below trend in 1982.

17. This is an estimate of the immediate disruption to the economy caused by the pandemic, not an estimate of what society would be willing to pay to avoid a pandemic. That amount would be much larger than the loss of GDP because it would include, among other things, the net present value of expected future lifetime earnings of those who died from the disease. See Meltzer, Cox, and Fukuda, "The Economic Impact of Pandemic Influenza in the United States."

Effects Under a Mild Pandemic Scenario. The economic effects of a mild pandemic would be much smaller and might not even be distinguishable from the normal ups and downs of economic activity. To calculate the supply-side effect, CBO assumed that the attack rate would be 25 percent (except in the farm sector, where it was assumed to be 5 percent), the case fatality rate would be just over 0.1 percent, and the time out of work would be one-quarter of the duration assumption for the severe scenario (that is, just less than four days absent, on average). Under those assumptions, GDP would decline by about 1/2 percent (about \$70 billion in 2004) as a result of supply-side factors. For the demand-side effects, CBO assumed that the declines in each industry would be one-quarter of the declines under the severe scenario, which amounted to 1/2 percent of GDP (about \$60 billion in 2004). In total, the decline in output amounts to about 1 percent of GDP, relative to what would have happened in the absence of a pandemic. Compared to the long-run growth trend, a mild influenza pandemic would cause growth to slow, but would probably not cause real GDP to fall (or cause a recession).

Comparison with SARS. Past studies of the epidemic of severe acute respiratory syndrome that affected Southeast Asia, China, and Canada provide a point of comparison for CBO's estimates. The scale of the SARS epidemic—more than 8,000 cases worldwide and nearly 800 deaths—was much smaller than the pandemics considered in the scenarios CBO developed for this analysis. Nevertheless, that experience is applicable to a potential avian flu pandemic because people's reaction to the SARS outbreak could be considered similar to what might be expected in a flu pandemic. A study by Jong-Wha Lee and Warwick McKibbin used a global macroeconomic model to estimate the impact of the SARS epidemic on GDP in 2003. Lee and McKibbin estimate that the decline in GDP was largest in Hong Kong, where output was 2.6 percent lower in 2003 than it would have been without a pandemic. Hong Kong was followed by China, according to the authors, with a decline of 1.1 percent of GDP relative to a base case without a pandemic, and by Taiwan and Singapore, with declines of about 0.5 percent.¹⁸

However, a separate study by Alan Siu and Richard Wong, which focused exclusively on Hong Kong, concluded that the SARS epidemic had had only a mild impact on output in 2003.¹⁹ Although they do not present their own estimates, they conclude that private-sector forecasts predicting that SARS would knock 1.2 percentage points off the growth of GDP proved to be too pessimistic. That the disease's impact was mild was not because aggregate demand did not fall. The authors document declines in travel, tourism, and retail trade that were severe: year-over-year declines in retail

18. See Jong-Wha Lee and Warwick McKibbin, *Globalization and Disease: The Case of SARS*, Working Paper No. 2003/16 (Australian National University, August 2003).

19. See Siu and Wong, "Economic Impact of SARS." Hong Kong accounted for about 22 percent (about 1,800) of the total number of SARS cases worldwide and 40 percent (about 300) of the deaths.

trade of 15 percent in April 2003, a decline of 63 percent in total visitors arriving in Hong Kong, and sharp declines in restaurant spending.²⁰ The authors argue that SARS's economic impacts were concentrated in the sectors that were most directly affected by the epidemic and were relatively short-lived. Moreover, the epidemic caused no major disruption to international trade nor to Hong Kong's manufacturing base in the Pearl River Delta region of China.

An August 2005 study by the investment firm BMO Nesbitt Burns also examined the economic impact of the SARS. It describes the reaction to the epidemic in Toronto (which included sharp drops in travel, retail trade, and tourism) and documents the strains on the health care system. Citing a study by the Bank of Canada, the study estimates that the crisis cut GDP in the second quarter of 2003 by 0.6 percent, which implies that economic activity in Toronto declined by about 3 percent in that quarter and roughly 0.75 percent for the year.

The estimates of the economic effects of the SARS epidemic provide a useful benchmark for CBO's estimates of the impact of an influenza pandemic. The SARS estimates also show how difficult it is to estimate the economic effects of an epidemic. Even though all of the studies were performed after the fact (using actual data), their results vary widely. Nevertheless, the estimates suggest that the impact of SARS on Hong Kong's economy (which is where the effects were concentrated) was roughly similar to a mild business-cycle recession, although the studies differ sharply about the degree of the slowdown. CBO's estimates of the effects of the two influenza pandemics are roughly comparable. The effect on GDP in the severe scenario is larger than any of the estimates of SARS' effects, whereas the estimated effects from the mild scenario are in the middle of the range of SARS estimates.

One could argue that what happened with SARS is not relevant for an analysis of the effects of an influenza pandemic in the United States because people with influenza, unlike those with SARS, are contagious before the onset of case-defining symptoms. As a result, control measures that are based on case identification (which worked well for SARS) will be ineffective for the flu, and a much larger proportion of the population is likely to be infected.²¹ Consequently, an influenza pandemic might be expected to have a larger impact on the economy than did SARS.

There are also reasons, however, to think that the SARS epidemic is relevant for analyzing the effects of a flu pandemic. First, Hong Kong is a densely populated city; the impact of the flu in cities like New York and Boston might exceed that of SARS in Hong Kong by a wide margin, but the flu's impact on the overall economy might be

20. Tourism makes up a much larger share of Hong Kong's economy—about 6 percent—than it does of the United States' economy, and tourists contribute more to retail sales there than they do in the United States.

21. See Christina Mills, James Robbins, and Marc Lipsitch, "Transmissibility of 1918 Pandemic Influenza," *Nature*, vol. 432 (December 16, 2004), pp. 904-906.

considerably less. Second, the economic effects of the SARS outbreak appear to have been disproportionate to the virulence of the disease. The disruption to travel, transport, and tourism was substantial in Hong Kong and Toronto, as people shunned public places and public transportation, thus limiting the scope for even larger declines in economic activity in response to a deadlier disease.

Long-Term Effects

The most important long-term impact of a pandemic is the reduction that would persist in the population and in the labor force after overall demand in the economy returned to normal. The effects of that drop in the population would depend, in part, on the characteristics of the outbreak. If, for example, mortality was concentrated among the very young and the very old, then a pandemic would have relatively small effects on the subsequent growth of GDP. By contrast, if the disease struck workers who were in their prime working years more heavily, then the effects on GDP growth during the years following the pandemic would be more significant. However, predictions of the size and direction of those effects are ambiguous. Under standard assumptions, for example, a one-time reduction in the labor force would raise the ratio of capital to labor and lower the rate of return to capital, thus slowing the pace of capital accumulation and GDP growth for many years. However, under other types of analyses that include the influence of human capital, reduction in the labor supply would encourage investment in human capital, which would tend to speed the growth of per capita output during the transition period, when the economy was recovering from the shock.

How big a reduction in the U.S. labor force would a severe pandemic produce? In 2004, the labor force totaled 147.4 million people. Under the assumption of an attack rate of 30 percent and a case fatality rate of 2.5 percent—the same assumptions applied to the population as a whole—a severe pandemic would cause the deaths of more than 1 million labor force participants, or about 0.75 percent of the labor force. Since growth in the labor force averaged 1.6 percent during the 1948-2005 period, losing 0.75 percent of the labor force would be equivalent to a pause of one-half year in the growth of the work force.²² Under the assumptions for infection and mortality associated with the mild-pandemic scenario—an attack rate of 25 percent and a fatality rate of just over 0.1 percent—the number of workers killed would be 50,000, or 0.03 percent of the labor force.

There is little evidence available to use to determine which theoretical prediction best describes the long-term impact of an influenza pandemic. One study that analyzed whether the decline in population associated with the plague in Europe during the 14th century caused an increase in wages (and, therefore, in per capita output) re-

22. A decline of that magnitude is not particularly large relative to the normal yearly variation in labor force growth. For example, the standard deviation (a measure of the variability of a data series) of labor force growth during the 1948-2004 period is 0.8 percentage points, which indicates that labor force growth was within 0.8 percentage points of its mean value (of 1.6 percent) about two-thirds of the time during the historical sample period.

ported inconclusive evidence.²³ That study also looked at the effect of the 1918 influenza pandemic on agricultural production across 13 Indian provinces and found no relationship between changes in population and agricultural output. By contrast, in a study that analyzed the effects of the 1918 flu pandemic on economic growth using data from U.S. states, the authors found that after controlling for other variables—such as population density, education levels, share of foreign-born population, and climate—states that were harder hit by the epidemic experienced faster per capita growth during the 1919-1930 period.²⁴ The authors caution, however, that their results may be picking up a transitional effect—a return to trend growth—rather than an increase in steady-state growth. Moreover, because the study looks at growth rates among the states, it does not address the question of whether the growth of overall GDP would be faster or slower.

Finally, there is evidence that a potential influenza pandemic could have an impact over the very long term, lowering the incomes and socioeconomic status and harming the health of children who were born after the pandemic and were *in utero* during its height.²⁵

Current Policies and Options for the Future

Preparedness for a flu pandemic lies within the nation's overall capacity to address public health emergencies. Growing concern about a flu pandemic occurs at a time when the public health system overall and the parts of it directly associated with influenza are under increased scrutiny, and when heightened concerns about terrorism have been the primary driver of increased public health funding.

Options for addressing potential pandemics in the near and long term fall into four broad categories: detecting and controlling viruses at their source, developing and using vaccines to prevent diseases, developing and using treatments with antiviral drugs and other medications, and building the capacity of the health care system (facilities, equipment, and people) to deliver care. Decisions made in the near term may alter the availability of vaccines and treatment options in the longer term. In making decisions about how to proceed, there are competing risks. The risk of inaction is that a pandemic will occur that could have been prevented or mitigated. The risk of action is

23. See David Bloom and Ajay Mahal, *Does the AIDS Epidemic Really Threaten Economic Growth?* Working Paper No. 5148 (Cambridge, Mass.: National Bureau of Economic Research, June 1995). That paper was later published under the same title in the *Journal of Econometrics*, vol. 77, no. 1 (1997). See also Bloom and Mahal, "AIDS, Flu, and the Black Death: Impacts on Economic Growth and Well Being," in David Bloom and Peter Godwin, eds., *The Economics of HIV and AIDS: The Case of South and South East Asia* (Delhi: Oxford University Press, 1997).

24. See Elizabeth Brainerd and Mark Siegler, *The Economic Effects of the 1918 Influenza Epidemic*, Discussion Paper No. 3791 (London: Centre for Economic Policy Research, February 2003).

25. See Douglas Almond, "Is the 1918 Influenza Pandemic Over? Long-term Effects of *In Utero* Influenza Exposure in the Post-1940 U.S. Population" (mimeo, Columbia University, July 2005).

that it is costly, diverts resources from other priorities, and could be damaging by itself, as was the case in the reaction to the swine flu scare of 1976.

Context

Rising concerns in the 1990s about the spread of disease as a result of international commerce and travel, antibiotic resistance, biological and chemical terrorism, and new and evolving pathogens led to an increased focus on improving the public health system. Federal funding, initially targeted toward efforts to stockpile medicines and improve laboratory capacity, increased substantially in the face of concern about the medical consequences of terrorism after the terrorist attacks of September 11, 2001, and the anthrax attacks in that same year. Between 2001 and 2005, policymakers appropriated almost \$30 billion for activities to address the nation's preparedness against infectious diseases; improve cooperation between federal, state, and local authorities in the event of a public health emergency; upgrade the nation's laboratory capacity and expand the ability of local governments to deal with large numbers of people needing health care. Over half of that funding was for expanding research on vaccines and therapies against infectious diseases. Other funds aim to encourage private firms to develop new vaccines and other remedies to respond to biological terrorism and improve the national stockpile of and distribution strategy for remedies in the event of such an attack.

Countering bioterrorism has been the main priority of those efforts and about \$15 billion was appropriated for those purposes between 2001 and 2005. Many of the preparedness activities supported by that spending contribute to stronger health care systems and improved processes for combating epidemics of infectious diseases, including pandemic influenza. But concerns remain about how to specifically address an influenza pandemic. First, are concerns about the health system's ability to care for a large number of people in all parts of the country who are sick at the same time. Second, the declining number of suppliers of flu vaccine and the vaccine production problems that occurred in the 2001-2002 and 2004-2005 flu seasons highlight concerns about the national capacity to produce vaccines that would mitigate the damage a pandemic outbreak might cause. Concerns about a pandemic flu may have increased the urgency to resolve problems that rose to prominence last year in relation to the pace of technical improvement in the vaccine industry—an issue of long-standing concern for public health analysts—and may have increased the willingness to pay for solutions. Third, heightening those worries are more-recent developments indicating that the worldwide demand for antiviral drugs that might blunt the impact of an outbreak far exceeds current production capabilities.

Over the past several months, both the Administration and Members of Congress have proposed appropriating between \$4 billion and \$8 billion specifically for programs to respond to the prospect of a flu pandemic. Those proposals raise a number of questions. For example, how would costs compare with net expected benefits? Has the right balance been struck between spending for health system response and vaccines and drugs? How can significant new spending for a flu pandemic be best incor-

porated in the larger public health effort? What lessons have been learned thus far, about how government policies can improve and guarantee the supply of vaccines and antiviral drugs? And how can effective policies be formulated in the presence of great uncertainty?

This section summarizes the Administration's recently released plan and some Congressional alternatives. It also lists and examines specific policies now in effect and options being considered whose intention is to limit the harm of a pandemic flu. Those proposals and policies may be revised as scientists and policymakers learn more about the virus and possible countermeasures. In keeping with CBO's mandate to provide objective, nonpartisan analysis, this paper makes no recommendations.

The discussion of options and policies addresses both measures that are directed toward a near-term outbreak and measures that increase the nation's capability to deal with a pandemic several years into the future. Uncertainty is an ever-present concern, prompting such questions as, Will the H5N1 strain be the pandemic strain? Will the vaccines currently being stockpiled prove effective? Likewise, will antiviral drugs prove useful? And can the public health system cope with the surge in demand that an outbreak would bring? Not surprisingly, most of the policies now in effect and those being contemplated can be analyzed only by making heroic assumptions about how such uncertainty is resolved. Some small comfort may be found in the fact that in several instances, the issues being raised are not unique to policy regarding flu pandemics. Such issues include, for example, how incentives to produce new antiviral drugs can be preserved if the patent rights of the current producers of those drugs are not respected or how liability for the harm a vaccine might cause can be best distributed among producers, consumers, and taxpayers.

The Administration's Proposal and Congressional Alternatives

In November 2005, the President requested a total of \$7.1 billion in emergency funding for influenza pandemic preparedness. About 95 percent of that amount was to be spent on producing and stockpiling vaccines, antiviral drugs, and other medical supplies and on enhancing surveillance systems both internationally and domestically, as described in the Department of Health and Human Services (HHS) Pandemic Influenza Plan (hereafter referred to as the HHS plan).²⁶

26. Sources for CBO's discussion of the HHS plan include Michael O. Leavitt, Secretary of the Department of Health and Human Services, *Pandemic Influenza*, statement before the Subcommittee on Labor, Health and Human Services, and Education of the Senate Committee on Appropriations, November 2, 2005, available at <http://appropriations.senate.gov/hearings/Leavitt.htm>; a speech by President Bush at the National Institutes of Health on November 1, 2005, "President Outlines Pandemic Influenza Preparations and Response, available at www.whitehouse.gov/news/releases/2005/11/print/20051101-1.html; "White House Fact Sheet: Safeguarding America Against Pandemic Influenza," November 1, 2005, available at <http://www.whitehouse.gov/news/releases/2005/11/20051101.html>; and Department of Health and Human Services, *HHS Pandemic Influenza Plan* (November 2005), available at <http://www.hhs.gov/pandemicflu/plan/>.

Several other proposals that have been introduced in the Congress also address preparedness for an influenza pandemic. Although they share the same general goals, they differ from each other and from the Administration's proposal in levels of funding, relative emphasis on vaccine stockpiling versus other activities, the extent to which vaccine manufacturers and providers would be protected from liability lawsuits, and the share of the costs that state and local governments would be required to contribute. Several proposals would provide greater funding for antiviral drugs than for vaccines, whereas others would allot greater funding for public health preparedness. Recent proposals to expand Project Bioshield (discussed later) would fold incentives for the development of pandemic flu vaccines and drugs into broader efforts to provide incentives for developing drugs to treat effects arising from bioterrorist attacks. Still other proposals would focus narrowly on liability protections for manufacturers and providers of vaccines and other flu countermeasures.

Under the HHS plan, \$4.7 billion would go toward investments in creating production capacity for pandemic influenza vaccine and a stockpile of enough vaccine against each circulating influenza virus with pandemic potential to provide a course of inoculation for 20 million people by 2009.²⁷ The ultimate goal is to have a "surge" capacity sufficient to produce enough vaccine for the entire U.S. population (almost 300 million people) within six months of a pandemic outbreak.

The Administration argues that sufficient capacity cannot be achieved from egg-based production alone; its proposal is based on only 20 percent of surge capacity coming from that source and 80 percent coming from new cell-based vaccine-manufacturing facilities. To achieve that goal, HHS would spend \$2.8 billion to finance the establishment of new cell-based vaccine manufacturing facilities that could open by 2010. The department would also finance the retrofitting of existing domestic egg-based manufacturing facilities.

Following are several other features of the HHS plan:

- HHS would work with industry and academia to support development of dose-sparing technologies (that is, technologies that stimulate a strong immune response using less antigen, the raw material of vaccines) and would invest in research to develop a universal vaccine that would work against all strains of the flu.

27. A course is two doses of vaccine, each with 90 µg (micrograms) of antigen.

- The Administration proposes liability protections for vaccine manufacturers and providers on the grounds that the threat of litigation is an obstacle to the development and production of new vaccines.
- Under the HHS plan, \$1.4 billion would go toward purchasing antiviral drugs and accelerating the development of new antiviral drugs. About \$1 billion of those funds would be used to purchase 50 million courses of treatment of antiviral drugs and to subsidize the states' purchase of an additional 31 million courses under federal contracts.²⁸
- HHS would spend \$555 million to expand domestic and international surveillance, strengthen public health infrastructure, and communicate with the public about the risks of an influenza pandemic. Because state and local governments would be largely responsible for distributing vaccines, antiviral drugs, and other medical supplies, the plan designates \$100 million of the \$555 million for state and local pandemic preparedness efforts.

Near-Term Options

Over the next several months, the options available to prevent a possible pandemic or to diminish its effects are limited. The United States could provide technical and financial support for national and multilateral public health organizations that monitor potential outbreaks and control them at their source by culling flocks of infected birds. On the domestic front, were an outbreak to occur, limited production capacity of vaccines and antiviral drugs would be used strategically to slow a potential pandemic and limit the impact on the health care system. Equally important, policy decisions in several of those areas would have the potential to improve the longer-term national capability to cope with an outbreak.

28. HHS would subsidize 25 percent of the cost of the antiviral drugs purchased by state governments.

Source Control and Surveillance. The longer the H5N1 virus remains transmissible only to humans who are in close contact with infected birds, the more likely it is that vaccines, antiviral drugs, and public health preparedness in general will be useful in limiting the effects of a possible pandemic. In the event that the virus becomes easily transmissible from person to person, the sooner that fact is known, the more time there will be to gather and deploy the available public health resources.

Current policy recognizes the importance of source control and surveillance. The United States participates in and contributes to the World Health Organization's (WHO's) and other international agencies' efforts to contain the H5N1 epidemic among poultry flocks (by educating farmers in proper bird handling, for example) and to detect new outbreaks. For example, the U.S. Agency for International Development is spending \$13.7 million for avian influenza control, prevention, and preparedness in Asia, complementing \$6 million in spending on international surveillance by the Centers for Disease Control and Prevention (CDC).

As the H5N1 epidemic has progressed in bird populations, source control has become an increasingly important tactic to delay the onset of a potential H5N1-based pandemic in humans. Although the social benefits of identifying and culling infected flocks are clear, the incentives for individual farmers to actively cooperate are less clear-cut. Providing compensation to farmers who are vigilant and proactive could improve the likelihood that source control will be successful. Accordingly, ensuring that poorer countries have the funds necessary to provide such compensation as well as undertake surveillance and educational activities is in the interest of the United States and other developed countries. A November 2005 report prepared by the United Nations Food and Agriculture Organization questions whether the funds currently committed on a bilateral and multilateral basis are sufficient to implement the best strategy to control avian flu in the animal population.²⁹

Although support for countries and individuals coping with avian influenza in their domesticated bird populations may be desirable, certain risks are evident. Nations or farmers who expect outside help to pay for a problem that affects them as well as everyone else will have diminished incentives to spend resources of their own to identify infected flocks and cull them. Thus, the payoff from more aid for those purposes is likely to be offset in part by recipients' weaker incentives to take action because they are expecting someone else to pay.

29. U.N. Food and Agriculture Organization, *A Global Strategy for the Progressive Control of Highly Pathogenic Avian Influenza (HPAI)* (Rome: U.N. Food and Agriculture Organization, November 2005), p. 13-14.

Another option for source control in the near term is vaccinating the domestic bird flocks of nations where avian influenza has been detected. The Chinese government is undertaking such an effort, and some recent research suggests that vaccinating chickens may be an effective means of source control.³⁰ Again, it may be in the interests of developed nations to subsidize vaccination programs in poor countries. But inefficient vaccination giving only partial immunity to inoculated flocks could do more harm than good by making it more difficult to detect a lethal strain of avian flu in domesticated flocks.

Vaccines. Currently, no licensed human vaccine is available for the strain of the avian influenza virus now circulating in Southeast Asia. The National Institutes of Health (NIH) has contracted with private manufacturers to produce developmental vaccines against the H5N1 strain and has tested those vaccines in healthy adults; it plans more testing among children and the elderly. This past fall, the U.S. government awarded \$162.5 million in contracts for additional vaccine development to two firms: Chiron and sanofi pasteur.³¹ Very recent reports indicate that the government intends to have a stock of vaccines sufficient to immunize 4 million people against the H5N1 virus by February 2006.

If the H5N1 flu strain triggered a pandemic in the next several months, the Food and Drug Administration (FDA) would probably request that producers switch from manufacturing seasonal flu vaccine to producing vaccine effective against the pandemic strain. Currently, the only manufacturer of flu vaccine located in the United States is sanofi pasteur, which can produce 60 million doses of seasonal vaccine about every six months. Each dose of seasonal vaccine contains 45 µg (micrograms) of antigen, the raw material from which vaccines are made. The best available science indicates that two doses of vaccine, each requiring 90 µg of antigen, are necessary to protect against the H5N1 strain.³² Thus, the raw material that currently can be used to inoculate 60 million people against the seasonal flu would provide immunity to only

30. J.A. van der Goot and others, "Quantification of the Effect of Vaccination on Transmission of Avian Influenza (H7N7) in Chickens," *Proceedings of the National Academy of Sciences*, vol. 10 (December 5, 2005).

31. Chiron's contract was awarded in October and is for \$62.5 million; sanofi pasteur's contract was awarded in September and is for \$100 million.

32. Statement of Michael Leavitt, November 2, 2005, p. 5.

15 million people every six months during a pandemic caused by the H5N1 strain.³³ Optimal vaccination of the United States' 300 million people would require many times that amount. That shortage of capacity results in part from problems in the market for pandemic influenza vaccine, many of which are present in the seasonal influenza market as well (see Box 1).

Some experts believe that it is overly optimistic to assume that antigen yields from using the capacity available to produce seasonal influenza vaccine would be realized in producing a vaccine effective against the H5N1 virus. Because H5N1 is lethal to birds, it both threatens the supply of chickens able to provide the necessary eggs and increases the number of eggs required for each dose. The pharmaceutical manufacturer GlaxoSmithKline has conducted tests that indicate that the yield for a pandemic strain could be 20 percent to 50 percent lower than it is for each strain of seasonal vaccine—which would reduce the number of people who could be vaccinated proportionately.³⁴

In the event of a near-term flu pandemic, the short supply of vaccine and the likelihood of extraordinary demand for it could require the public health system to take a forceful role in distributing and administering the limited supplies of vaccine. The HHS plan lists priority groups as recommended by its Advisory Committee on Immunization Practices (ACIP) and its National Vaccine Advisory Committee (NVAC). The plan states that the “primary goal of a pandemic response considered was to decrease health impacts including severe morbidity and death; secondary pandemic response goals included minimizing societal and economic impacts.”³⁵ ACIP and NVAC recommendations give priority to medical workers (8 million to 9 million people) and people critical to the manufacturing of vaccines and antiviral drugs (40,000 workers). The recommendations then give priority to the elderly with

33. Experience to date indicates that the H5N1 strain presents special problems for vaccine development. For example, laboratories have been unable to prepare the candidate H5N1 seed strain in the same manner as they prepare the candidate seasonal influenza A seed strains. Those seasonal seed strains are prepared by genetic reassortment using a strain that improves growth performance. If the candidate H5N1 seed strain was prepared in that manner, it would still be capable of causing severe disease and therefore would not be suitable for manufacturing. Instead, the candidate H5N1 seed strain must be prepared by reverse genetics to make it incapable of causing disease and suitable for manufacturing. MedImmune holds the patent rights for a reverse-genetics process useful in vaccine manufacturing. It has allowed manufacturers to produce pandemic influenza vaccines from seed strains prepared by this process for research purposes but not for distribution. However, according to officials at NIH, MedImmune has agreed to license the technology to vaccine manufacturers in return for a licensing fee. Resolving such license issues now might speed up the production of pandemic flu vaccine in the event of an outbreak.

34. Andrew Jack, “Fighting Flu: Vaccine Makers Roll Up Their Sleeves,” *Financial Times*, October 30, 2005.

35. Department of Health and Human Services, *HHS Pandemic Influenza Plan*, Part 1, Appendix D, p. D-10.

Box 1.**Problems in the Market for Influenza Vaccine**

Planning, production, and distribution of influenza vaccine follow an annual cycle. The Centers for Disease Control and Prevention (CDC) runs a domestic flu surveillance program and works with the World Health Organization (WHO) and other groups to monitor flu internationally. Each year, those efforts culminate in a decision about which strains of flu should be included in that year's seasonal vaccine. The WHO Collaborating Centers for Influenza, the U.S. Food and Drug Administration (FDA), and other agencies' laboratories prepare candidate high-growth seed strains and provide them to manufacturers licensed by the FDA. The manufacturers report back to the WHO Collaborating Centers and the FDA on the candidates' suitability for vaccine production. Sometime between February and March, FDA announces the selected strains to be included in the vaccine for the upcoming flu season. Manufacturers must then produce enough vaccine for the market by October to November (the optimal time for vaccinations), using a process that can take six months or more and is based on growing the viruses in fertilized chicken eggs.¹

Experience in both the 2000-2001 and 2004-2005 flu seasons makes it clear that much can and does disrupt that annual cycle.² The following are among the problems in the flu vaccine market:

- The lengthy egg-based manufacturing process means that production cannot be scaled up quickly if flu vaccine demand is higher than predicted. Also, demand is hard to predict and can depend on such things as the timing and media coverage of the current flu season and the severity of previous flu seasons. Demand for vaccine for a pandemic flu is even more variable, ranging from none in most years to perhaps 10 times more (by quantity of antigens) in a pandemic year than the average flu vaccine demand.

1. This description of the annual seasonal-flu cycle was drawn from Catherine Gerdil, "The Annual Production Cycle for Influenza Vaccine," *Vaccine*, vol. 21 (2003), and personal communication to the Congressional Budget Office from staff of the National Institutes of Health.
2. Government Accountability Office, *Flu Vaccine: Supply Problems Heighten Need to Ensure Access for High-Risk People*, GAO-01-624 (May 2001), and *Influenza Vaccine: Shortages in 2004-05 Season Underscore Need for Better Preparation*, GAO-05-984 (September 2005).

Box 1.**Continued**

- Besides being highly variable, demand for flu vaccinations is likely to be smaller than the socially optimal level. Flu vaccine helps not only the person vaccinated but also people with whom that person comes in contact, because each vaccinated person adds to “herd immunity” and decreases the possibility of transmission. Individuals’ decisions about the desirability of getting a flu vaccination may not take into account that additional social benefit, however. People may also choose not to get vaccinated if they believe that everyone with whom they come in contact will be vaccinated.
- Flu vaccine cannot be stored from one flu season to the next because flu strains change from year to year. Consequently, if manufacturers supply more vaccine than demanded, the excess vaccine is destroyed.
- The manufacturing process is prone to contamination, which upon inspection will cause vaccine to be withheld from the market.
- Although the government accounts for less than 20 percent of the market for flu vaccine, the CDC’s role in allocating vaccine during shortages discourages the establishment of reserve capacity. In the event of shortages, the CDC recommends that vaccine be given only to people in priority groups in order to decrease the health effects associated with the flu, including severe morbidity and death. If, instead, market incentives were allowed to determine the allocation of vaccine during periods of scarcity, manufacturers would have a greater incentive to increase their production capacity. In that case, however, people in priority groups who were unwilling to pay enough might not get vaccinated.

Because of those risky market conditions, few manufacturers of flu vaccine serve the U.S. market, which makes that market vulnerable to supply disruptions.

conditions that put them at high risk for hospitalization and death if they become infected with influenza (18.2 million people) and to people ages 6 months to 64 years with two or more conditions that put them at high risk for hospitalization and death if they become infected with influenza (6.9 million people).³⁶

Some critics argue that younger and healthier individuals should be given priority over the elderly and over people with conditions that put them at high risk for hospitalization and death if they become infected with influenza. Such critics argue that younger and healthier individuals are more mobile than older, less healthy people and therefore are more likely to spread the flu to others. Healthier individuals are also more likely to play critical roles in supply chains for food, water, electricity, and the like.³⁷ Another factor arguing for giving priority to younger people is that the seasonal flu vaccine produces a weaker immune response in the elderly, making it less effective in flu prevention. Finally, a potential pandemic flu could have characteristics similar to those of the flu of 1918, which caused a disproportionately high number of deaths among the young and healthy.

The discussion above assumes that two doses of 90 µg each is the course of treatment administered to each person. An alternative strategy would be to reduce that course and inoculate a much larger number of people. What level of immunity might be provided from a diluted course is unknown—although initial studies by NIH found that diluted courses did not achieve the desired immune response. The risk of the dilution strategy is that sufficient immunity will not be provided to key priority groups whose immunization is essential to mitigating the effects of a pandemic—groups such as medical workers and people critical in manufacturing vaccines and antiviral drugs.

Even if supplies of vaccine were adequate, having the government conduct a mass immunization campaign for a potential epidemic is an enterprise not without challenges and risk. The swine flu response in 1976 serves as a cautionary tale for mass vaccination programs and raises the question of whether the risks of such a program merit action before an outbreak actually occurs. Concerned that the infection of four soldiers at Fort Dix with the swine flu presaged a pandemic akin to the 1918 Spanish flu, health officials pressed for a national vaccination campaign. Although some health officials expressed doubts about the likelihood of an epidemic, the government initiated a mass inoculation program and requested that manufacturers produce 150 million new doses to vaccinate the entire U.S. population. After hundreds of people receiving the vaccine came down with Guillain-Barre syndrome (GBS), a rare neurological disease thought to be caused by the swine flu vaccine, the government terminated the

36. For the remaining priority groups, see the HHS plan (Appendix D, p. D-13, Table D-1).

37. Tyler Cowen, *Avian Flu: What Should Be Done*, Working Paper Series (Mercatus Center, George Mason University, November 11, 2005), p. 11.

campaign and indemnified manufacturers, ultimately paying out \$93 million in claims.³⁸ The epidemic never occurred.

More recently, efforts to vaccinate several million health care workers against smallpox fell short as a result of doubts about the vaccine's safety and the low probability of a smallpox attack. The government spent about \$500 million to build a stockpile of vaccine against smallpox for the entire population and began an immunization program that would prioritize health care workers. However, the vaccine caused an unexpected number of injuries and deaths, and only about 40,000 individuals have been vaccinated to date.

Antiviral Drugs. A key part of the current strategy for preparing for a flu pandemic is the purchase and stockpiling of antiviral drugs to prevent infection in people exposed to the virus and to treat illness. Should an outbreak occur, antiviral drugs would be a key factor in treating the sick and halting further spread of the flu. Other drugs, especially antibiotics, would also be necessary to treat the sick.

Only two antiviral drugs, oseltamivir and zanamivir, have shown promise in treating avian influenza. Oseltamivir is licensed as Tamiflu and manufactured under patent by the Swiss firm Roche Laboratories in tablet form. A treatment course for Tamiflu includes 10 pills, taken over five days. Zanamivir is licensed as Relenza and manufactured by GlaxoSmithKline. Relenza is administered by oral inhalation and is not recommended for people with chronic lung problems.³⁹ The FDA has approved both antiviral drugs for treating influenza; Tamiflu has also been approved to prevent influenza infection.

Because antiviral agents can be stored—Tamiflu and Relenza have shelf-lives of three and five years, respectively—developing a stockpile has advantages as part of a strategy for a flu pandemic. Several countries, including Japan, the United Kingdom, France, Norway, the Netherlands, and New Zealand, are pursuing a stockpiling approach. By the end of 2005, more than 4 million treatment courses of Tamiflu and 84,000 treatment courses of Relenza will be in the U.S. Strategic National Stockpile.⁴⁰ The United States has ordered 12 million more treatment courses of Tamiflu from Roche, but the company's production capacity is committed to filling previous contracts for the next two years. Even if the order could be filled, that amount would be enough to cover only about 5 percent of the population, far short of WHO's recommendation that governments have enough antiviral treatments on hand for at least 25 percent of their population.

38. Sarah Lister, *Pandemic Influenza: Domestic Preparedness Efforts*, CRS Report for Congress RL33145 (Congressional Research Service, November 10, 2005), p. 28.

39. *The Pill Book*, 11th ed. (New York: Bantam Books, 2004), p. 1169.

40. Department of Health and Human Services, *Pandemic Influenza Plan*, p. F-39.

Securing antiviral drugs, however, is not simply a matter of funding because there are currently shortages of them. The demand for Tamiflu from governments and private entities exceeds Roche's production capacity, and the firm temporarily suspended shipments of the drug to the United States in late October to prevent hoarding and ensure adequate supplies to treat seasonal flu cases this winter. In the event of an influenza pandemic in the immediate future, sufficient quantities would not be available to treat the sick. That situation may improve, however, since Roche will soon begin to manufacture Tamiflu in the United States (in six new FDA-approved facilities) and claims that the firm will increase 10-fold over 2003 levels.⁴¹

Even if the supply of antiviral drugs were adequate, questions would remain about relying too heavily on them for protection. Many of those who died from H5N1 influenza were given Tamiflu, although the drug may have been administered too late or in too small a dose to be effective.⁴² (Tamiflu needs to be taken within two days of the initial flu symptoms, when many people may not yet be aware that they have the flu.) Some research in mice has suggested that Tamiflu is less effective against recent strains of H5N1 than it was against the 1997 strain.⁴³ Additionally, the nature of the treatment (10 pills over five days) might make it difficult for overburdened medical facilities to provide Tamiflu and for patients to comply with the dosage regimen.

An additional concern about antiviral drugs is the location of stockpiles and the distribution of drugs, should an outbreak occur. That concern overlaps with concerns about health care system readiness, discussed below. Without an adequate plan that accounts for limited supplies and the predominantly local character of health care delivery, a national stockpiling plan will not be effective. Federal, state, and local efforts to devise such a plan are ongoing.

Health Care System Readiness. If a pandemic occurred in the next several months, the United States would have to rely primarily on the existing public and private health system (and its current capacity for hospitalization, antibiotics, and ventilators) to treat infected people. The effectiveness of that response would depend not only on the federal government but also on the state and local health authorities and the private sector, which traditionally play large roles in immunization, laboratory services, and deciding on and implementing public health actions. Health system response, while relatively more important than other options were an outbreak to occur in the near term, would also remain critical for the foreseeable future, in that the effectiveness of antiviral drugs is uncertain and vaccines, even if produced in mass quantities in the future, would not be available for at least six months after an outbreak. Limiting the

41. "Roche Plans Big Increase in Tamiflu Production," *New York Times*, November 10, 2005; and "Run on Drug for Avian Flu Has Physicians Worried," *Washington Post*, October 22, 2005.

42. Garrett, "The Next Pandemic?"

43. "Mouse Studies of Oseltamivir Show Promise Against H5N1 Influenza Virus," *NIH News*, Monday, July 18, 2005, available at www.nih.gov/news/pr/jul2005/niaid-18.htm.

harm of a pandemic flu outbreak may also depend on social distance measures—for example, closing schools and shopping malls.

Across the nation, pandemic influenza would bring people to physicians' offices and health care facilities, which could quickly face overcrowding. Higher-end estimates of the number of sick individuals treated by hospitals range from 5 million to 10 million.⁴⁴ Those figures, even when converted to a bed-day basis, would far exceed the number of staffed hospital beds. Currently, the United States has approximately 970,000 staffed hospital beds and 100,000 ventilators, with three-quarters of them in use on any given day. As a result, shortages could occur in critical areas such as ventilators, critical care beds, and drugs to treat secondary infections. The ability of facilities to maintain strict infection control would be challenged. Pandemic flu would be widespread and would restrict the flexibility to shift resources to other communities. Surge capacity is particularly a concern for the services of health care personnel, especially nurses, epidemiologists, and laboratory technicians. In many regions of the country, surge capacity would be further limited by the likelihood that health care personnel might themselves be sick or be called upon to care for sick family members at home.

Communities and health care facilities may have to look to other facilities to hold the sick and adopt diversion strategies for non emergency patients. Additional hospital bed capacity may be created by setting up field hospitals and using auxiliary sites such as shelters, schools, religious facilities, nursing homes, hotels and day care centers. Wide variations exist among communities in the ability of local officials to cope with an outbreak, with smaller jurisdictions likely at a disadvantage. The suggestion has been made that government facilities and health care personnel could provide a significant surge capacity, but as Box 2 discusses, the medical capacity of the Departments of Defense, Veterans Affairs, and Homeland Security is also limited. Policymakers may need to adopt a strategy to encourage home treatment for those with less serious symptoms to reduce overcrowding in hospitals and also to contain the spread of pandemic flu by reducing the number of contacts between infected and noninfected individuals. A home treatment strategy would require a system to provide training and support for home caregivers.

Some public health experts have argued that quarantine measures to combat pandemic flu will fail. As noted earlier, such measures worked well in slowing the spread of SARS, but SARS is much less contagious than the flu and has a longer incubation period. Unlike people with SARS, people with the flu can transmit the virus beginning one day before symptoms develop. Less stringent social distance measures—closing public places such as schools, shopping malls, and movie theaters—may be more effective because those measures do not require that infectious people be identified. As time goes by and the flu dissipates, however, people may begin to resume normal activities, which could lead to a second wave of flu infections.

44. Lister, *Pandemic Influenza*, p. 10.

Box 2.

“Surge” Medical Capacity of the Departments of Defense, Veterans Affairs, and Homeland Security

One of the resources that might be drawn on in the event of an outbreak of pandemic influenza is the medical facilities and staff of the Departments of Defense (DoD) and Veterans Affairs (VA). Many of those individuals also participate in the Department of Homeland Security’s National Disaster Medical System (NDMS), whose teams of medical personnel support other professionals in the event of a major emergency or disaster. In addition, the military has mobile facilities that might provide hospital and medical capacity during a pandemic.

Department of Defense Facilities

The Department of Defense has more than 50 military hospitals and medical centers in the continental United States, providing more than 3,500 staffed beds for active-duty personnel and their dependents and for military retirees and their families. On any given day, about 70 percent of those beds are occupied, although many are used by patients seeking elective or nonurgent care that could be deferred if beds were needed for flu victims. In addition, DoD operates more than 400 outpatient clinics. In the event of a pandemic, those facilities might be able to treat ambulatory cases, thus providing some additional capacity for treating flu victims. Staffing could be supplemented by calling up medical personnel in the National Guard and Reserves. However, that approach, rather than adding to the total number of medical personnel available nationally to treat avian flu cases, would instead merely shift medical personnel from the civilian to the military sector.

Facilities Operated by the Department of Veterans Affairs

The Department of Veterans Affairs’ 157 hospitals provide over 18,000 acute care beds. VA also operates more than 860 outpatient clinics. Those facilities serve 7.5 million veterans who are enrolled in the VA medical system. Although most of those facilities currently operate at high occupancy or utilization rates, in the event of a pandemic outbreak, treatment of many patients who were seeking elective or nonurgent care could be deferred if VA facilities and personnel were needed. In addition, VA could increase its inpatient capacity by reassigning personnel and adding beds where possible. However, VA is likely to be faced with an influx of veterans seeking treatment for avian flu, who may quickly fill VA hospitals to capacity.

Box 2.**Continued**

The National Disaster Medical System

The National Disaster Medical System, a section within the Department of Homeland Security, supports other federal agencies in responding to the medical aspects of major emergencies and federally declared disasters, including natural disasters, major accidents, and events that involve weapons of mass destruction. The NDMS includes a Disaster Medical Assistance Team, National Nurse Response Team, National Pharmacy Response Team, and other key support teams. Those groups treat victims in and responders to domestic disasters by providing medical care at a disaster site, in transit, and in hospitals and other treatment facilities that participate in the system.

Because many team members work in the medical field on a daily basis, the teams do not necessarily add to the number of medical professionals who would be available to treat avian flu cases. They would, however, add to the number of people trained to work together to provide care and manage resources in case of a disaster or emergency.

Mobile Medical Facilities

The military also has mobile medical facilities (which include the Army's field hospitals, the Navy's hospital ships and expeditionary medical facilities, and the Air Force's theater hospitals) that are intended to provide medical and surgical care to military forces deployed in combat zones. Those facilities are designed to be set up rapidly and to be self-supporting. Many are prepositioned overseas. The facilities are intended to be staffed by military medical personnel drawn from fixed facilities (such as military hospitals) as well as by medical personnel activated from the National Guard and Reserves. Although such resources might be needed to care for military personnel, nondeployed mobile medical facilities in the United States might be available to provide care to civilians in case of an avian flu pandemic. One advantage of the mobile hospitals is that they are self-sustaining, providing their own power and traveling with prepackaged sets of drugs, medical supplies, and equipment. Field hospitals might be particularly useful if medical facilities were needed in remote areas without access to power, water, and other services. Several thousand beds could be made available by setting up these facilities in the United States, but the actual number would vary depending on deployment and training schedules.

Options for the Longer Term

If an avian flu pandemic did not start for several years, the United States would have many more opportunities to improve its response capability. Although monitoring and source control could continue to be effective in helping to prevent a potential pandemic, the possibility of new vaccine techniques, coupled with the effective use of larger stockpiles of vaccines and antiviral drugs, might offer a way to ameliorate pandemics in the future. Within the next year or two, currently available drugs could be produced in larger quantities and stockpiled. The major risk associated with that approach, however, is that those stockpiled agents will prove to be ineffective. Also of concern is protection of the patent rights of existing producers of antiviral drugs to ensure that incentives to develop new such drugs remain strong.

For the future, new drugs and methods of production, particularly for vaccines, could be developed and put in place. However, a better long-term outlook may depend on policies that are implemented in the very near term. Yet that approach has pitfalls as well—for example, those associated with active government intervention in private investment and production. Direct investment by the government in production facilities runs the risk of the government’s essentially picking winners and losers—which it does poorly. Less risky alternatives might be to contract for research into new drugs and production technologies, guarantee purchases, build the market for annual influenza vaccinations, and address a number of issues that some observers contend are obstacles to private investment, including liability protection for vaccine producers, and patent protection for innovations. The measures listed above are not mutually exclusive and could be put in place in conjunction with direct government financing of production facilities.

Vaccines. Over the long term, policies could be pursued to help ensure a sufficient supply of vaccine—in part by taking advantage of new technologies—and to develop a more effective process for distributing it to the public. Over the next year, stockpiles of vaccine against the H5N1 strain could be built, and the H5N1 strain could be added to the regular annual flu vaccine. Later, new dose-sparing approaches and immunization techniques could be developed to increase the number of people who could be inoculated with a fixed supply of vaccine raw material.

Build a Stockpile of H5N1 Vaccine. Under this policy, manufacturers would produce H5N1 flu vaccine in the “off-season” (that is, the time of the year when they are not producing at full capacity), using their existing technology and their capacity for producing the seasonal flu vaccine. Nevertheless, vaccines stockpiled to inoculate people against the H5N1 strain could turn out to be ineffective against a mutated strain, and shortages would persist.

Some people have raised concerns that manufacturers will decline to participate in government stockpile programs because Securities and Exchange Commission (SEC) guidance requires revenue recognition to be delayed until the buyer takes delivery or, in the case of vaccines, until they are delivered from the stockpile. However, on

December 5, 2005, the SEC released new guidance that allows companies to recognize revenue for vaccine sales to federal government stockpile programs.⁴⁵

Vaccinate People with the H5N1 Vaccine. Vaccinating people with an H5N1 strain now might provide some of the population with additional immunity in the event of an H5N1 pandemic. However, a pandemic flu strain might be significantly different from the current H5N1 strain, which would make advance vaccinations with the current strain ineffective. Adding H5N1 to the regular seasonal flu vaccine would require manufacturers either to make fewer doses of the seasonal vaccine or to remove one of the current strains that it includes. Such a strategy might increase the likelihood that more people would get the flu from the removed strain.⁴⁶

Develop Dose-Sparing Vaccines and New Immunization Techniques. New technologies may be available in the near future that will have the potential to reduce the amount of antigen needed for a vaccine to be effective. Promising dose-sparing technologies include intradermal administration (injected between the layers of the skin) as opposed to intramuscular administration (injected within the muscle) and adjuvanted vaccines. Adjuvants are substances that are included in the vaccine to make it effective at a lower dose; they are routinely used in childhood vaccines. Currently, the United States has no approved influenza vaccines that contain adjuvants. In October, Chiron announced promising results from a clinical study that tested its investigational adjuvanted vaccine against another avian influenza virus, H9N2. In that study, adjuvanted vaccine doses containing as little as 3.75 µg of antigen proved highly capable of producing an immune response.⁴⁷

Data from clinical trials are required to gain regulatory approval from the FDA for those technologies. NIH has in place a network of vaccine and treatment evaluation units (VTEUs) to quickly conduct clinical trials. Using its VTEUs, NIH completed trials of a seasonal influenza vaccine manufactured by GlaxoSmithKline to accelerate the FDA approval process and increase the supply of vaccine in the United States in time for the 2004-2005 flu season.⁴⁸ NIH has also just completed trials comparing intradermal with intramuscular administration using a candidate H5N1 vaccine manufactured by sanofi pasteur and expects to have published results within the year. In addition, trials of an H5N1 adjuvanted vaccine will begin soon.

45. That guidance is available at <http://www.sec.gov/rules/interp.shtml>.

46. The seasonal flu vaccine is a trivalent vaccine—that is, it contains antigens from three influenza virus strains (two influenza A virus strains and one influenza B virus strain).

47. “Chiron Announces Promising Data from Clinical Study of Adjuvanted Avian Influenza Vaccine; Results Confirm Previous Clinical Studies: Chiron’s MF59 Adjuvant Significantly Enhances Immune Response,” *Chiron News*, October 28, 2005 available at <http://phx.corporate-ir.net/phoenix.zhtml?c=105850&p=irol-newsArticle&ID=774795&highlight=>.

48. Personal communication to the Congressional Budget Office from NIH staff.

Strengthen Demand-Side Incentives. A government commitment to purchase influenza vaccines that are effective against potential pandemic strains would be a strong market signal to producers that investment in new capacity and technologies will be rewarded. An increase in the demand for annual flu vaccine would amplify that signal. Increasing the market for the seasonal flu vaccine would also provide the immediate benefit of reducing the cost of the seasonal flu.

An example of demand-side incentives in the bioterrorism area for development of vaccines and treatments against biological agents is Project BioShield, begun in 2004. The program is designed to encourage such development through the use of advance purchase agreements that offer the promise of a government sale to encourage drug manufacturers to develop products that have limited markets with no commercial application. (Without advance purchase, manufacturers might be reluctant to invest in expensive clinical trials and production capacity.) To date, funds appropriated for such purchases total \$5.6 billion; about \$3.4 billion of that total is currently available for obligation. The government has entered into only a few contracts, the largest of which (\$800 million) is for an anthrax vaccine scheduled for delivery in 2007. Product development has been slow, however. The government has paid out only \$70 million for the delivery of final products. Critics of this kind of approach question whether the government should be providing funding to companies during this stage of the development process and whether the approach provides a strong incentive to manufacturers.

In terms of the market for the seasonal flu vaccine, the CDC currently recommends that about 190 million people get a flu shot each year, and in recent years when supplies were adequate, about 45 percent of that number were actually vaccinated. The annual market might be expanded by intensifying efforts to get more individuals in the recommended groups inoculated (for example, only about 40 percent of health care workers were inoculated in 2003) or by including more groups among those for whom vaccination is recommended—all college students, for instance. Yet the gains from such a strategy might be limited: the government and the news media actively promote flu shots now, and more of the same might not produce large increases in the size of the market.

Another demand-expanding strategy for the seasonal flu vaccine would be for the CDC to increase the recommended dosage particularly for the elderly, a group that is a disproportionately large consumer of flu vaccine and one for which the standard dosage of the seasonal flu vaccine generally provides a lower immune response. More dramatically, the government could implement the recommendations of an Institute of Medicine panel that in 2004 called for a federal mandate on insurers, accompanied by offsetting subsidies, to cover the cost of vaccines (influenza and others) under their policies, as well as a vaccine voucher program for people who do not have health insurance.⁴⁹

49. Institute of Medicine, *Financing Vaccines in the 21st Century: Assuring Access and Availability* (Washington, D.C.: National Academy Press, 2004), pp. 11-14.

Strengthen Supply-Side Incentives to Increase Capacity and Improve Technologies. The Administration's plan and the various Congressional proposals span a wide range of supply-side stimulants that include additional funding and other incentives for research and development and clinical trials, government support for construction and renovation of facilities, streamlined regulatory procedures, and liability protection for manufacturers.

- *Provide financial assistance to enhance vaccine production capacity.* An important part of the Administration's proposal to increase the nation's capacity to produce influenza vaccine is, as HHS Secretary Michael Leavitt testified, "financing the establishment of new cell-based vaccine manufacturing facilities."⁵⁰ President Bush, in his speech announcing the proposal, noted that the HHS plan included a request for 2.8 billion dollars for cell-culture technology. Presumably, financing for production facilities is included in that total. Also provided in the Administration's plan is financing for the retrofitting of egg-based manufacturing facilities.

Detailed information about financing, however, is not provided in the HHS plan; thus, financing could involve a number of different mechanisms ranging from outright grants to loans (subsidized and unsubsidized) to loan guarantees. Government financing might not take into account the value of production capacity as an investment, and such choices by the government discourage outsiders or active participants in the industry that wish to pursue a different approach. Consequently, the use of demand-side incentives—such as stockpiling, guaranteed purchases, and the like—gives market forces wider latitude.

- *Establish incentives for research and development.* Assistance from the government for research and clinical trials might encourage manufacturers to apply for licenses for new technologies if the approaches proved cost-effective. Both the Administration's proposal and those of Members of Congress include such measures. New technologies might comprise cell culture-based influenza vaccines that could circumvent possible problems presented by H5N1 strains that are lethal to chicken embryos. That technology might be available in three to five years. Other approaches that are not as far along in their development include recombinant DNA production and the development of a universal vaccine that would work against all strains of the flu. Some scientists argue that a live-attenuated flu vaccine (that is, containing live but weakened influenza viruses) or a whole-virus vaccine could provide a stronger immune response at lower doses. (MedImmune's Flumist is a live-attenuated flu vaccine for seasonal flu that is administered as a nasal spray.) Other researchers argue that it would be too risky to create live-attenuated or whole-virus pandemic flu vaccines.

Manufacturers may be unwilling to incur the regulatory costs of getting new technologies approved when prices for seasonal flu vaccines are low. NIH could, as it

50. Statement of Michael Leavitt, November 2, 2005, p. 6.

did in response to last year's seasonal influenza vaccine shortage, use its network of vaccine and treatment evaluation units to quickly conduct clinical trials of vaccines made from new technologies and thus accelerate the FDA approval process, reducing regulatory costs for manufacturers. Policymakers could also provide tax incentives, prizes, or other rewards to firms that developed certain technologies to achieve stated goals.

- *Provide liability protection.* Faced with having their products used in a public health emergency, manufacturers contend that the federal government should offer them liability protection. Liability exposure associated with vaccine injuries is often cited as one of the reasons for the small number of vaccine manufacturers and the lack of innovation in the industry. As the need for protection from infectious diseases and bioterror agents has grown, so have demands for broad federal shielding of manufacturers from the financial risk associated with vaccine production, particularly for vaccines distributed to large numbers of healthy people in a public health emergency.

However, there are questions about the extent to which potential liability exposure discourages future investment in vaccines and vaccine technologies. Some observers view liability as a minor problem for vaccine manufacturers and assert that low profit margins for certain vaccines, together with the lack of a dependable market, are the main reasons companies do not invest in vaccines.⁵¹ Those observers also note that companies invest in other vaccine ventures (for example, vaccines to protect against HIV and cervical cancer) without extra liability protection. Opponents of broad federal liability protection argue as well that individuals should have access to judicial remedies in vaccine injury cases and that without an avenue to address injuries, people might be deterred from seeking immunization.⁵²

The federal government has several options for addressing liability concerns of manufacturers; they include limiting the circumstances in which individuals can sue, indemnifying manufacturers, providing assistance with liability insurance, and establishing or broadening vaccine injury compensation programs. An existing no-fault compensation system for injuries related to childhood vaccines—the National Vaccine Injury Program (VICP)—compensates individuals who are harmed by certain vaccines and protects manufacturers by limiting suits that can be pursued outside of the program. That program covers the seasonal influenza vaccine but not vaccines against a flu pandemic. An additional program provides compensation to health care workers who are injured by the smallpox vaccine. One option for addressing liability concerns about vaccines against pandemic influenza might be to include them in the VICP. However, because the fund's financing comes from ex-

51. American Trial Lawyers Association, "Liability Concerns Are Not Affecting Vaccine Production," *ATLA Factsheets* (November 3, 2005), available at www.altalaw.org/FACTS/products/vaccineshortage.aspx.

52. See Congressional Budget Office, *The Economics of U.S. Tort Liability: A Primer* (October 2003), for a broad discussion of liability issues.

cise taxes levied on covered vaccines, that avenue may not be the most appropriate for a mass campaign against pandemic influenza. Instead, a separate compensation fund similar to the smallpox fund could be set up to work alongside other strategies to limit liability exposure for firms.

Antiviral and Other Drugs. A reason for the lack of availability of antiviral drugs is weak current sales, in part a consequence of the very short window in time in which a doctor can prescribe the drugs and expect them to be effective. By the time a doctor is consulted by an infected patient with the seasonal flu, it is often too late for antiviral drugs, hence the preference for flu vaccination. As with vaccines, the supply of currently available antiviral drugs will be greater, and new drugs will be more likely to become available over time. For the next year or so, significant obstacles stand in the way of increasing production of currently available drugs by enough to meet worldwide demand (see Box 3).

Strengthen Demand-Side Incentives to Increase the Production of Currently Available Antiviral Drugs. Steady demand from the federal government to build a stockpile of antiviral drugs and influenza drugs purchased at a price that producers considered adequate could provide greater incentives for companies to invest or deploy existing resources to large-scale production of those agents. However, for manufacturers to invest in and convert production to pandemic influenza drugs would probably require assurances from the government regarding how much it will pay and for how long.

During an outbreak, the federal government might threaten to confiscate intellectual property rights as a way of motivating manufacturers. During the anthrax attacks of October 2001, for example, the Secretary of Health and Human Services extracted deep cuts from Bayer for its antibiotic Cipro (paying only one-quarter of the market price for the crucial drug) by threatening the company's patent protection.⁵³ Repeating actions of that type, however, will make companies less likely to invest in research and development for drugs against pandemics.

Over the long term, individuals and private entities making their own assessment of the risk of pandemic flu may also contribute to higher demand and establish their own stockpiles of antiviral drugs. Some observers argue that in the event of a pandemic, government distribution of Tamiflu and Relenza would be too slow so it would be better to distribute them prior to a pandemic. Others caution that incorrect dosing could be ineffective and that flu viruses with increased resistance to Tamiflu could develop if people take the drug incorrectly.

Strengthen Supply-Side Incentives to Develop New Antiviral Drugs. The Administration's proposal includes support for research and development for new antiviral drugs. But maintaining the intellectual property rights held by the current producers of such

53. "Fearing Avian Flu, Bioterror, U.S. Scrambles to Fill Drug Gap," *Wall Street Journal*, November 9, 2005.

Box 3.

Obstacles to Increasing the Production of Currently Available Antiviral Drugs

As with influenza vaccines, manufacturing mass quantities of certain products to address a flu outbreak could require substantial investment in facilities and might strain existing production processes. According to Roche, the maker of Tamiflu (also known as oseltamivir), production of that drug takes six to eight months and requires scarce ingredients and specialized facilities.¹ The active ingredient in Tamiflu—shikimic acid—comes from the star anise, a rare Chinese cooking herb. Researchers at Michigan State University have developed a synthetic version of shikimic acid; however, the production process for that compound requires using specialized fermentation equipment that companies may want to use for producing other products instead.

The manufacturing process for oseltamivir includes other complicating factors, such as the potentially dangerous use of sodium azide, a highly reactive chemical (also used to make automobile air bags inflate). Many companies, including Roche, contract out that step in the production process.

Even if those production issues were resolved, questions would arise about whether to depend on existing producers in the near term or to require compulsory licensing so that generic manufacturers who claim they are willing

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1. Andrew Pollack, "Is Bird Flu Drug Really So Vexing? Debating the Difficulty of Tamiflu," *New York Times*, November 5, 2005.

drugs is also likely to be as important as subsidies for new drug development in determining whether such activities actually occur.

On the research front, some researchers suggest that the government provide more money for research and development and for clinical trials to support the development of a new generation of antiviral drugs. Some observers have pointed out the effectiveness of statins (cholesterol-lowering drugs) in reducing flu symptoms from the H5N1 virus. Yet even without additional government resources for antiviral research, private firms are likely to view new antiviral drugs and antibiotics (some of which may treat pandemic influenza as well as other diseases) as potentially profitable enterprises.

Improve Readiness of the Health Care System. Over the long term, the preparedness of health care facilities to deal with a pandemic poses different challenges than those associated with purchasing vaccines and antiviral drugs. The construction of new hospi-

Box 3.**Continued**

and technically able to produce oseltamivir could do so. Having multiple companies produce antiviral drugs could increase worldwide supply and prevent manufacturing problems from contributing to shortages in an emergency. However, the global market in which drug production takes place complicates intellectual-property issues. The Indian drug company Cipla announced in October that it would begin manufacturing small amounts of generic Tamiflu without a sublicense from Roche; Taiwanese researchers have already produced small quantities of Tamiflu; and a Japanese company, Sankyo, has developed a new version of Relenza (zanamivir, another drug for treating influenza virus).

Intellectual-property concerns weigh into companies' decisions about whether to invest in products; a weakening of intellectual-property laws could deter firms from producing necessary antiviral drugs now and (equally important) in the future.² Roche, however, is in negotiations with some generic manufacturers to sublicense Tamiflu production.³

2. For a discussion of the relationship between future innovation and the protection of intellectual-property rights, see Congressional Budget Office, *Copyright Issues in the Digital Media* (August 2004), pp. 21-26.
3. James Kanter, "Roche Offers to Negotiate on Flu Drug," *New York Times*, October 19, 2005.

tal wings or clinics to add beds to the system would be a costly policy option. A way to begin to address the issue would be to adopt measures that allowed facilities to maintain the flexibility to use beds in a local stadium or community center, should an outbreak occur. But those solutions are by their nature local ones and not easily addressed by the federal government. At the federal level, assistance could be provided by continued stockpiling of medical equipment (such as ventilators and antibiotics) and technical assistance to communities, clinics, and hospitals. Federal support might also be used to increase the supply of health care personnel in short supply.

Technical Appendix

Calculating the economic effects of a potential influenza pandemic with any degree of precision is extremely difficult. There do not appear to be any empirical estimates of the effects of the three flu pandemics that occurred during the twentieth century.

However, it is possible to develop a rough estimate of the likely effects by examining the possible effects on the supply side of the economy and then adding the effects of declines in demand that result from people trying to avoid social contact in stores and other public places.

Supply-Side Effect

To calculate the supply-side impact of a pandemic, CBO calculated the effect of the loss of employee work days on GDP in the five sectors of the economy—nonfarm business, farm, households, nonprofit institutions, and general government—using average productivity per employee calculated in 2004 (the last full year for which data are available). That calculation required assumptions about (a) the gross attack rate in each sector, (b) the case fatality rate for each sector, and (c) the number of weeks that the “average” infected worker would miss because they were sick. Combining those assumptions with the level of employment in each sector, allowed CBO to calculate the “lost employment” for the year in which the pandemic occurs.¹ That lost employment is then multiplied by average productivity in the sector to compute the impact on GDP.

Specifically, the number of infected workers in a given sector is calculated by multiplying the gross attack rate by the level of employment in 2004. The infected workers are assumed to miss the “average” number of weeks of work; those who are assumed to die from their illness—computed by applying the case fatality rate to the number who take ill—are assumed to miss a full year of work. Clearly, those workers will not rejoin the labor force, but the calculation assumes that the reduction in the labor force will raise real wages, thus encouraging some people who were not part of the labor force to join it and eventually allowing the level of employment to regain its previous trend.

The specific values for the assumptions are given in Table A-1. For the severe scenario, CBO assumed that, on average, 30 percent of the workers in each sector (except for the farm sector) would take ill and, of those workers, 2.5 percent would die. CBO assumed that those who survived would miss 3 weeks of work either because they were sick or because they needed to care for family or friends that became sick.² Given the less social nature of work in the farm sector, CBO assumed a milder impact: one-tenth of the workers are affected and survivors miss only a single week of work (the

1. Implicit in the exercise is the assumption that the pandemic runs its course within 12 months, a span that could occur in more than one calendar year.

2. Three weeks out of work is likely to be at the high end of the range for those who are infected. However, it is also meant to account for healthy workers who are absent because they are caring for sick family members or children who are home from school and because they are too fearful of becoming sick to leave their homes.

Table A-1.

Assumptions Underlying Estimates of the Supply-Side Impact of an Avian Flu Pandemic

Economic Sector	Gross Attack Rate (Percent)		Weeks Out of Work		Case Fatality Rate (Percent)	
	Severe	Mild	Severe	Mild	Severe	Mild
Nonfarm Business	30	25	3	0.75	2.5	1.14
Farm	10	5	1	0.25	2.5	1.14
Household	30	25	3	0.75	2.5	1.14
Nonprofit Institutions	30	25	3	0.75	2.5	1.14
Government	30	25	3	0.75	2.5	1.14

Source: Congressional Budget Office.

Note: The gross attack rate is the percentage of the population that is infected with a disease. The case fatality rate is the percentage of infected persons who eventually die from the disease or complications.

case fatality rate was unchanged). Using data for 2004, CBO used average productivity per worker, by sector, to compute the impact on GDP of the employment lost to the pandemic.³

For the mild pandemic CBO assumed a 25 percent attack rate (except in the farm sector, which was assumed to be 5 percent), a case fatality rate of just over 0.1 percent, and cut the time out of work to one-quarter of the duration assumed for the severe scenario (i.e., just under four days absent, on average).

Demand-Side Effect

To calculate the demand-side effect, CBO examined GDP by industry and assumed different declines in demand for different industries, based on judgments about the degree of social interaction required in different industries. Given that there is little historical evidence available to form these estimates, they are admittedly extremely rough. Industries that require interpersonal contact are assumed to have the largest declines in demand. For example, CBO assumed that demand would fall off by 80 percent (for three months) in the entertainment, arts, recreation, lodging, and restaurant industries, a set of industries that composed just under 4 percent of GDP in 2004 (see Table A-2). Other industries were assumed to suffer a smaller decline in demand. Retail trade, for example, was assumed to suffer a 10 percent decline, as were the wholesale trade and manufacturing industries.⁴ In contrast, there would be a surge in demand for medical care, which CBO assumed would rise 15 percent relative to a base case without a pandemic. For the mild scenario, CBO assumed that the demand-side declines in each industry were one-quarter of the declines in the severe scenario.

3. The analysis ignores the possibility that productivity among workers who remain on the job would be likely to rise.

4. The government sector would not have any demand-side impact in addition to the supply-side impact.

Note that some of the impact on overall GDP of the drop in demand would already be accounted for by the decline in supply. Therefore, CBO subtracted the supply-side impact of the pandemic on each industry from the estimate of demand-side impact before adding the two effects together to calculate the effect on GDP. That procedure avoided double-counting the supply-side effects.

Table A-2.

**Assumed Declines in Demand, by Industry, in the
Event of an Avian Flu Pandemic**

(Percent)

	Severe Scenario	Mild Scenario
Private Industries		
Agriculture	10	3
Mining	10	3
Utilities	0	0
Construction	10	3
Manufacturing	10	3
Wholesale trade	10	3
Retail trade	10	3
Transportation and warehousing		
Air	67	17
Rail	67	17
Transit	67	17
Information (Published, broadcast)	0	0
Finance	0	0
Professional and business services	0	0
Education/health care		
Education	0	0
Health care	-15	-4
Arts/entertainment/ accommodation/food		
Arts and recreation	80	20
Accommodation	80	20
Food service	80	20
Other services except government	5	1
Government		
Federal	0	0
State and local	0	0

Source: Congressional Budget Office.

Note: The severe scenario describes a pandemic that is similar to the 1918-1919 Spanish flu outbreak. It incorporates the assumption that a particularly virulent strain of influenza infects roughly 90 million people in the United States and kills more than 2 million of them. The mild scenario describes a pandemic that resembles the outbreaks of 1957 to 1958 and 1968 to 1969. It incorporates the assumption that 75 million people become infected and about 100,000 of them die from the illness or complications.
