REPORT TO THE PRESIDENT ON U.S. PREPARATIONS FOR 2009-H1N1 INFLUENZA

Executive Office of the President

President's Council of Advisors on Science and Technology

August 7, 2009

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EXECUTIVE OFFICE OF THE PRESIDENT
PRESIDENT'S COUNCIL OF ADVISORS ON SCIENCE AND TECHNOLOGY
WASHINGTON, D.C. 20502

August 7, 2009

President Barack Obama
The White House
Washington, DC 20502

Dear Mr. President:

We are pleased to transmit to you the report, *U.S. Preparations For 2009-H1N1 Influenza*, prepared by your Council of Advisors on Science and Technology (PCAST). This report examines the strategic issues raised by the likely resurgence this fall of the novel influenza virus called 2009-H1N1.

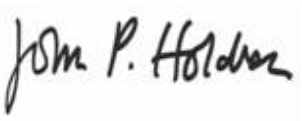
The report reviews the full range of response options for minimizing negative impacts from a fall 2009-H1N1 epidemic and provides an integrated set of recommendations about how to think about hard issues and key policy decisions regarding the epidemic. The nation's response to the threat of a fall epidemic involves decisions by government on a wide range of issues --- medical, scientific, social, and financial. We have tried to assess these, keeping in mind your interest in having the best available scientific insights and perspectives to inform your thinking about the nation's response to the continued spread of this new virus.

To provide a solid scientific basis for our recommendations, the Council assembled a PCAST Working Group of non-governmental experts, including one other member of PCAST, from a number of relevant fields (virology, public health, pediatrics, medicine, epidemiology, immunology, and others). On July 16-17, the Working Group met with government officials and others to discuss various aspects of the 2009-H1N1 pandemic, and then developed an in-depth report based on its own knowledge, the information provided during the meeting, and additional consultations with government, academic, and industry experts. The results of that report were presented to PCAST at its meeting on August 6-7, and the Council then approved an Executive Report of findings and recommendations for transmittal to you along with the in-depth Working Group report to PCAST.

The Working Group report discusses the complexities posed by influenza epidemics, and the uncertainties inherent in an epidemic that is still in progress. The report identifies the key decisions and actions to be taken, while recognizing that many decisions (for example, relating to use of vaccines and to school closures) cannot be resolved now but will need to be made rapidly as the epidemic unfolds. In these instances, the Working Group report instead offers guidance about how decisions should be made over the coming weeks and months.

PCAST hopes that its Executive Report and the full Working Group report help lay a foundation for the medical, scientific, social, and financial decisions you and others in the Federal Government must make this fall. We are grateful for the opportunity to serve you and the country in this way.

Sincerely,



John P. Holdren
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The President's Council of Advisors on Science and Technology

Executive Report

U.S. Preparations for the 2009-H1N1 Influenza

In April 2009, a novel influenza A (H1N1) virus (2009-H1N1) appeared in Mexico, causing pneumonias and 59 deaths in Mexico City alone. The virus soon spread to the United States and to other continents. Within two months, the World Health organization (WHO) declared that the viral outbreak met the criteria of a level 6 pandemic. Although initial concerns of an extremely high fatality rate have receded, the expected resurgence of 2009-H1N1 in the Fall poses a serious health threat to the United States.

Since the initial report of the outbreak, the Federal Government, through various departments, agencies, and offices, has been actively studying the course of events, responding to them, and planning for a resurgence of the pandemic this fall. In late June, President Obama requested that his Council of Advisors on Science and Technology (PCAST) undertake an evaluation of the 2009-H1N1epidemic and the nation's response to a probable recurrence.

In this Executive Report, PCAST assesses the emerging Federal response to a second wave, identifies critical questions and gaps in this response, and suggests additional opportunities for mitigation. PCAST's observations, conclusions, and recommendations presented here are based on the analysis of its 2009-H1N1 Working Group, consisting of 3 PCAST members and a further 11 non-governmental experts in virology, public health, pediatrics, medicine, epidemiology, immunology, and other relevant scientific fields. The Working Group's deliberations were informed by discussions with government officials and others on various aspects of the 2009-H1N1 pandemic.

2009-H1N1 in Historical Context

Based on the history of influenza pandemics over the past hundred years, PCAST places the current outbreak somewhere between the two extremes that have informed public opinion about influenza. On the one hand, the 2009-H1N1 virus does not thus far seem to show the virulence associated with the devastating pandemic of 1918-19; moreover, medical science now has many potent tools at our disposal to mitigate an influenza pandemic in ways that were not possible ninety years ago. On the other hand, the 2009-H1N1 virus is a serious threat to our nation and the world, unlike the "swine flu" episode in 1976 that led to the vaccination of over 40 million Americans in the absence of any spread of the virus beyond an initial four cases at a single Army base.

The Current Situation and a Plausible Scenario

Indeed, the 2009-H1N1 influenza is already responsible for significant morbidity and mortality worldwide — from its appearance in the spring, its continued circulation in the U.S. this summer, and its spread through many countries in the Southern Hemisphere during their winter season. While the precise impact of the fall resurgence of 2009-H1N1 influenza is impossible to predict, a plausible scenario is that the epidemic could:

- **produce infection of 30–50% of the U.S. population this fall and winter**, with symptoms in approximately 20–40% of the population (60–120 million people), more than half of whom would seek medical attention.
- **lead to as many as 1.8 million U.S. hospital admissions during the epidemic**, with up to 300,000 patients requiring care in intensive care units (ICUs). Importantly, these very ill patients could occupy 50–100 percent of all ICU beds in affected regions of the country at the peak of the epidemic and could place enormous stress on ICU units, which normally operate close to capacity.
- **cause between 30,000 and 90,000 deaths in the United States**, concentrated among children and young adults. In contrast, the 30,000–40,000 annual deaths typically associated with seasonal flu in the United States occur mainly among people over 65. As a result, 2009-H1N1 would lead to many more years of life lost.
- **pose especially high risks for individuals with certain pre-existing conditions**, including pregnant women and patients with neurological disorders or respiratory impairment, diabetes, or severe obesity and possibly for certain populations, such as Native Americans.

There is an important issue with respect to **timing**:

- The fall resurgence may well occur as early as September, with the beginning of the school term, and the peak infection may occur in mid-October.
- But significant availability of the 2009-H1N1 vaccine is currently projected to begin only in mid-October, with several additional weeks required until vaccinated individuals develop protective immunity.

This potential mismatch in timing could significantly diminish the usefulness of vaccination for mitigating the epidemic and could place many at risk of serious disease.

PCAST emphasizes that this is a planning scenario, not a prediction. But the scenario illustrates that an H1N1 resurgence could cause serious disruption of social and medical capacities in our country in the coming months. The circumstances underscore the importance of:

- ensuring that the nation's complex and distributed healthcare systems are prepared to deal with the potential surge in demand, especially with respect to critical care.
- ensuring that all feasible steps are taking to protect the most vulnerable populations.

Preparations for the Pandemic: Observations and Recommendations

Preparation for the predicted fall resurgence has been constrained by time and materials: the virus appeared in late spring and its resurgence is anticipated in early fall, while vaccine production currently requires at least 6 months. On the other hand, the development of preparedness plans was greatly stimulated by the recognition a few years ago of the threat posed by a highly lethal avian influenza; preparations developed for this potential threat facilitated the response to the current, quite different strain of influenza virus.

PCAST is impressed by the efforts underway across our government—including the breadth and depth of thinking, energy being devoted, and awareness of potential pitfalls. The response is probably the best effort ever mounted against a pandemic, reflecting past preparedness efforts and the quality and commitment of the people involved.

Still, PCAST found some aspects of the decision-making and preparation processes that we believe could be improved, even in the short time remaining before the fall. These findings and recommendations are discussed at considerable length in its Working Group report.

Reflecting the rapid pace of response in the Federal Government, some of the suggested actions are already being considered, planned, or initiated by relevant agencies. In these cases, our recommendations are intended to provide support and additional focus to such efforts. Our recommendations fall into seven major categories:

1. **Coordination**. We suggest that coordination of the decision-makers could be more effectively orchestrated if a single person in the White House were assigned the responsibilities of clarifying decision-making authorities and processes, ascertaining that all important issues are resolved in a timely fashion, and reporting to you about actions to be taken.

2. **Scenarios**. We believe that preparations could be strengthened if the Federal Government developed and disseminated a few specific planning scenarios that Federal, state, local, and private entities could use to assess their capacities and plans for medical and non-medical interventions.

3. **Surveillance**. The ability to respond to the epidemic will depend on reliable and timely information about its course at the national, regional, and local level. We believe there are opportunities to make important upgrades to existing national surveillance systems in time for the expected fall resurgence.

4. **Response**. There are four critical pillars of a mitigation effort: vaccines, anti-viral drugs, medical care, and non-medical interventions that diminish virus spread. In particular, we focus on decisions that could reduce instances of severe disease and death by accelerating the delivery and use of vaccines; developing integrated plans to protect especially vulnerable populations; and ensuring access to intensive care facilities.

5. **Barriers**. Some legal, social, and financial barriers exist that may reduce compliance with some recommended measures for mitigation and we propose ways that the Federal Government and others could work to overcome such barriers.

6. **Communication**. Communication plans for relaying to the states, health workers, and the general public the government's recommended actions for mitigation are in some cases inadequate and should be strengthened.

7. **Future Preparedness**. The current outbreak highlights gaps in our capacity to combat epidemics caused by influenza and other agents. We outline steps that can be taken in the next few years, including improving vaccine production and design, anti-viral drug development, and health surveillance systems.

Action Items

In the report, PCAST makes a number of recommendations about specific aspects of the national preparations. Several are of special importance and warrant consideration for immediate or near-term action. Specifically, PCAST proposes that the President:

i. Designate a senior member of the White House staff, preferably the President's Homeland Security Advisor, to be responsible for **coordination** of all major decision-making about the 2009-H1N1 pandemic.

and that the relevant Federal agencies:

ii. Produce and disseminate several **planning scenarios** and work with Federal, state, local, and private entities to **anticipate potential 'surge' demand** (especially for critical care, e.g., ICUs and respirators) and **develop logistical plans** for such contingencies.

iii. Expand CDC's existing **surveillance systems** to track information about influenza-like illnesses from an integrated network of sites, including data from population sampling, emergency rooms, and hospitals, with emphasis on critical care units.

iv. **Accelerate production** of an initial quantity of **finished vaccine** as early as mid-September, to allow vaccination of up to 40 million people, with emphasis on the most vulnerable age and disease groups, as soon as initial data are available on safety and immunogenicity. This decision would need to be made almost immediately.

v. **Develop focused plans** to identify, reach, and **protect members** of the most **vulnerable groups** and their health care providers in time to make use of the protective methods at the nation's disposal.

vi. Prepare a **communication plan** that would deliver appropriate and effective messages about the range of available medical and non-medical interventions, including especially vaccination, to the public in a timely fashion.

vii. **Organize a multi-agency effort**, under the direction of the National Security Council, to improve the **design and production of influenza vaccines**, so that effective vaccination programs can begin more promptly in the course of future epidemics caused by new strains of influenza virus.

Caveats About the Report

The urgency of an ongoing pandemic, one that is likely to worsen in the next month or two, has compelled PCAST and its Working Group to perform its tasks rapidly. Under these circumstances, some of the information gathered by the Working Group for this report (such as the schedule for availability of vaccines and clinical data on infected individuals) must be viewed as provisional and subject to change.

Given the complexity of the situation and the many activities underway to deal with it, PCAST recognizes that the Working Group could not analyze the problem from every perspective and has doubtless failed to acknowledge all of the useful work that is already being done by members of the Obama Administration. In particular, the report does not rigorously address the measures that might need to be taken in the unlikely event that the pandemic proves to be much more severe than we currently envision.

Next Steps

PCAST hopes that its report and that of its Working Group help guide the urgent work that the Administration has undertaken to mitigate the effects of the 2009-H1N1 pandemic. PCAST and its Working Group are prepared to respond to additional questions that members of the Administration might have in the coming months.

The President's Council of Advisors on Science and Technology

2009-H1N1 Working Group Report

PCAST
2009–H1N1 Working Group

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I. Introduction and Charge

CHAPTER SUMMARY

In April 2009, a novel influenza A/H1N1 virus (2009-H1N1) appeared in Mexico, causing pneumonias and 59 deaths in Mexico City alone. The virus soon spread to the United States and to other continents. Within two months, the World Health Organization (WHO) declared that the viral outbreak met the criteria of a level 6 pandemic. As of August 2009, the virus continues to spread in the United States and elsewhere.

Although initial concerns of an extremely high fatality rate have receded, the expected resurgence of 2009-H1N1 in the fall poses a serious health threat to the United States. Further, although most cases are mild, serious complications arise in some individuals, especially those with underlying medical complications such as pregnant women and those with neurological conditions. Under some models, seriously ill influenza patients could require 50 to 100 percent of intensive care unit (ICU) beds at the epidemic's peak, stressing the medical and public health systems to the point of overwhelming some hospitals, and could cause from 30,000 to 90,000 deaths, concentrated among children and young adults.

Since the initial report of the outbreak, the Federal Government, through various departments, agencies and offices, has been actively studying the course of events, responding to them, and planning for a resurgence of the pandemic this fall.

Under the aegis of the President's Council of Advisors on Science and Technology (PCAST), a Working Group on 2009-H1N1 influenza was formed in response to the President's request for an expert external review of the epidemic and the nation's response to an anticipated resurgence in the fall of 2009. Overall, the Working Group was deeply impressed by the efforts underway across the Federal Government—including the breadth of issues being anticipated and addressed, the depth of thinking, the overall level of energy being devoted, and the awareness of potential pitfalls.

The Working Group did identify some potential ways to strengthen the response, and it has provided recommendations. In many cases, the relevant agencies are already aware of these opportunities and are taking steps in these directions. The Working Group's recommendations are intended to provide support for and additional focus to such efforts.

On April 15, 2009, the first case of infection with novel influenza A (H1N1) virus ("swine flu," hereafter "2009-H1N1") was confirmed in the United States. In March and April, Mexico had experienced an outbreak of unexplained pneumonia, with hundreds of reported cases and 59 deaths in Mexico City alone. It soon became clear that 2009-H1N1 was associated with the Mexican pneumonia outbreak and that the virus was spreading within North America; it was soon detected in many other countries. On April 29, the World Health Organization (WHO) raised its influenza pandemic alert level to Phase 5, just short of declaring that a global influenza pandemic was underway. In those early days of the outbreak, severe cases were the most readily counted because they were usually hospitalized. As of April 29, 8 of 148 individuals with confirmed 2009-H1N1 infection worldwide had died (5.4 percent), initially raising

the possibility that the virus was extremely virulent, comparable to or even worse than the viral strain that caused the 1918-19 influenza pandemic. But uncertainty about the number of unconfirmed cases—especially infected individuals with mild or no symptoms—made it impossible to assess severity accurately. In fact, subsequent data revealed that the case-fatality ratio was actually much lower—although still a cause for serious public concern.

As more cases were confirmed around the United States in late April and early May, the Centers for Disease Control and Prevention (CDC), in coordination with state and local public health departments, increased surveillance efforts and issued interim guidance to control the virus's spread. Intensified surveillance rapidly clarified that many mild cases had been missed in the early phases of the epidemic, easing concerns that the new virus was extremely virulent, but still leaving uncertain the overall spectrum of illness and incidence. Media coverage was intense. Advisories warned against travel to Mexico and soon against travel to the United States. In regions of the United States with reported cases, some schools were closed just days or weeks short of the end of the school year. By June 11, the virus had spread to 74 countries and all continents but Antarctica, and WHO declared the outbreak an influenza pandemic (Phase 6) on the basis of its geographic spread. As summer began and schools adjourned, travel advisories were rescinded and media and public attention waned.

Although influenza usually becomes almost undetectable during the summer, transmission of 2009-H1N1 virus continues in the United States (albeit at a lower level) and in other Northern Hemisphere countries, notably the United Kingdom. While monitoring of clinical outcomes to date suggests that most 2009-H1N1 infections are mild, there have been notable reports of people with severe illnesses, many of them requiring intensive hospital care, and deaths, predominantly among relatively young people. Certain groups—such as the First Nation people in rural Manitoba, Canada—appear to have been particularly hard hit. And even mild outbreaks have in many cases been socially disruptive.

The Southern Hemisphere's regular influenza season is now underway, and 2009-H1N1 has spread rapidly within Argentina, Australia, Chile, and New Zealand, appearing to eclipse infection with the expected seasonal influenza virus and stressing the medical and public health systems to the point of overwhelming some hospitals and filling some intensive care units (ICUs) to capacity. For example, in Australia, 11 percent of over 20,000 confirmed cases of 2009-H1N1 influenza have been hospitalized. And of the 410 cases now hospitalized, 110 are in ICUs.

As the influenza season in the Northern Hemisphere approaches and schools reopen, the pandemic is expected to accelerate, with the potential for significant health consequences in the United States, Europe, and other regions. Based on past pandemics, this acceleration is likely to occur before the normal (i.e., seasonal) influenza season, starting in September and peaking in October. In a typical (non-pandemic) season, influenza becomes prevalent in winter and causes an estimated 30,000 to 40,000 deaths in the United States, with about 90 percent of those deaths occurring in patients ages 65 years or older.

A plausible scenario, given current data (and described in more detail in Chapter 3), is that 2009-H1N1 influenza could place enormous stress on U.S. medical and public health systems, as well as on an American economy already under stress. It could cause anywhere from 30,000 to 90,000 deaths in the United States in fall 2009, mainly among younger adults and children (unlike the situation with seasonal influenza, which causes death mainly in the elderly) and those with certain pre-existing conditions.

Moreover, as much as 50 to 100 percent of ICU capacity in the United States could be required solely to treat 2009-H1N1 patients at the peak caseload, in hospital units that typically run at 80 percent of capacity. Such stress on ICUs and emergency departments would cause severe disruption of hospital function, necessitating marked curtailment of all but the most urgent admissions and surgeries.

These estimates assume that the clinical severity of infection with the 2009-H1N1 virus will be the same this fall as it was in the spring. Even so, the estimates of serious disease and death could be off by several-fold because the total number of infected persons to date—and proportion of severe infections—remain extremely uncertain. In addition, there is a possibility, difficult to quantify, that severity could change, either up or down, as the virus evolves (see Box 1A). Various public health measures can be taken to attempt to mitigate the pandemic. It is clear, however, that many of the decisions about whether and when to employ these mitigation measures will have to be made rapidly, before many uncertainties are resolved.

Since the outbreak began in late April 2009, the Federal Government—through various departments, agencies, and offices, especially the Department of Health and Human Services (DHHS), the Department of Homeland Security (DHS), and components of the White House staff—has been actively studying the course of events, responding to them, and planning for a resurgence of the pandemic this fall. As a consequence of concerns since 2004 about the possibility of a pandemic involving the highly pathogenic avian (H5N1) influenza virus, the United States has been especially well positioned to organize a response to the 2009-H1N1 pandemic. Preparedness activities have included:

- releasing antiviral drugs from the national stockpile;
- contracting with several pharmaceutical companies to develop and manufacture vaccines against 2009-H1N1 as quickly as possible;
- removing restrictions on the use of unapproved medical treatments and tests under public health emergency conditions;
- increasing surveillance at multiple levels (e.g., virus identification and characterization; data on outpatients, hospitalized patients, and mortality);
- convening a summit of states, tribes, and territories to plan responses to the epidemic;
- overseeing congressional passage of an emergency funding measure (described in greater detail below) for a variety of uses, including purchase of vaccines and drugs, support of non-Federal public health initiatives, and additional needs at CDC and the Food and Drug Administration (FDA);
- providing funds to state and local public health offices and health care systems to step up their preparedness efforts;
- undertaking public communication efforts; and
- issuing guidance for the general public, clinicians, laboratories, pregnant women, schools, and communities.

BOX 1A: THE 2009-H1N1 INFLUENZA VIRUS

In the few months since its first isolation, the 2009-H1N1 influenza virus has been quickly subjected to intense study of its molecular properties, illustrating the capacities of modern virology and genetics.

Like other influenza viruses, the genes of the 2009-H1N1 virus are arrayed on eight segments of single-stranded RNA that, in the aggregate, constitute the viral genome. Genomes of these viruses are inherently unstable, with frequent changes in each RNA segment accounting for genetic "drift," and reassortment of segments when cells are co-infected with two or more viruses, accounting for more dramatic genetic "shift." The 2009-H1N1 virus is a "triple reassortant," as it contains RNA segments from avian-, human-, and swine-origin viruses. The majority of RNA segments, including the segment coding for the hemagglutinin protein, come from swine-origin viruses. Hemagglutinin mediates immune protection against influenza viruses, is notable for rapid changes in its composition, and forms the basis for the annual reformulation of influenza virus vaccines. It is also one of the two major proteins on the viral surface, hemagglutinin (H) and the neuraminidase (N), that determine the subtype classification of type A influenza viruses as 'H1N1,' 'H3N2,' etc.

Of all of the H1 subtype hemagglutinins in viruses isolated from humans in the 20th and 21st centuries, the hemagglutinin of the 2009-H1N1 appears to be genetically most similar to those of the 1918-19 H1N1 pandemic virus and of the H1N1 virus of swine-origin that caused the limited human outbreak at an army base in New Jersey in 1976. It is less closely related to the hemagglutin in other strains of H1N1 virus responsible for seasonal influenza in recent years.

The relatively low virulence of 2009-H1N1 virus may be attributed, in part, to the absence of a major determinant of virus virulence—the expression of a protein called PB1-F2 that is known to cause cell death and was found in viruses responsible for the major influenza pandemics of 1918-19 (H1N1), 1957 (H2N2), and 1968 (H3N2).

The 2009-H1N1 virus is atypical in some ways, including its transmissibility during warm seasons and its apparent infection of the gastrointestinal tract in approximately one-third of serious cases. These and other properties of the new virus will be subject to more intensive study and comparisons with earlier isolates in the near future in order to understand its mode of pathogenesis, virulence, transmission rate, and immunogenic properties.

On June 24, 2009, President Obama signed into law the Supplemental Appropriations Act, 2009 (Public Law 111-32). Within the Act, Congress appropriated $7.65 billion to DHHS to prepare for the 2009-H1N1 influenza outbreak, including a $5.8 billion contingent appropriation. After spending an initial $1.85 billion on procurement of vaccines, expansion of surveillance activities, and preparation for a possible immunization campaign, on July 16 the President designated an additional $1.825 billion as emergency funds to support additional measures related to influenza vaccination efforts, leaving $3.975 billion in reserve as contingency funds.

In early July, President Obama asked his Council of Advisors on Science and Technology (PCAST) to provide an expert external assessment of the epidemic and to offer guidance about the nation's plans

to respond to its likely resurgence in the fall. PCAST established a Working Group on 2009-H1N1, co-chaired by Drs. Harold Varmus and Eric Lander, consisting of experts in the fields of virology, public health, and medicine, with experience in the academic, governmental, philanthropic, and industrial sectors.

PCAST's charge was several-fold:

- to identify critical questions for which timely answers are needed by decision-makers;
- to survey and assess preparations currently underway in the Federal Government;
- to highlight major challenges and gaps; and
- to make specific recommendations concerning additional opportunities to help mitigate a serious 2009-H1N1 flu pandemic this fall.

The Working Group worked on an accelerated schedule during the month of July 2009 to respond to its charge. It met July 16–17, 2009, in Washington, D.C., to hear presentations from Federal agency leaders, epidemiologists, state and international public health officials, vaccine and drug developers, and experts in social mitigation strategies, including public information and marketing. In addition, interviews were conducted at other times with government officials and experts on various aspects of the influenza epidemic.

The Working Group's goal was not to predict the severity of any next wave of the epidemic or to prescribe specific responses. Instead, the goal was to provide guidance to support and strengthen the many efforts already underway to prepare the country for the expected resurgence of 2009-H1N1 in the fall.

MAIN CONCLUSION

Overall, the Working Group was deeply impressed by the efforts underway across the Federal Government—including the breadth of issues being anticipated and addressed, the depth of thinking, the overall level of energy being devoted, and the awareness of potential pitfalls. The response is probably the best effort ever mounted against a pandemic, reflecting both past preparedness efforts and the quality and commitment of the people involved.

The Working Group did identify some potential ways to strengthen the response. In many cases, the relevant agencies are already aware of these opportunities and are taking steps to address them, while recognizing that time is short and that some goals may not be achievable. The Working Group's recommendations are intended to provide support for and additional focus to such efforts.

To present its observations in a logical narrative, this report is organized in chapters focused on the Nation's prior experience with influenza; scenario planning; surveillance of the current epidemic; decision-making about measures to mitigate the epidemic; lowering legal and economic barriers to response; communications; and steps to strengthen the response to future epidemics. In addition to providing specific guidance to relevant agencies, the report aims to provide sufficient background to be readable by members of the general public, who are understandably concerned about the current outbreak and the Nation's response.

II. The U.S. Experience with Influenza Over the Last Century

CHAPTER SUMMARY

Seasonal influenza epidemics occur every winter and are estimated to cause some 30,000-40,000 deaths in the United States alone, primarily in young children, the elderly, and others with underlying medical conditions. Several times in the last century new subtypes of influenza have swept through the human population—which has little or no immunity to them—and caused global pandemics.

Preparation for influenza pandemics is shaped in large part by the experiences of the pandemic of 1918-19, when 40-100 million people perished worldwide, and the swine flu "fiasco" of 1976, when 45 million Americans were vaccinated for a virus that never spread beyond a tiny cluster. In 2005, concerns that the highly lethal avian H5N1 virus could precipitate an influenza pandemic led to significant investments and improvements in Federal preparedness, although significant transmission among humans has fortunately not occurred to date. Based on available information, the influenza pandemics most analogous to the current 2009-H1N1 outbreak may be those of 1957 and 1968, in which the death rates were two- to four-fold higher than normal.

The main lessons from these experiences are that vigorous preparation and action can save lives, but that it is critical to maintain situational awareness and flexibility as a pandemic unfolds.

Introduction

Seasonal influenza epidemics occur every winter, peaking between December and February, and are estimated to cause 30,000 to 40,000 deaths in the United States alone, primarily in children under age 2 and adults over age 65, and more than 250,000 hospitalizations per year. The economic impact of seasonal influenza is estimated at $37 billion each year.

Since 1977, two influenza A virus subtypes and one influenza B subtype have circulated each winter. Seasonal influenza viruses undergo frequent mutations that can cause small changes in proteins necessary for entry into human cells, allowing them a measure of protection against immune responses, even in people who were infected with prior strains. (Influenza viruses are classified by these proteins, called hemagglutinin [H] and neuraminidase [N]; see Box 1A in Chapter 1.) This genetic variability means that people experience repeated influenza infections over their lives and vaccine formulations must be updated nearly every year.

At irregular intervals, new subtypes of influenza burst on the scene and sweep through the human population, which has no significant immunity to them. Such global pandemics appear to occur three to four times per century. In the twentieth century, pandemics were caused by new variants of influenza

A virus in 1918 (H1N1), 1957 (H2N2), and 1968 (H3N2). These pandemics varied in severity, for reasons related both to the level of pre-existing immunity in the human population and to the genetic makeup of the virus. In spite of extraordinary scientific advances in understanding influenza viruses, they remain highly unpredictable.

Responses to new pandemics should be informed by historical experience. The severe pandemic of 1918–19 offers some lessons about the benefits of rapid action, and the swine flu vaccination campaign of 1976 is instructive about the risk of an overly aggressive response to an unproven threat. Over the past five years, the emergence of human cases of a highly pathogenic avian H5N1 influenza has stimulated unprecedented pandemic planning efforts.

1918–19 Influenza Pandemic

The 1918–19 pandemic was the worst natural calamity of the twentieth century, with an estimated mortality worldwide of 40–100 million lives. In the United States, between 500,000 and 750,000 perished at a time when the U.S. population was one-third its current size. In contrast to seasonal influenza, mortality was especially high among previously healthy young adults. In cities that adopted early measures of "social distancing," such as cancelling public gatherings and closing schools, the epidemic appeared to have spread more slowly and reached a lower peak incidence.

What is most informative about the 1918–19 pandemic for current planning purposes is its pattern of spread. A first, or spring, wave began in March 1918 and spread unevenly across the United States, Europe, and Asia. Although illness rates were high, death rates in most locations were not significantly above those of seasonal influenza. The spring outbreak was mild enough that the public health and medical communities saw no cause for alarm. However, a second, fall wave spread globally from September to November 1918, with death rates approximately ten-fold higher than in the spring. Cities that responded rapidly by closing schools, churches, and theaters, restricting public gatherings, and otherwise discouraging social interaction appear to have reduced transmission and mortality while the measures were in effect. However, most cities could not sustain these measures, and many experienced the return of influenza as control efforts lapsed. In some places, a third wave occurred in early 1919. Death from pneumonia was a hallmark of the 1918–19 fall and winter waves. The 1918–19 pandemic vividly illustrates what can happen when the public health and medical communities lack knowledge, contingency plans, and effective vaccines or treatments.

1976 Swine Flu "Fiasco"

The events of 1976 serve as an example of a public health response premised only on the "worst case" scenario, which ended up being a false alarm. In January 1976, a novel H1N1 virus first appeared in a group of army recruits at Fort Dix, New Jersey. Four were hospitalized and one died. In March, on the advice of public health experts, President Gerald Ford announced on television that he was asking Congress for $137 million "to inoculate every man, woman, and child in the United States" against swine flu. Within 10 weeks of the launch of the fall vaccination campaign, about 45 million people, or 1 in 4 Americans, had received swine flu immunizations. Public confidence, however, was soon shaken by the deaths of three elderly adults in Pittsburgh soon after they received their swine flu shots. Although such

events are expected by chance, local public health officials and the media raised the possibility that the deaths were due to the immunizations. Later reports found Guillain-Barré syndrome, a paralyzing neuromuscular disorder, to be associated with 1976 vaccination at a frequency of approximately 1 per 100,000 vaccinations. With no disease from the swine flu virus having appeared since the outbreak at Fort Dix, even this relatively rare complication was enough to lead to the suspension of the immunization program.

The key policy error in 1976 was to bundle all decisions (e.g., make the vaccine, immunize everyone, make a Presidential announcement) into a single "go" or "no-go" decision, with no provision for the monitoring of the situation and continual reconsideration of policy directions based on new evidence. The experience of 1976 highlights the challenge of coordination horizontally across different agencies of the Federal Government; vertically across the various levels of government (Federal, state, local); among public officials and health professions and institutions; and between the public and private sectors. The 1976 swine flu immunization program highlighted other lessons, including the importance of communication to the public, the long-term need to preserve credibility, and the need for preparations relating to vaccine liability insurance anticipation of coincident deaths in a mass immunization program, the potential impact of vaccine side effects, and the role of chance.

In applying these lessons to present circumstances, it is worth noting a number of crucial differences between then and now. Among them: (1) the current 2009-H1N1 is continuing to spread, unlike the single, self-quenching outbreak at Fort Dix; (2) a wider array of interventions, including antiviral medications, is available; (3) more sophisticated characterization and surveillance systems for circulating viral strains are in place; (4) the Federal Government has a more complex structure and a larger number of relevant agencies and officials; (5) the media are vastly more varied and operate on a continuous news cycle; and (6) widespread international travel contributes to accelerated transmission around the world.

Other Pandemics

The two other influenza pandemics in the last century also provide insight into the current situation. The so-called "Asian Flu" of 1957 appeared in the United States in late spring. Small outbreaks occurred over the summer, but transmission accelerated in the late summer through early fall, peaking in October before vaccine supplies were widely available. Public health authorities learned an important lesson about the potential value of early protection against influenza. After a lull following the October peak, there was a smaller upsurge in transmission in early 1958, in which the elderly were disproportionately affected. Mortality in 1957–58 was high—an estimated 70,000 deaths in a population of about 170 million. Although death rates were highest among the elderly, about 30 percent of all deaths occurred in those under age 65.

The mildest of the twentieth century pandemics occurred in 1968, with an estimated 34,000 deaths in a population roughly two-thirds of today's; death rates were highest in the elderly, but about half of all deaths occurred in people under age 65. The 1968 virus emerged first in Hong Kong in mid-1968 and appeared in the United States in September, but did not peak until December 1968/January 1969. One reason for the slower spread and reduced death toll during the 1968 pandemic may be that the virus (H3N2) shared some similarities with the virus that was already circulating (H2N2), so the population may have been partially immune.

In the decade following each of the twentieth-century pandemics, seasonal epidemics continued and excess deaths in younger age groups remained elevated above normal seasonal levels. These recent pandemics illustrate that the timing of peak pandemic activity may be earlier than that of normal flu season, but unpredictable in that younger age groups suffer more during pandemics than during seasonal influenza outbreaks, and that the impact of new strains on these younger groups persists into subsequent seasons.

Avian Flu

In Hong Kong in 1997, a highly pathogenic avian H5N1 virus was found to have infected large numbers of poultry and a small number of humans. Following initial control by extensive slaughter of poultry flocks, the virus disappeared, only to reappear in 2003–2004. The virus was felt to be a potential pandemic threat because, although the rate of bird-to-human transmission was low and person-to-person spread was rare, the mortality rate was over 60 percent.

The possibility that H5N1 could acquire the ability to transmit efficiently between humans and thereby start a new and severe pandemic spurred major pandemic-planning efforts at the state, Federal, and global levels. Beginning in 2005, the Federal Government undertook a number of initiatives to address this threat, including: (1) developing a "National Strategy for Pandemic Influenza" to guide the preparedness efforts of Federal departments and agencies, state and local authorities, businesses, and the public; (2) requesting that Congress appropriate $7.1 billion to establish a domestic stockpile of antiviral medications and pre-pandemic vaccine and to significantly expand domestic influenza vaccine production capacity; (3) developing guidance on pandemic influenza preparedness for the public and a broad spectrum of stakeholders outside of the Federal Government; (4) establishing policies to guide the pandemic response in areas such as border management and prioritizing allocation of pre-pandemic vaccine; and (5) creating the International Partnership on Avian and Pandemic Influenza to facilitate global surveillance and preparedness actions.

These and other efforts in response to the H5N1 threat have informed and guided many of the actions undertaken in response to the 2009-H1N1 outbreak to date.

Lessons for Fall 2009

Given the concern about avian influenza and awareness of the catastrophic results of the 1918–19 pandemic, much of the effort for pandemic planning has been directed toward responding to an extremely severe pandemic. This worst-case-scenario planning has led to improvements in the efficiency of vaccine production and testing, stockpiling of antiviral drugs, and other measures that will be valuable in the fall, if used appropriately. However, unless the severity of the 2009-H1N1 influenza increases markedly, it is unlikely that community mitigation on the scale envisioned for a more severe pandemic will be required. On the other hand, as described in the next chapter, it is already clear that the current pandemic is no false alarm (as in 1976) and has the potential to cause serious health consequences, especially in relatively young age groups and in individuals with certain pre-existing medical conditions.

While the features of 2009-H1N1's next wave cannot be accurately predicted, history teaches us that the most effective responses will be achieved by advanced planning, knowledgeable judgments about the range of possible events, continued situational awareness about the pandemic, and flexibility in thinking and decision making.

III. Anticipating the Return of 2009-H1N1: Envisioning Scenarios

CHAPTER SUMMARY

While the course of the 2009-H1N1 pandemic cannot be accurately predicted, it is important to have a clear picture of our current knowledge and to envisage a range of specific scenarios against which to make plans and assess our capabilities.

Our current knowledge is that the virus is readily transmissible, especially to younger age groups, and causes severe clinical manifestations in a small but significant proportion of cases, with most of the severe cases in people under age 65. The proportion of influenza cases that ends in death appears similar to that for seasonal influenza (perhaps 1 per 1,000 patients seeking medical attention), but the absolute number of deaths is expected to be at least as high, if not substantially higher, than for seasonal flu because a higher proportion of the population is likely to become infected (perhaps 40 to 60 percent for pandemic flu versus perhaps 5 to 20 percent for seasonal flu). Moreover, the distribution of deaths is likely to cause a greater loss of expected years of life because the virus predominantly affects younger people. Some specific individuals appear to be at much higher risk, including patients with neurological disorders, pregnant women, and patients with asthma. Certain ethnic groups also may be at higher risk, such as Native Americans. Notwithstanding these observations, there remains great uncertainty about the likely course of the pandemic.

The Working Group believes that planning activities would be aided by development of a small number of specific, shared scenarios describing the possible evolution of the pandemic.

We believe it would be valuable for DHHS to develop a limited number of specific scenarios for dissemination to Federal, state, local and private decision-makers, to be used for assessing capabilities and planning responses.

For planning purposes, we describe a plausible scenario in which the pandemic causes between 30,000 and 90,000 deaths and requires at its peak 50 to 100 percent of ICU beds in affected regions of the country, placing extreme stress on a system in which 80 percent of ICU beds are already otherwise occupied. Analysis of this scenario and alternative scenarios should facilitate decision making about the use of mitigation methods in response to new information about the epidemic.

Introduction

Because the course of the 2009-H1N1 pandemic cannot be accurately predicted, it is important to have a clear picture of our current knowledge and to envision a range of specific scenarios against which to test our planning and capabilities. While changes in the virus remain possible, the current picture of 2009-H1N1 is as follows:

- *The virus is transmitted readily between people* at a rate comparable to that estimated for previous pandemic strains. In most places where surveillance is available, there is clear evidence of ongoing transmission even through the summer.
- *Confirmed cases are concentrated in younger age groups, up to age 24*. According to CDC, infection risk in the 0 to 24 age group is 4 to 5 times greater than for those in the 25 to 49 age group, and 20 times greater than those over age 65.
- *Almost all severe cases are in people younger than age 65*. To date, 83 percent of deaths and 71 percent of hospitalizations from 2009-H1N1 in the United States have been in people between the ages of 5 and 64. This is in stark contrast to seasonal influenza, in which two-thirds of hospitalizations and almost 90 percent of deaths occur in persons 65 or older. This means that the years of anticipated life lost per death are much greater than is usual as a result of seasonal influenza.
- *The case-fatality ratio (i.e., proportion of infected individuals who die as a result of the infection) appears to be similar to seasonal influenza—possibly on the order of 0.1 to 0.3 percent of medically attended cases (i.e., those infections requiring hospitalization or primary care), and perhaps 0.05 to 0.2 percent of all symptomatic cases, whether or not medical care is sought*. However, these numbers are highly uncertain, in particular because the number of medically attended cases is not well measured and the number of mild cases that do not come to medical attention is essentially unknown.
- *Despite a similar case-fatality ratio as for seasonal influenza, the number of deaths from 2009-H1N1 is likely to be substantially higher and the deaths and severe illness in the population will likely be concentrated among much younger people than is the case for seasonal influenza*. Because most of the population lacks significant immunity to a new pandemic strain, the proportion of people infected in a pandemic is usually substantially higher than for seasonal flu (50 to 70 percent for pandemic flu versus perhaps 5 to 20 percent for seasonal flu). Second, as noted above, the consequences of infection in this epidemic are already known to be far more severe for children and young adults, and seemingly milder for people over age 65 (with deaths mainly among children and young adults, compared to seasonal influenza).
- *Individuals with certain underlying medical conditions—including those with neurological disorders and pregnant women—appear to be at substantially elevated risk of severe outcomes*. According to CDC, as many as one-third of fatal cases and one-fifth of hospitalizations have been in persons with neurological (e.g., neurocognitive, neuromuscular, seizure) disorders. Pregnant women accounted for 8 percent of deaths and 6 percent of hospitalizations, although they make up about 1 percent of the population. Asthma, diabetes, immunodeficiencies, chronic obstructive pulmonary disease (COPD), and other chronic conditions appear to be associated with severe outcomes as well.
- *Certain populations appear to be at elevated risk of severe outcomes, including Native American groups*. American Indians and Alaska natives historically are at high risk for severe respiratory infections; while it is unclear what toll they have suffered from 2009-H1N1, a cluster of severe 2009-H1N1 disease among First Nation people in remote Manitoba, Canada, suggests that

these groups may be at high risk. Cases of 2009-H1N1 virus infection in these clusters have had rapidly progressive, diffuse, lower airway disease (compared to seasonal influenza, which more commonly involves the upper airway), resulting in development of acute respiratory distress syndrome (ARDS) and prolonged ICU admission.

The Need for Concrete Scenarios for Response Planning

The Working Group is concerned that uncertainty about the course of the 2009-H1N1 pandemic may be hampering planning. While uncertainty is inherent in pandemics, planning activities may be aided by development of a limited number of specific, shared scenarios that describe the possible evolution of the pandemic. Dissemination of a limited number of plausible scenarios would provide a framework against which decision-makers at the Federal, state, and local levels could test current capabilities and also structure specific plans and decision points. In the absence of such frameworks, decision-makers may fail to adequately assess capabilities relative to potential needs. They also may fail to foresee key decision points and be forced into hasty decisions in the "heat of battle." A scenario-based approach already has been embraced by the United Kingdom, which has defined and made public its planning assumptions for a "reasonable worst case" scenario.

MAIN RECOMMENDATION (CHAPTER 3)

We recommend that DHHS rapidly develop a limited number of specific scenarios and disseminate them to Federal, state, local and private decision-makers for planning purposes. Components of these scenarios ideally would include:

- **i. timing and magnitude of the fall epidemic;**
- **ii. peak burden on primary care providers, emergency rooms, hospital admissions, and ICUs;**
- **iii. number of doses and timing of vaccine availability;**
- **iv. dosing requirements and efficacy of vaccine; and**
- **v. efficacy and supply of antiviral drugs and medical materiel.**

These scenarios would allow Federal, state, local and private entities to assess their capacity and develop plans for deployment and targeting of medical and non-medical interventions under the various scenarios.

In addition, it would be valuable for DHHS to define trigger points related to changes in circumstances (e.g., change in severity) to facilitate timely action, as well as the data and data streams that will be required to activate these trigger points.

To illustrate this approach, we describe in Box 3A a scenario that we consider to be a reasonable model for planning, followed by sample decision points that might be appropriate. We also suggest indicators and triggers to redirect decision making should an unanticipated event emerge within the scenario. The assumed characteristics of the model scenario are described in Table 3-1.

BOX 3A: A MODEL SCENARIO: A POSSIBILITY, NOT A PREDICTION

One plausible scenario is that there will be resurgence in transmission of 2009-H1N1 this fall that is comparable to that seen in spring-summer 2009 but with higher rates of transmission due to the resumption of school and the cooler, drier weather. Following a relatively steady or declining burden of cases in August, the number of new cases will begin to rise exponentially in the first week of September, growing 10-fold about every 10 to12 days. Hypothetically, the peak incidence of infection nationally will occur around October 15, with minor variations across the country such that peak incidence almost everywhere will occur during the month of October. At this peak, perhaps 1 to 2 percent of the population will become infected each day.

Predicting demand on the health care system during this peak is fraught with uncertainties, but the following numbers from one possible scenario are illustrative. During the peak, 1 or 2 out of every 2,000 Americans might be hospitalized. Cases requiring mechanical ventilation or intensive care could reach 10 to 25 per 100,000 population, requiring 50 to 100 percent or more of the total ICU capacity available in the United States and placing great stress on a system that normally operates at 80 percent of capacity. Because adult ICUs are not prepared to care for pediatric patients, there could be a particular shortage of facilities for sick children. In particular locations, the stress on the health care system could grow even more acute, as large outbreaks occur in prisons, schools, and isolated communities with limited health care access, such as Native American reservations. As awareness of the pandemic spreads, pressure on emergency departments could mount, with long lines and a need for triage of mild cases and non-influenza cases.

Alongside these health-related burdens, substantial absenteeism from work and school could occur, as sick children stay home, schools with large outbreaks close, and parents are forced to stay home either because of their own illness or to take care of sick children. Key members of the social infrastructure, such as police officers and firefighters, are increasingly home ill. Exposure of healthcare workers to sick patients is continual and antiviral supplies prove inadequate for ongoing prophylaxis of these workers. Retail pharmacies run out of antiviral supplies in late September or earlier, and states face the demand to replenish these supplies from state stockpiles and state Strategic National Stockpile allocations; however, many states lack the ability to move antiviral drugs into the retail supply chain and focus on delivery to hospitals. Hospitals face competing pressures to dispense antiviral drugs for prophylaxis of their workers, to provide them to patients appearing in the emergency room, or to save them for the sickest admitted patients. Debates intensify about the value of antiviral use for long-term prophylaxis or early treatment for mild infection in high-risk groups such as pregnant women and immunocompromised patients, treatment of severely ill patients, and prophylaxis of essential healthcare workers.

In this model scenario, around October 15, as the epidemic peaks, a major supply of 2009-H1N1 influenza vaccine becomes available. Immunization starts within days, with considerable geographical variation in the rate at which administration occurs. Immunization of priority groups is completed by early or mid-November, resulting in immunity in vaccinated adults by mid-late November, as the epidemic wanes in most populations. Children require two doses and do not acquire immunity until December, when new infections will have become rare.

By the end of 2009, 60 to 120 million Americans would have experienced symptomatic infection with 2009-H1N1; nearly 1 to 2 million would have been hospitalized, with about 150,000-300,000 cared for in ICUs; and somewhere between 30,000 and 90,000 people would have died, the majority of them under 50 years of age.

We emphasize that this is a plausible scenario, not a prediction. By way of comparison, it is less severe by a factor of three (in terms of expected deaths per capita) than the "reasonable worst case" planning assumptions, publicized by the UK government, for the H1N1 resurgence in that country.

TABLE 3-1: A POSSIBLE (NOT PREDICTIVE) SCENARIO TO HELP PLAN FOR THE FALL RESURGENCE OF 2009-H1N1 INFLUENZA IN THE UNITED STATES	
Peak incidence date (unmitigated)	October 15
Peak incidence of symptomatic disease	1–2% of U.S. population (3–6 million people) on the U.S. epidemic's single peak day
Percent of U.S. population (and approximate numbers) assuming no change in virus	
Infected (indicated by seroconversions, with or without symptoms)	30–50% (90–150 million)
Symptomatic	20–40% (60–120 million)
Needing medical attention	15–30% (45–90 million)
Needing hospital care	0.3–0.6% (0.9–1.8 million)
Needing Intensive Care Unit (ICU) facilities	0.05–0.1% (150,000–300,000)
Deaths	0.01–0.03% (30,000–90,000)
Peak occupancy of ICU beds due to 2009-H1N1	10–25 ICU beds/100,000 population[1]
Peak occupany of hospital beds due to 2009-H1N1	50–150 hospital beds/100,000 population[2]
High-risk groups for death or hospitalization	Pregnant women; children (0–4 years old); patients with neuromuscular/neurocognitive disorders, asthma, chronic obstructive pulmonary disease, cardiovascular disease, diabetes, severe obesity, or immunocompromising conditions[3]

Notes:

[1] The United States has 20 ICU beds/100,000 population. The number of ICU beds available for pediatric patients is especially limited.

[2] The United States has 211 hospital beds/100,000 population.

[3] Cetron M, 2009 Pandemic Novel Influenza A (H1N1): Community Mitigation, powerpoint presentation to PCAST H1N1 Working Group, July 16, 2009.

Beyond this scenario, alternative scenarios are needed to take into account the possibility that major assumptions are incorrect. In particular, four variations are of notable importance:

1. A milder scenario in which the number of deaths and severe cases is much lower than outlined here, perhaps because many mild cases or infections without symptoms were missed in the spring, leading to an overestimate of the severity.
2. A modified scenario in which a large fraction (e.g., one-third) of 2009-H1N1 cases are resistant to oseltamivir (Tamiflu) by the peak of the epidemic, reducing the effectiveness of an important method for mitigating the epidemic.
3. A more severe scenario, in which changes in the virus result in elevated rates of hospitalization, intensive care demand, and death. In this case, the focus of severe disease may shift more toward the general population, making focused attention on groups that showed high-risk in the spring less of a priority.
4. A delayed scenario in which transmission does not increase dramatically in the early autumn, so that vaccine availability precedes the peak of the epidemic, reducing the number of subsequent cases by conferring protection through immunization.

We emphasize again that the baseline scenario and the alternatives above are given as examples for planning purposes; they are not predictions of what will happen. DHHS should exercise its own expert judgment in defining the most relevant scenarios, with the caveat that scenarios other than the most likely also should be considered. In addition, planning should include at least one scenario in which the peak of the epidemic precedes the availability of significant vaccine supplies.

To illustrate the value of scenario-based analysis, it is useful to consider issues in vaccine allocation, since the timing of availability of significant quantities of vaccine is still uncertain.

- In the model scenario, we assume that vaccine administration will commence around the peak of the pandemic, with substantial population-level immunity occurring only 2 to 8 weeks after the peak. In this case, vaccination will have limited value in reducing transmission. There may be a strong rationale for vaccinating certain high-risk groups as rapidly as possible, by accelerating the availability of at least some vaccine.
- If transmission is substantially delayed compared to the model scenario, vaccination of children may be of high value epidemiologically: it may be possible to immunize many before exposure, protecting them and decreasing spread.
- Conversely, if an increase in severity is detected with the expected rate of transmission, broader administration of vaccine before complete clinical trial data are available may be appropriate, and the use of adjuvant (as discussed in Chapter 5) might offer an improved risk-benefit profile.

In addition to analyzing specific scenarios in advance, it will be important to define indicators that could trigger the need to make changes in plans, and to incorporate these indicators into scenarios. We believe that it would be valuable for DHHS to define specific triggers in advance to the extent possible, since this will allow orderly decision making when unexpected events arise. (It is worth noting that beyond these triggers, public pressure in response to events, such as a cluster of child deaths, may force certain communities to change their strategies.) Examples of potential triggers are shown in Box 3B.

BOX 3B: EXAMPLES OF INDICATORS THAT MIGHT SERVE AS TRIGGERS FOR ACTION

Indicators of unacceptable burdens on health care might trigger guidance to intensify community mitigation to spread out the peak burden.

- observations of intense burdens on health care providers, particularly emergency department visits and ICU admissions, in developed countries in the Southern Hemisphere (during our summer);
- observations of intense burdens on emergency departments and ICUs in leading areas of the Northern Hemisphere in autumn;
- early evidence of intense burdens on health care providers without evidence that the infection is peaking, including more healthy adults or children among severe cases.

Indicators of substantially increased severity that might justify changes in plans for antiviral use, vaccine formulation (adjuvant use), or community mitigation.

- observations of novel symptomatology in the Southern Hemisphere or in isolated Northern Hemisphere groups during summer, especially if combined with evidence of viral changes associated with this symptomatology;
- increased ratios of ICU admissions to overall hospitalizations for influenza-like illnesses (ILI) (probably not observable unless very large changes occur);
- early evidence of intense burdens on health care providers without evidence that the infection is peaking; changes in risk groups to include more healthy adults or children among severe cases.

In addition, concentrations of unusually severe cases could occur in a population subgroup defined by geography/ethnicity (e.g., a remote Native American population), by underlying medical condition (e.g., pregnancy or a novel risk factor), or by place of residence (e.g., nursing home, prison). In such cases it will be urgent to provide adequate treatment for affected persons, consider accelerating vaccine delivery to similar groups, and ascertain reasons for this increased severity, distinguishing viral changes from infectious cofactors, host factors, or other reasons.

IV. Ensuring Adequate Data for Decision Making: Surveillance Systems

CHAPTER SUMMARY

Decisions about how to respond to the fall resurgence of 2009-H1N1 will have to be made quickly in response to rapidly evolving information about the epidemic. The quality of decision-making will depend on reliable and timely estimates of the number of people and specific subgroups that are infected, ill, seeking medical care, being hospitalized, requiring intensive care, and dying from 2009-H1N1; changes in the virus; stresses on health systems; and effectiveness of various medical and public health interventions.

CDC, in close coordination with local and state public health departments, supports a number of important systems for surveillance of influenza activity. These systems have provided valuable data through the spring and summer, but they have shortcomings that will limit their ability to provide the data needed to make informed decisions. While it is not possible to remedy all of these limitations before Fall 2009, there are a number of short-term steps that could be taken to significantly improve the data available for decision making.

The Working Group believes there is an important opportunity to upgrade national surveillance systems in time for Fall 2009 by knitting together and extending existing systems. We are aware that CDC is developing plans along these lines and strongly support these efforts.

Introduction

Decisions about how to respond to the fall resurgence of 2009-H1N1 will have to be made quickly in response to rapidly evolving information about the epidemic. The quality of decision making in response to the 2009-H1N1 pandemic will depend on accurate and timely data to answer six key sets of questions:

1. *Approximately, how many people are becoming infected, experiencing illness, seeking medical care, being hospitalized, requiring intensive care, and dying from 2009-H1N1?* These data allow estimates of severity, which help determine the intensity of response that is justified. A subsidiary but important challenge is to estimate the same numbers for seasonal strains of influenza that may be circulating over the same period.
2. *How are these numbers changing over time?* Are they increasing or decreasing, and how quickly?
3. *Who is becoming infected and who is at greatest risk of severe outcomes (i.e., hospitalization, ICU admission, death)?* Specifically, what are the ages, underlying conditions, and other risk factors for infection and severe outcome?

4. *How is the virus changing?* Most important, are there changes in illness severity, antigenic character (which could compromise immunity acquired from natural infection or a vaccine), or drug resistance of the circulating virus?

5. *Are the medical and public health systems able to respond adequately?* Is there adequate capacity in physician offices, emergency rooms, hospitals, ICUs, morgues, points of dispensing (PODs), and other public health venues set up for the pandemic?

6. *How well do medical and public health responses work?* Does the vaccine protect against infection or severe outcome? Is the vaccination strategy (e.g., mass vaccination clinics) able to target effectively the recommended population groups? Does antiviral treatment reduce severity? Do social mitigation measures reduce transmission?

Federal decision-makers need data that answer these questions to inform policies and recommendations about the priority groups for vaccination and treatment, to calibrate the intensity of social mitigation interventions, and to provide guidance to clinicians about appropriate treatment and prevention. State and local decision-makers need the data for the same reasons, but they also need to understand the situation in their communities, which may differ from the national average. Clinicians need data especially related to questions 3 and 5 in order to target scarce treatment to the appropriate patients, improve clinical treatment, and implement surge capacity plans in the event of increased demands on the health care system. The general public needs to understand the size and severity of the epidemic and be motivated to comply with social mitigation measures. Historically, compliance improves when the epidemic is perceived to be severe. All of these data are needed as close to instantaneously as possible.

Existing Data Streams

CDC, in close coordination with local and state public health departments, supports a large number of systems for surveillance of influenza activity. The output of many of these systems is summarized publicly on FluView www.cdc.gov/flu/weekly/, and includes measures (some more nationally representative than others) of outpatient consultation for influenza-like illnesses (ILI), hospitalization for influenza, pediatric deaths from influenza, population-wide deaths from pneumonia and influenza, and virus characteristics (subtype and drug resistance). Federal decision-makers have relied on these systems as the main source of data on trends in case numbers, age distribution, and virus characteristics.

A second key source of data on the epidemic in the early days of the spring wave of 2009-H1N1 was the relatively detailed reports from state and local health departments describing individual confirmed cases, noting (with varying completeness) key variables such as age, underlying conditions, and outcome (i.e., recovery, hospitalization, ICU, death). By early May, this level of reporting had become unsustainable; most jurisdictions stopped testing most mild cases for 2009-H1N1 virus and ceased detailed reporting of individual cases. Local authorities in many communities continued gathering data on the most severe cases, but these data were not systematically reported to CDC. Thus the clinical picture of confirmed infection at the national level is relatively static, based on the first case reports in the epidemic, and it has not been possible to track the evolution of the epidemic in the United States.

Shortcomings of Current Data Streams

While the data collected about 2009-H1N1 thus far have been extremely valuable, they have a number of limitations. The key shortcomings of existing data streams are:

- **Some key data are not updated continuously**. Since individual-level case reporting ended in early May, there has been no systematic way to update national data on high-risk groups (i.e., according to age and predisposing conditions) for confirmed infection and severe outcome at the national level. Some of these data exist locally but are not being aggregated into a national picture now that reporting to CDC is not at the individual level. Up-to-date information on these variables is needed, for example, to inform decisions on who should receive priority for vaccination and antiviral treatment.
- **Current systems are geographically limited**. Influenza activity is geographically heterogeneous, as was apparent in the spring wave of 2009-H1N1 and as is known for seasonal influenza. Responses, therefore, should vary locally, but they can do so only with local information. For national decision-makers, geographic coverage is important to ensure a nationally representative picture of the epidemic. Many of the most detailed data feeds, such as the influenza-confirmed cases at hospitalization monitoring sites funded by CDC through the Emerging Infections Program (EIP), are geographically limited. By chance, during the spring none of these EIP sites was in an area with a heavy burden of 2009-H1N1 disease.
- **Current systems do not provide reliable estimates of influenza morbidity and mortality**. For many purposes it is critical to know, for example, approximately how many people are infected or hospitalized, measured as total numbers of people or numbers per 100,000 population. Most of these systems do not answer that question, but instead measure what proportion of visits to health care providers or emergency departments are for ILI, and what proportion of ILI cases that undergo viral testing are positive for 2009-H1N1.
- **No systematic approach yet exists to monitor the capacity of the health care system to respond**. Although many jurisdictions monitor emergency department volume, national integration of these data is geographically spotty. For total burden of hospitalizations and intensive care admissions due to influenza, few if any representative data are available. Such a system, called "HAvbed," is planned by DHHS but has not yet been implemented.
- **Laboratory capacity to confirm diagnosis and isolate viruses for further characterization is limited**. Most public health laboratories now restrict virus testing to patients with severe disease and many laboratories will be unable to maintain even this practice if the number of cases grows much higher in the fall. Commercial testing for pandemic 2009-H1N1 and other viral respiratory pathogens is not widely available or widely used, so 2009-H1N1 infection in most patients may not be confirmed in fall 2009; as a result, diagnosis will be based empirically on clinical symptoms and knowledge of which respiratory viruses are circulating in each community.
- **Current systems cannot monitor the burden of mild illness that does not come to medical attention**. Reliable estimates of this burden are needed to understand the severity of illness—

the more people are becoming infected without coming to medical attention, the smaller we expect the overall burden of morbidity, mortality, and health care system stress to be for a given prevalence of infection. At present we do not know this number.

- **Current systems for reporting and analyzing adverse events associated with vaccination may not be well suited to challenges likely to arise during a vaccination campaign for 2009-H1N1**. The Working Group has identified two concerns in this area. First, adverse event surveillance and analysis depends to a large degree on the ability to link vaccination to possible adverse events via medical records, but the administration of vaccine in settings other than traditional medical care may circumvent this linkage. Second, high-risk groups that are prioritized for vaccination also are likely to experience adverse health events at high rates. Existing systems may not be able to rigorously evaluate elevated rates of such common events in high-risk groups, e.g., spontaneous abortions (miscarriages) in pregnant women or various complications in neurologically impaired patients.

In a rapidly growing pandemic wave, most state and local health departments do not have the capacity to count every hospitalization or death without depleting limited public health resources. Therefore, more efficient and sustainable surveillance methods are necessary to obtain the key data needs during a moderate or severe pandemic, including a qualitative assessment of local influenza activity combined with virologic sampling of a representative number of viral isolates.

Recommendations

It is not possible to address all of these limitations before the autumn wave of 2009-H1N1. (In Chapter 8, we recommend long-term measures to erect a comprehensive and population-based influenza surveillance system that would address data needs for decision making in seasonal influenza and future pandemics.)

The Working Group believes, however, that CDC can take a number of steps in the coming weeks to significantly improve critical data for decision making.

MAIN RECOMMENDATION (CHAPTER 4)

We recommend that DHHS take rapid advantage of available opportunities to upgrade national surveillance systems to improve decision making during the fall resurgence The critical surveillance information for decision making includes data on influenza-like symptoms in the population, emergency room admissions, health system utilization, hospitalized patients, and adverse events.

Below, we suggest several specific measures that may improve situational awareness and decision making through the autumn wave. These recommendations attempt to balance the need for improved data with the practical constraints of assembling systems to acquire these data in a short time frame. We recognize that efforts to address many of these needs, and many other aspects of surveillance, are ongoing; we highlight here aspects that appear to be both urgent and addressable within a short time frame.

RECOMMENDATION 4-1: EMERGENCY ROOM DATA

We recommend that CDC rapidly assemble an integrated system, by combining syndromic surveillance and emergency department data from existing local and state surveillance systems into a geographically representative national network, that rapidly reports total and ILI-related emergency visits.

Needs/gaps in existing systems and possible approaches: Most states and many large cities have implemented their own syndromic surveillance systems in emergency departments. These electronic systems provide valuable information on ILI trends based on symptoms that bring patients to medical care centers. These systems often collect data within 12 to 24 hours of patient visits. However, these state and local systems currently are not integrated, making it difficult to obtain regional or national situational awareness of influenza activity based on reports from individual centers.

For example, the International Society of Disease Surveillance has implemented a simple and flexible integrated system and collects aggregate counts of ILI syndromes by age group in order to monitor and compare ILI activity throughout the United States very quickly (e.g., see the International Society of Disease Surveillance's DiSTRIBuTE system). However, only nine jurisdictions (a mix of cities, counties, and states) participate. This system could form a natural template for additional data feeds. We believe it may be feasible to expand this or other systems in the coming weeks and we are aware of efforts by CDC to do so.

Expected benefits: This system would provide a national picture, with some local resolution, of trends in the numbers of patients visiting emergency departments, the percentage of such patients with ILI, and the distribution of ILI by age. Such information would allow Federal, state, and local officials to obtain a better sense of the trajectory of the outbreak (in scale, scope, and pace) in different regions of the United States over time. Systems of this type already are proving useful for evaluation of local control measures, although additional information is required to assess the severity of disease associated with the 2009-H1N1 virus (e.g., cases requiring hospitalization or case fatality rates).

RECOMMENDATION 4-2: POPULATION SAMPLING

We recommend that CDC implement a system to measure the burden of ILI on a weekly basis. Although nationally representative data would be valuable, it may be beneficial for these surveys to oversample in jurisdictions that have relatively robust surveillance plans in place for tracking influenza-related primary care visits, hospitalizations, and deaths in order to more accurately monitor changes in rates of more severe illness over time.

Needs/gaps in existing systems and possible approaches: Existing systems do not establish the number of ILIs occurring in place and time as a rate per 100,000 population. This precludes estimates of severity because the severe cases, which are better ascertained, cannot be related to overall levels of infection.

This may be accomplished through web-based or telephone-based surveys.

Expected benefits: These studies would provide approximate denominators of mild and medically attended illness against which more detailed data on hospitalizations and fatalities can be compared. Such denominators are especially important for estimating severity of infection and consequently for predicting peak burdens on health care: for a given number of severe outcomes, the overall severity is much less if there are many cases of mild illness or of symptoms that do not cause a patient to seek medical attention. Data from random public surveys would reduce, although not eliminate, the uncertainties cited above concerning overall severity. In addition, the surveys would provide an independent measure of the number of people affected by illness that may be attributable to 2009-H1N1 and to the rate of change in these numbers. The interpretation of ILI activity due to 2009-H1N1 will depend on the proportion of 2009-H1N1 compared to other circulating respiratory viruses in each community where surveillance is taking place. In the spring, 2009-H1N1 was more prevalent; but in the fall, other viruses will likely be circulating, such as respiratory syncytial virus (RSV) and seasonal influenza. Thus, these numbers will be best interpreted in conjunction with virologic data.

RECOMMENDATION 4-3: HEALTH SYSTEM UTILIZATION

Because hospital facilities may become dangerously scarce in the fall, we recommend that DHHS implement an integrated system to monitor health care system utilization overall and attributable to respiratory infection, with an emphasis on incidence and prevalence of cases occupying hospital beds, ICU beds, and mechanical ventilators.

Needs/gaps in existing systems and possible approaches: Hospital and intensive-care utilization are not routinely monitored in the United States. Southern Hemisphere countries are reporting stress on ICUs from 2009-H1N1 illness even during a period of school holidays, and the epidemic probably has not yet peaked. As noted above, DHHS is developing the HAvBED system, which may be expanded to meet present needs. An alternative or complementary approach may be to integrate existing state and local systems, such as the New York State Health Emergency Response Data System (HERDS). In any system, it would be valuable for such data to be immediately available to state and local providers. Since most hospitals maintain such information on a daily basis, the key is to implement a simple system that allows defined information to be regularly uploaded.

Expected benefits: Acute stress on ICUs or increased demand for ventilators may be a trigger for resource reallocation from less affected areas and/or for intensifying community mitigation measures. Accurate measures of health care system utilization would facilitate more efficient sharing of resources.

RECOMMENDATION 4-4: HOSPITALIZED PATIENT DATA

We recommend that CDC define a mechanism to gather timely clinical, epidemiologic, and virologic data on a representative sample of patients hospitalized for respiratory illness and ensure that those data are available to inform national recommendations to clinicians, public health officials, and the public. Such data could be gathered by assembling a network of participating sites, such as sites currently specializing in influenza surveillance; healthcare systems with appropriate electronic record-keeping systems; and states and localities interested in participating.

The data ideally would include:

- **A. Results of systematic testing of patients hospitalized for respiratory infection to determine the presence of respiratory viruses including 2009-H1N1. To improve representativeness of data, such testing would ideally be done within a defined population according to prospective criteria rather than according to clinician discretion.**
- **B. Clinical data—including age, predisposing conditions, course of hospitalization (whether admitted to ICU or ventilated), duration of hospital/ICU stay, and resolution (death, discharge), vaccine status, presence/absence of bacterial secondary infections, and identity and timing of antibiotic and antiviral administration—should be reported for a representative sample of hospitalized cases of 2009-H1N1 infection.**

In addition, it would be valuable for CDC to define explicitly the most important clinical studies needed to guide response during the autumn wave, gain Institutional Review Board approval, identify and fund sites to perform these studies during the early autumn, and put in place a mechanism for rapid dissemination of results

Needs/gaps in existing systems and possible approaches: There is an important gap in our ability to assess the clinical features of pandemic influenza infections in an ongoing way to inform treatment and prevention decisions. CDC's Emerging Infections Program (EIP) reports population rates of infection with confirmed influenza. These data are valuable but are limited by variation in the sensitivities of immunological and nucleic-acid-based assays and by clinician discretion regarding whether to test. Adequate personnel and funding should be available so that EIP sites have capacity to perform PCR-based tests (which are more sensitive) and to test systematically rather than at clinician discretion.

For clinical information, existing data streams are limited and state and local health departments are unable to follow up most hospital admissions to determine clinical course. Such data are particularly critical and may change over time as the pandemic progresses, either due to changing susceptibility in the population or changes in the virus. While it is not feasible to obtain clinical information for all hospitalized patients, sentinel hospitals or EIP sites could be used to gather detailed clinical data in a standardized fashion. In addition to these standard data, clinical studies—for example, on optimal management of severe cases that do not respond to antiviral therapy—will be needed, and little time is left to ensure that they will be ready to commence early enough to have maximal impact. In addi-

tion, waiting for peer-reviewed results to be published will likely diminish the value of any findings, as a manuscript submitted in mid-September might not be published until November, after the possible peak of the epidemic.

To address these needs, CDC should work with existing sites that specialize in influenza surveillance, or research centers, to prospectively monitor for changes in the clinical or epidemiologic characteristics of the virus over time. Other states or locales that have interest and capacity to participate should be included, when possible, to improve geographic representativeness. These "sentinel sites" should use standardized protocols and data collection instruments to ensure that timely and up-to-date clinical, epidemiologic, and virologic data on patients hospitalized for respiratory illness are available to inform national recommendations to clinicians, public health officials, and the public. Adequate funding will be needed to support these sites.

Expected benefits: Such data streams, and CDC's guidance based on them, would be of primary benefit to clinicians and to vaccine planners in targeting prevention and treatment to groups at high-risk of severe disease. Changes in risk groups or changes in clinical spectrum (e.g., more rapid progression to death, increasing need for ICU care or ventilation among hospitalized cases) may be early signs of changes in the virus or in other factors, such as bacterial superinfection, that would warrant changes in control measures or clinical management. Such changes are not observable now because of the lack of ongoing clinical characterization of severe cases. A rapid means to disseminate clinical data and results of key clinical studies would provide clinicians with needed information while it is most valuable.

RECOMMENDATION 4-5: ADVERSE EVENTS

We recommend that DHHS ensure the adequacy of surveillance systems and signal evaluation systems for vaccine-associated adverse events (VAE), with particular focus on the risk of *common* adverse events that are likely to occur at high rates in high-risk populations (e.g., pregnant women) and whose association with vaccination may be difficult to assess rapidly.

In addition, we believe it would be valuable for DHHS to assess the adequacy of existing systems for VAE reporting to detect rare events in settings of nontraditional vaccine distribution (e.g., in public settings, such as malls) and take steps to improve these systems where needed.

Needs/gaps in existing systems and possible approaches: Existing VAE detection systems and surveillance planned for the fall focus on detection of rare complications, such as Guillain-Barré syndrome. In an atmosphere of heightened public concern, common adverse events occurring in high-risk groups likely to be early candidates for vaccination (e.g., spontaneous abortions) may be expected to occur frequently among early vaccine recipients, even if the vaccine is perfectly safe. A mechanism is needed to evaluate the possible contribution of vaccine to such common adverse events to address public concerns, even if the plausibility of such associations is low.

Major existing adverse event detection systems such as CDC's Vaccine Safety Datalink rely on linked medical records, including vaccination and adverse events for the same persons. If public distribution

of vaccine occurs, these systems might not accurately record vaccination status, hence may be unable to function as normal to detect and evaluate signals of adverse events.

Expected benefits: Systems to address vaccine safety are crucial to the success of any vaccination program but will be of particular importance this fall given likely heightened awareness of such issues during a pandemic and during a rapid mass vaccination campaign.

Conclusions

Given the short time until the expected resurgence of 2009-H1N1, it is not feasible to create entirely new surveillance systems. Nonetheless, we believe that it may be feasible to significantly improve surveillance capabilities by upgrading existing systems. Such improvements could have the following direct benefits for decision making.

- Continuously updated clinical information will provide a basis for national recommendations to physicians, with reliable data on who is at highest risk and which treatments are most effective for such patients.
- Emergency department surveillance, combined with a system to monitor demand on hospitals, can provide a considerably stronger basis for decisions about resource allocation to overtaxed areas and for assessing the need for enhanced community mitigation measures to slow demand on the health system.
- Emergency department surveillance and population-based surveys will inform estimates of the current stage of the epidemic and its trajectory.
- Adequate reporting and analysis of adverse events is crucial to ensuring vaccine safety and to maintaining public acceptance of the vaccine.

We are aware that CDC is developing plans to expand its surveillance efforts for fall 2009 and we strongly support such efforts.

V. Responding to the Pandemic

CHAPTER SUMMARY

The impact of influenza epidemics can be mitigated by four methods: vaccination, administration of anti-viral drugs, symptomatic medical care, and non-medical interventions that reduce viral transmission. Decisions to implement these approaches depend on a variety of factors, especially the nature and course of the epidemic and the availability of materials, personnel, and delivery systems.

Because the influenza virus spreads rapidly and often efficiently, little time is generally available to respond once medically significant outbreaks occur. It is thus critical that scenario-based plans be made in advance for each of these interventions. It is equally important that a well-defined process for decision making be established, with clear assignments of responsibility and logical, agreed-upon guidelines for evidence-based decision making.

The Working Group was impressed with the very active engagement by many highly competent people in multiple Federal agencies who are thinking about the decisions that need to be made. However, as the fall resurgence nears it is especially important to be certain the roles and responsibilities of these individuals in decision making, as well as the processes used to arrive at decisions, are clear. The Working Group believes that it would be valuable to (1) clarify decision-making authorities and processes, and (2) adopt a more structured decision-making framework for certain key decisions.

We recommend that the Homeland Security Advisor assume responsibility for identifying the people, agencies, and processes for making decisions in the next phases of the 2009-H1N1 pandemic; for guaranteeing that all necessary decisions are made in a timely fashion; and for presenting recommended courses of action to the President.

In addition, we examine critical issues in each of the four areas of intervention and make specific recommendations about the processes and information required for decision making in those areas. In particular, we encourage the responsible agencies to focus immediately on decisions that could reduce severe disease and death in especially vulnerable populations by accelerating the delivery and use of vaccines, increasing the appropriate use of anti-viral drugs, and ensuring access to intensive care facilities.

Finally, we comment on the ways in which decisions made to mitigate disease in the United States might affect the many other countries likely to be affected by the 2009-H1N1 pandemic.

Introduction

Influenza epidemics cannot be prevented with currently available tools, but four categories of methods are available to mitigate the effects of an epidemic:

1. **Vaccines** to prevent infection. For seasonal influenza, vaccines reduce the risk of serious disease in infants and children, pregnant women, older adults, people who have chronic medical conditions, or those who might infect high-risk people through their work or household contact.

2. **Antiviral drugs** to decrease the likelihood of infection or severe disease in uninfected individuals (usually those with known or suspected exposure); to reduce the severity and duration of disease in patients already infected and ill; and to lower the rate of virus shedding in infected individuals, thereby decreasing the likelihood of transmission to others.
3. **Medical care** to manage clinical illness, which may range from mild to extreme, delivered at home, in out-patient clinics, hospitals, and intensive care units.
4. **Non-medical mitigation** practices, including isolation of infected individuals, hand washing, and several forms of social distancing such as school closures, cancellation of sporting events, etc., to lower the chances of person-to-person transmission of virus.

Because the influenza virus spreads rapidly and often efficiently, little time is generally available to respond once surveillance methods reveal medically significant information. For this reason, it is critical that plans be made in advance for the production, acquisition, and delivery of medical interventions, such as vaccines and drugs; the provision of facilities and materials for patient care; the mobilization of necessary health personnel; and the communication of information about both medical and non-medical mitigation strategies. In addition, a well-defined process for decision making needs to be established well in advance, with clear assignments of responsibility and logical, agreed-upon guidelines for decision making.

Responding to the anticipated 2009-H1N1 influenza epidemic in the coming months will require complex coordination—across different agencies of the Federal Government, vertically across the various levels of government (Federal, state, local), between public officials and health professions and institutions, and between the public and private sectors. "Coordination" across agencies and participants can be wasteful and frustrating if there are ambiguous responsibilities and unclear lines of authority. Rather than focusing on coordination per se, it is more productive to emphasize clarity about leadership, responsibilities, roles, and communication.

The Working Group has been impressed by the active engagement by many highly competent people in multiple Federal agencies who are thinking about the decisions that need to be made about efforts to mitigate the effects of the spread of 2009-H1N1 influenza virus in the United States this fall and winter.

The Working Group has some concerns, based on conversations with representatives of the various agencies involved, that decision-making authorities and processes may not be completely clear in all cases. Primary Federal responsibilities for response to an epidemic are lodged in two departments (DHHS and DHS), with significant involvement of others (Education, Defense, State, Agriculture, Labor), and coordination by White House staff. While the National Strategy for Pandemic Influenza Implementation Plan provides a comprehensive list of assignments for a multitude of offices, agencies, and departments involved in the Federal planning process, the large number of tasks and responsible units tends to obscure the primary seat of responsibility. (See www.pandemicflu.gov/plan/federal/pandemic-influenza-implementation.pdf.) The Working Group believes it would be valuable to clarify these matters before events accelerate in September and assign to the Homeland Security Advisor the responsibility for ensuring that all of the important decisions are made in a timely fashion and with appropriate consultation with the President.

In addition to clarifying authorities, the Working Group believes it would be valuable to adopt structured frameworks for making certain key decisions. At the time of our study, agencies had not yet formalized decision frameworks but were moving to do so. We strongly endorse these efforts. We urge that they attempt to be as precise as practical with respect to overall goals, scenario-based assumptions, required data elements, quantitative trigger points, expected benefits, and expected costs. It would be valuable to circulate these analyses within the government. Where feasible, it could also be desirable to share them publicly through an appropriate channel to gain the benefit of expertise outside government; this would be consistent with the Administration's commitment to open government.

MAIN RECOMMENDATION (CHAPTER 5)

As the fall resurgence nears, important decisions will have to be made rapidly and based on limited data. It is important to be certain that roles and responsibilities in decision making, as well as the processes used to arrive at key decisions, are clear. The Working Group believes that the White House is best positioned to ensure that these systems are in place, building upon the strong coordination role it is already playing.

We recommend that the White House designate an individual, preferably the Homeland Security Advisor, to be responsible for coordinating all policy development for the 2009-H1N1 response; identifying the people, agencies, and processes for making key decisions; guaranteeing that all necessary decisions are made in a timely manner; and presenting recommended courses of action to the President.

Concerning decision-making authority, it will be important to identify the individual(s) responsible for organizing the decision-making processes for each of the mitigation measures. For most key decisions discussed in this Chapter, the responsible individual should be the Secretary of DHHS.

Concerning decision-making processes, it would be valuable to employ structured decision frameworks incorporating scenarios—including an assessment of required data, specific trigger points for action, and a forecast of benefits (e.g., decreased morbidity and mortality, decreased transmission) and costs (e.g., financial loss and social disruption). We are aware of and endorse efforts already underway to create such structured analyses. Such documents should be shared within government and, where feasible, shared with experts outside government.

The most urgent attention should be given to the priority decisions necessary to support vaccine and antiviral allocation and deployment, the national medical response, and the implementation of non-medical mitigation strategies, as described below.

In the sections that follow, we discuss specific issues that should be addressed in making decisions about each of the categories of mitigation methods, and we offer specific recommendations about how to approach those issues.

Vaccines and Antiviral Drugs

The two main medical lines of defense are vaccination and antiviral drugs. Vaccination constitutes the best defense against an epidemic, but its effectiveness depends on timing and coverage of the population. Both inactivated and live attenuated influenza vaccines are approved for use. (See Box 5A) Antiviral drugs can provide a powerful tool for prophylaxis for exposed individuals and for treatment, especially if used within 48 hours of the appearance of symptoms, but with possible benefits for treatment of severe cases thereafter. Two inhibitors of influenza neuraminidase, oseltamivir and zanamivir, are approved and effective against 2009-H1N1 virus. (See Box 5B)

BOX 5A: INFLUENZA VIRUS VACCINES

Two types of vaccines are FDA-approved, recommended for seasonal influenza among the elderly and young children, and now being manufactured at five pharmaceutical companies in response to orders from the Federal government for use in the 2009-H1N1 influenza pandemic.

Inactivated vaccines **are the most widely used. They are prepared by growing viruses in embryonated chicken eggs and then inactivating them by treatment with ethyl ethers or detergents. Inactivated vaccines contain all the viral structural proteins and are administered via injection, usually in a single 15 microgram dose that is made available in multi-dose vials or single-dose syringes.**

Live attenuated vaccines **are made from cold-sensitive variants of the virus that are also produced in chicken eggs, partly purified, and administered to the nasal mucosa, usually with a nasal spray device.**

Other approaches to making influenza vaccines by growth of virus in cell culture or by recombinant DNA methods are being studied and are described in Chapter 8. In addition, it may be possible to augment the effectiveness of influenza vaccines through the use of **adjuvants**, **substances that stimulate the immune response to viral proteins. Use of adjuvants with influenza vaccines has not yet been approved by the FDA, but is permitted in Europe. Depending on the outcome of clinical tests, adjuvants could be added to 2009-H1N1 vaccines under the terms of an Emergency Use Authorization (EUA) from the FDA.**

BOX 5B: ANTIVIRAL DRUGS FOR INFLUENZA

Two classes of antiviral drugs have been developed and approved for use in the treatment of influenza.

One class, the amantadines, blocks the virus life cycle by interfering with a small viral protein called M2. This class of drug is not effective in the treatment of either 2009-H1N1 virus or the current seasonal influenza viruses and is thus not considered further here.

The second class, the neuraminidase inhibitors, includes two agents—oseltamivir (TamiFlu, taken orally) and zanamivir (Relenza, inhaled)—that are FDA-approved and widely used as prophylaxis against disease (among those known or likely to be exposed to infected individuals) and as treatment (for patients diagnosed with influenza). Treatment is most successful when begun soon after infection; the agents also reduce the amount of infectious virus produced by infected individuals. The drugs are often used in the management of severe influenza, but intravenous delivery of these two agents, or of a third agent (peramivir), in advanced stages of development, has not yet been approved by the FDA. Resistance to these agents, especially oseltamivir, as a result of viral mutation or genetic recombination, can be a major factor limiting antiviral effectiveness; seasonal influenza viruses increasingly show resistance to oseltamivir, but thus far only a few of the many isolates of 2009-H1N1 virus have shown resistance to oseltamivir.

The Working Group has identified several important decisions that need to be taken—immediately in some cases, rapidly in all cases—if these two mitigation measures are to be employed to maximum effect this fall:

(1) Accelerate vaccine production. The expected timing of vaccine availability poses significant challenges, as seen from the following considerations:

- Although revisions of the schedule are under consideration by DHHS, plans announced in July by the HHS Secretary would provide the first significant quantities of 2009-H1N1 vaccine in mid-October; an effective immune response would take another 2 to 4 weeks to develop after vaccination. Under the model scenario described in Chapter 3, the resurgence of the epidemic would start in September and peak in mid-October. If this model is approximately correct with respect to timing, a vaccination campaign would not begin to protect vaccinees until well after the epidemic had peaked.
- Certain groups are already known or suspected to be at high risk for serious complications and death from 2009-H1N1, and are likely to account for a significant minority of serious morbidity and mortality. Based on current information, groups at relatively high risk include pregnant women, individuals with certain neurological impairments, asthmatics, and others (see Chapter 3). In addition, high numbers of severe cases and deaths were observed among children and young adults. These groups would disproportionately benefit from early access to vaccine.

Given these circumstances, it is important to consider options for accelerating the availability of vaccine supplies, at least for individuals at elevated risk, estimated to represent nearly 40 million in the U.S. Currently, vaccine availability is gated by results of clinical studies concerning safety and optimal dose (expected in mid-September), after which manufacturers can "fill and finish" the vaccines at the appropriate doses (which requires another 3–4 weeks). Inactivated vaccine for seasonal influenza is usually administered at a dosage of 15 micrograms; a similar dosage is expected to work for the 2009-H1N1 vaccine, but this will not be known with certainty until results from clinical studies are available.

RECOMMENDATION 5-1: ACCELERATING VACCINE AVAILABILITY FOR HIGH-RISK GROUPS

We recommend that DHHS accelerate the availability of a portion of the vaccine supply to mid-September by having manufacturers begin to "fill and finish" a subset of the bulk vaccine product at 15 micrograms. Such a decision would need to be taken almost immediately.

We thus recommend a "hedged" strategy in which an initial amount of product is packaged "on risk," assuming a 15 microgram dosage, and the remainder is packaged when dosing and safety information becomes available in mid-September following the first results of clinical trials conducted by the NIH and industry. The risks of this course of action appear to be relatively low: some vaccine product could be wasted by filling vials at sub-optimal doses. If a somewhat larger dose is required, however, physicians can administer additional vaccine (e.g., a second dose of 15 micrograms to achieve 30 micrograms). The optimal amount of vaccine will need to be determined from immunological responses in clinical tests and an appropriate decision analysis. However, it seems clear that filling and finishing up to 40 million doses could have a substantial effect on the incidence of disease and death in these vulnerable populations.

The Working Group recognizes that there are important considerations for manufacturers as they contemplate reconfiguring their "fill and finish" operations to meet accelerated deadlines. If DHHS elects to follow this approach, a highly knowledgeable Federal decision-maker would need to work promptly with one or more of the pharmaceutical companies already contracted to produce vaccine to execute this strategy.

We note that the National Biodefense Science Board has also encouraged accelerated production and that the strategy is under consideration by the relevant DHHS agencies.

(2) Focus on protecting those at highest risk. Because the most severe outcomes appear to be concentrated in certain groups, based on data thus far with 2009-H1N1, it is logical to assume that focusing mitigation efforts on those groups will have disproportionate public health benefits. In addition to accelerating the availability of vaccine, it is important to develop clear guidance about the means of access and appropriate use of vaccines and anti-viral drugs for these groups and to communicate that guidance to them and their health care providers promptly and effectively (discussed in Chapter 7). We note that the complex and distributed nature of the U.S. healthcare system poses logistical challenges in accomplishing these goals, which will require considerable planning.

This strategy will require attention to important questions about the specific recommended interventions, both medical and non-medical. To cite just one example, what guidance concerning antiviral prophylaxis should be given to a pregnant schoolteacher whose class has two students who are at home after contracting symptoms of 2009-H1N1 influenza?

RECOMMENDATION 5-2: PROTECTING HIGH-RISK GROUPS

We recommend that DHHS undertake a focused program to identify and maximize protection of individuals at high risk of severe outcomes if infected with 2009-H1N1.

This process should include:

- **A.** **reviewing existing knowledge about nH1N1 hospitalizations, ICU admissions and deaths to strengthen the list of groups at highest risk for these events;**
- **B.** **developing plans to mobilize these groups (and their health care providers), generate guidance for members of these groups to follow in deciding when to use such medication, and dispense antiviral drugs when indicated;**
- **C.** **using these mobilization strategies to reach the same groups for vaccination, and begin offering vaccine as soon as supplies become available; and**
- **D.** **considering plans to offer existing vaccines against other respiratory pathogens to members of such groups (severe consequences of influenza virus infection often result from secondary infection, such as pneumococcal pneumonia).**

(3) Manage anti-viral stockpiles. The United States currently has Federal and state stockpiles of approximately 90 million courses of antivirals (consisting of roughly 80 percent oseltamivir and 20 percent zanamivir). Each course represents one week of treatment; an individual taking prophylaxis for three months would thus consume 12 courses. There is little or no additional supply available for purchase through the end of 2009. The existing stockpile must thus be used prudently.

The Working Group has heard concerns expressed that there is a risk of depleting the stockpile if it is not managed properly (for example, if used for widespread and prolonged prophylaxis of health care workers or the general public). It is important that antiviral drugs be available for treatment and for prophylaxis for those at greatest risk of serious illness (prioritized groups directly exposed to virus). Once antiviral drugs are released from the national stockpile, the states and localities control their use. Still, CDC has an important influence through its guidelines on the use of these drugs. The Working Group heard concerns that the existing CDC guidelines may not be sufficiently strong and clear to promote optimal use.

RECOMMENDATION 5-3: ANTIVIRAL DRUGS

We recommend that CDC clarify and strengthen its guidelines for use of antiviral drugs, including for treatment, pre-exposure, and post-exposure prophylaxis, and contingency plans for the development of drug resistance. These guidelines and plans, and their rationales (including preservation of limited supply for those in greatest need), should be clearly communicated to state and local health departments, health care practitioners, and the public. State and Federal supplies of antiviral drugs should be monitored on a frequent basis.

(4) Intravenous antivirals. Severely ill patients may benefit from the intravenous use of neuraminidase inhibitors. (For example, in the model scenario described in Table 3-1, as many as 300,000 patients are envisioned to require treatment in an ICU). However, no antiviral drugs have been approved by FDA for intravenous use. There are some initial clinical data on intravenous use of the approved drugs oseltamivir and zanamivir and more advanced clinical data for peramivir, a new drug with a somewhat different resistance profile than oseltamivir. The Working Group urges FDA to work with drug manufacturers to determine whether these drugs can be used intravenously as a result of accelerated approval or under the terms of an Emergency Use Authorization (EUA).

RECOMMENDATION 5-4: INTRAVENOUS ANTIVIRALS

We recommend that FDA accelerate a decision about the availability of antiviral drugs (peramivir, zanamivir, or oseltamivir) for intravenous use.

(5) Trigger for using adjuvant. The effectiveness of vaccines can often be increased by co-administration with adjuvants, substances that can amplify an immune response when mixed with an appropriate antigen, allowing the dosage of antigen to be decreased. Thus a given amount of antigen can be used to immunize more individuals. This strategy may be important if a vaccine is poorly immunogenic (and thus requires a large quantity of antigen) or if vaccine supplies are insufficient to fill an urgent national need. A supply of one adjuvant (MF59) has been ordered and stockpiled for possible use with the 2009-H1N1 vaccine.

Adjuvants are not currently approved for use with influenza vaccines in the United States, although they have been approved and are being used with influenza vaccines in Europe. Accordingly, the use of adjuvants would require an EUA by the FDA. Given these circumstances, there is reluctance to use adjuvants unless they are clearly necessary to extend the vaccine supply.

The Working Group encourages DHHS to develop quantitative criteria (vaccine efficacy, severity of epidemic) that would trigger a decision to use adjuvants and to ensure that sufficient data are available for the FDA to grant an EUA.

(6) Plan for a national vaccination campaign. A decision to vaccinate portions or the entirety of the U.S. population against influenza virus is an important step, but the public health consequences of that

decision depend heavily on the manner in which the decision is announced, the recommendations that are made about who should receive vaccine, and the system(s) chosen to distribute and deliver the vaccine. Without those additional steps, actual use of the vaccine may be low or the vaccine may be used inappropriately. The Working Group encourages DHHS to accelerate the planning required for an effective campaign, taking into consideration some of the recommendations about communication practices offered in Chapter 6. The ACIP has already proposed to CDC that up to 160 million people should be considered preferentially for vaccination against 2009-H1N1 virus, and a subset of those individuals should be prioritized according to criteria mentioned earlier in this chapter. Plans for a national campaign will need to incorporate appropriately those priorities and target messages about the vaccine. The complex and distributed nature of the U.S. healthcare system makes a coordinated national effort particularly challenging; considerable attention will need to be focused on the many logistical challenges.

(7) Surveillance of vaccine effectiveness and vaccine-associated adverse events. Clinical testing of an influenza vaccine allows scientists to determine whether that vaccine produces a measurable immune response that has been correlated with some degree of clinical protection. However, it does not directly determine whether the vaccine elicits protective immunity against infection that is a conclusion that can only be firmly drawn by studying groups of vaccinated and control individuals over longer periods of time. Furthermore, initial clinical tests usually are conducted with small groups of healthy individuals, so rare adverse events and complications associated with pre-existing medical conditions are unlikely to be encountered. In view of these circumstances, it will be important that CDC, FDA, and NIH develop a collaborative plan to monitor appropriately designated groups of vaccinees, based on age, location, or pre-existing conditions, to assess the effectiveness of the vaccines and study any adverse reactions. These observations will be especially useful if a virus closely related to 2009-H1N1 returns in future years

Medical Response

As discussed in earlier chapters, even in the absence of changes in the characteristics of the 2009-H1N1 virus, the capacity of some communities to provide an appropriate medical response to ill patients is likely to be strained and possibly overwhelmed at the peak of the anticipated fall outbreak. It is impossible to predict where and when this will happen, so it is important that all communities be prepared for this possibility. During spring and summer 2009, the 2009-H1N1 pandemic has stressed the health care system in several countries, including parts of the United States, Argentina, Canada, Chile, and Mexico, and this has provided an opportunity to learn from the health system response in these places.

Given the structure of the U.S. health care system, the response to these "surge" requirements will be addressed at the local, state, and regional levels, with the majority of capacity coming from private and non-profit facilities that are outside of government. Nevertheless, the Federal Government will play a critical supporting role in this response—by providing guidance to communities on strategies that address the medical requirements; by relaxing legal and regulatory constraints; by mobilizing Federal personnel to assist in the response; and, in some cases, by providing medical materiel from the Strategic National Stockpile. Furthermore, while the Working Group recognizes that the potential inadequacy of the Nation's medical "surge" capacity cannot be closed in the immediate future, we believe that use of

existing capacity can be improved and made more equitable by expanded monitoring and allocation of scarce resources (such as ICU beds and ventilators) used to care for the most critically ill patients, as described in Chapter 4 (see Recommendation 4-4) and by the development of procedures to mobilize equipment, personnel, or patients.

RECOMMENDATION 5-5: MEDICAL RESPONSE

In its efforts to prepare the Nation's complex health care system for the likely increase in cases of severe 2009-H1N1 influenza, we recommend that DHHS emphasize the following approaches:

- **A.** **Using planning scenarios, forecast requirements for hospital beds, ICU beds, personnel, equipment, and medical materiel to inform state and local authorities in their planning efforts. Special attention should be given to the capacity to care for critically ill infants and children, as most adult ICU facilities are not fully equipped to handle these patients, and potentially high-risk populations for whom the Federal Government has specific responsibilities, such as American Indians/Alaska Natives. Guidance should be offered on (1) strategies and best practices to close critical gaps, and (2) Federal resources available to assist in this effort (e.g., through the Strategic National Stockpile).**
- **B.** **Use national surveillance systems, in collaboration with state health authorities, to maintain up-to-date situational awareness of the medical response across the country, as recommended in Chapter 4 (see Recommendation 4-4). These efforts should aim to determine which locations are under the greatest duress; track clinical presentation of infection and effectiveness of interventions; and understand which medical surge strategies are most effective.**
- **C.** **Determine the authorities, protections, and guidelines necessary to maximize a community's ability to allocate scarce resources in the most appropriate, ethical, and just manner, without fear of inappropriate penalties. The intent is to ensure uniformity in the allocation of scarce and perhaps life-saving medical resources, such as ventilators, across communities.**
- **D.** **Consult with relevant professional societies and health care organizations to ensure that guidance for protection of health care workers from the effects of 2009-H1N1 is supported by the evidence, feasible to implement, and is harmonized among multiple sources. Relevant societies include the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America (IDSA), and, where recommendations concern children, the American Academy of Pediatrics (AAP).**
- **E.** **Work closely with state and local health personnel to prepare the public to self-triage and manage illness at home or at alternative care facilities when appropriate, using scalable solutions such as national toll-free phone lines and web-based instructions where appropriate (as discussed further in Chapter 6).**

Non-medical Mitigation Measures

The Federal Government's planned response to a pandemic virus includes community mitigation measures, including "social distancing," cancellation of public gatherings, voluntary home quarantine, and school closure. Implementation of these measures has been linked to the severity of the pandemic, which the Federal Government has codified through a "Pandemic Severity Index" or PSI. The PSI for the 2009-H1N1 pandemic proved to be very difficult to assign early in its course in North America: the PSI depends primarily on the "case fatality rate," which cannot be calculated with certainty when the total number of infected persons is unknown. Implementation of the more significant interventions, such as school closure, has proved to be controversial, due to a perceived imbalance between the negative financial and social consequences of the intervention relative to the perceived mildness of the pandemic virus.

Valuable lessons about community mitigation have been learned in the United States, the United Kingdom, Japan, Mexico, and elsewhere since the emergence of the 2009-H1N1 virus, and have also been gleaned from historical accounts of past epidemics. The Working Group believes it is essential to capitalize on these lessons and ensure that communities are prepared to implement appropriate community mitigation measures depending on the course of the pandemic this fall.

The importance of such preparations is underscored by the following observations: (a) it is possible that the virulence of the virus could increase in subsequent waves, as happened in 1918–19; (b) even at the current level of virulence, the demand on the health care system in some communities is likely to exceed available capacity, necessitating measures to slow the spread of the virus; (c) the sheer number of cases in a given community, along with concern among the public, may lead to unplanned school closure and absenteeism in the workplace; and (d) it is unlikely that significant proportions of the population will have vaccine-mediated immunity at the time the 2009-H1N1 virus returns to a given community this fall.

The Working Group recognizes that many components of the Federal Government, including DHHS/CDC, NSC, and the Departments of Labor, Homeland Security, State, and Defense are engaged in discussions of non-medical mitigation methods and that national guidance is being developed. We suggest that adequately resolving these issues will require a greater quantitative specificity, in particular, of the trade-offs between the medical benefit gained and social disruption caused by school or institutional closure. The costs and benefits of these measures have not, to our knowledge, been adequately weighed in quantitative terms. For example: although there is significant evidence, as well as logic, to support the idea that school closure (and presumably similar social distancing actions) can reduce virus transmission, clear analyses are needed of what specific effects on the spread of infection in different types of communities are likely to result from school closures at different infection prevalence. Even more difficult to assess are the economic and social costs of implementing such measures. Although evidence-based estimates of such costs are difficult to make and inherently imprecise, they can help to advance the rationality of the debates, especially if performed in the context of specific scenarios for the severity of an epidemic.

Finally, we note that there currently appears to be no value in using border closures or travel restrictions as social mitigation measures, as the H1N1 influenza virus is already well-established in the U.S. This situation could change if a more virulent or drug-resistant variant of 2009 H1N1 in another country became a serious threat.

RECOMMENDATION 5-6: NON-MEDICAL INTERVENTIONS

We encourage CDC, working with other components of DHHS, the Departments of Education, Homeland Security, Commerce, Labor, and others as appropriate, to prepare a document that provides general guidance on non-medical interventions to mitigate the predicted recurrence of the 2009-H1N1 pandemic in the United States. This document could be the basis for communication of key messages to several different constituencies, including local governments, school officials, leaders of institutions and businesses with high concentrations of personnel, and organizers of various kinds of public events, and it should include several important components:

- **A.** **A description of the lessons that have been learned about community mitigation measures as a result of the experience in the United States, Japan, Mexico, and other places where these measures were implemented during the 2009-H1N1 pandemic, as well as a summary of lessons from earlier epidemics.**
- **B.** **An account of the second- and third-order consequences of measures such as closure of schools and other institutions or cancellation of public events, and strategies to limit their impact.**
- **C.** **An articulation of the goals of community mitigation measures if implemented (e.g., reduction in community-wide transmission, reduction in peak burden on health care system, protection of those most at risk for severe complications, reactive in response to absenteeism) under various scenarios, and the impact this would have on implementation.**
- **D.** **Triggers for implementation and adjustment of community mitigation strategies, based on data that are likely to be readily available to decision-makers. These plans should include strategies for communicating the recommendations to the public and state and local stakeholders, as discussed in Chapter 6.**
- **E.** **Methods for monitoring the effectiveness or ineffectiveness of these interventions during the expected fall outbreak, both to guide continued use in the fall and to gather knowledge for use in future influenza outbreaks.**

International Considerations Presented by the Pandemic

In preparing for the resurgence of the 2009-H1N1 epidemic, protecting the U.S population is the Federal Government's primary responsibility. In addition, the Federal Government is concerned about the impact of the pandemic on other countries in terms of health effects (diseases spread rapidly across borders and epidemics do not end until they subside everywhere); economic consequences (pandemics can disrupt the global economy, trade, tourism, political stability, and foreign policy); and, importantly, humanitarian reasons (rooted in deeply held national values).

There is reason to believe that under-resourced countries may be at special risk during influenza epidemics. For instance, a recent study projected that, if a 1918–19-like pandemic were to happen today,

96 percent of the deaths would occur in the developing world. Given the relatively young demographic profile, the widespread prevalence of co-morbidities such as malnutrition, HIV/AIDS, and tuberculosis, and the fact that many of these countries do not have functional health systems, the 2009-H1N1 pandemic could have a devastating impact on developing nations. Serious outbreaks already have been observed in underserved populations in the developed world. For example, aboriginal populations of Manitoba, which represent 10 percent of the population, appear to have accounted for 30 percent of cases of 2009-H1N1 influenza in the province so far and the majority of 2009-H1N1-infected patients requiring intubation in ICUs in Winnipeg.

While recognizing that issues with basic health infrastructure in developing countries cannot be remedied in the short run, the availability of materials—including 2009-H1N1 vaccine, antiviral medications, antibiotics, personal protective equipment, and other essential medical materials—may help mitigate the impact of the epidemic. Unfortunately, global supplies of the most important of these items—vaccines and antiviral medications—are expensive and severely constrained; thus, large quantities are unlikely to be readily available to developing nations. The vast majority of production capacity for 2009-H1N1 vaccine, for instance, already has been reserved by industrialized countries.

Since 2005, the United States has taken a number of steps, often in conjunction with WHO, to support global pandemic preparedness, including the open sharing of information about novel influenza viruses and establishing capacity in developing countries to rapidly detect and respond to influenza viruses with pandemic potential (see Box 5C).

BOX 5C: SAMPLING OF U.S. ACTIONS TO SUPPORT GLOBAL PANDEMIC PREPAREDNESS

- **Sharing viral isolates, sequence information, and technical expertise with WHO and regional and national laboratories;**
- **Providing technical assistance to support country-level pandemic planning over the past several years, including adaptation of community mitigation strategies to developing world contexts;**
- **Providing technical assistance to support in-country public health and medical responses,, including adaptation of clinical guidelines and implementation of medical surge plans;**
- **Providing resources to WHO, as well as personnel and technical assistance;**
- **Supporting the WHO Global Access Plan to establish vaccine production capacity in developing countries and the WHO-managed stockpile of antiviral medications;**
- **Providing extensive support of in-country laboratory and surveillance efforts; and**
- **Supporting the response to 2009-H1N1 influenza in Mexico this spring, including a donation of 400,000 courses of oseltamivir.**

Mindful of the urgency of protecting the U.S. population, the Working Group nonetheless believes that the United States can play an important role in efforts to reduce the impact of the 2009-H1N1 pandemic in developing countries, both independently and in collaboration with other countries and WHO. We recognize that the current lack of a U.S. Agency for International Development (USAID) Administrator and a Director of the Office of Global Health Affairs at DHHS has limited the institutional capacity to work on these issues. Nonetheless, we believe these issues should be addressed.

RECOMMENDATION 5-7: THREE ACTIVITIES TO REDUCE THE IMPACT OF THE EPIDEMIC ON DEVELOPING COUNTRIES

A. **Take action to produce, purchase, or redirect vaccines, antiviral drugs, antibiotics, and medical materiel to developing countries in need of such support;**

B. **Use the influence of the United States, in collaboration with WHO, to convince other developed nations to pay close attention to the needs of developing countries during the pandemic and to encourage manufacturers to make vaccines and drugs available under donation and/or tiered-pricing schemes to those developing countries that have the plans and the capacity to use them effectively, and in the same time frame as these materials are made available to developed countries;**

C. **Incorporate the international consequences of mitigation plans into Federal decision-making processes for the pandemic—for example, by recognizing that efforts to conserve antigen by use of adjuvants in vaccines or to conserve antiviral drugs by restriction on inappropriate use could liberate valuable materials for use in poor countries severely affected by the epidemic**

An Improbable Scenario Requiring More Stringent Non-Medical Measures

The 1918–19 pandemic was characterized by a relatively mild first wave of illness in spring 1918, followed by much more severe second and third waves. This pattern could conceivably be repeated with the 2009-H1N1 virus, leading to a far greater strain on communities than described in Chapter 3 or currently anticipated by the Federal Government. While the Working Group views this specter as highly unlikely and inappropriate as a driver of Federal preparedness efforts, the possibility of such a "step change" in the severity of the pandemic (e.g., to "Category 5" in the current Pandemic Severity Index) cannot be entirely ignored. If it should occur, the Federal Government would be confronted with a national crisis and the prospect of hundreds of thousands of deaths, millions of hospitalizations, and a dramatic impact on the functioning of communities due to school closure, workplace absenteeism, and fear-driven changes in people's behavior.

Such an event would stress the Federal Government in ways that are not discussed in this report. The Federal Government may be unable to respond to the number and scope of requests for Federal assistance from state and local authorities, whether for support of the healthcare infrastructure or the preservation of law and order. Communities may be unable to provide medical care to everyone in need, raising the prospect of rationing of services and mortality that would otherwise be preventable.

Federal, state, and local authorities may take unilateral action such as border closure, seizure of essential commodities, or curtailment of individual freedoms, out of fear or as a result of public pressure.

Under these circumstances, it would be necessary for the Federal Government to have streamlined mechanisms for decision making and coordination of the national response. The capability for such coordination extends well beyond the processes described earlier in this chapter, and falls into the realm of "national incident management." The Federal Government has spent a great deal of time developing systems for such coordination; the National Response Framework and associated documents are the result of that work. But these systems have never been tested by an event of the scope and scale described here. For this reason, it is essential that the Administration examine these systems of coordination and the roles and responsibilities of all players—particularly the Departments of Homeland Security, Health and Human Services, Justice, Defense, State, and Education—to ensure that the Federal response can be scaled to the magnitude of the health crisis as warranted by the circumstances.

VI. Lowering Financial and Regulatory Barriers to Effective Response

CHAPTER SUMMARY

Legal, social or financial obstacles may prevent institutions and individuals from taking useful actions to confront an epidemic.

In this chapter, the Working Group describes several such barriers to effective actions and proposes ways to overcome them in times of public health emergencies by providing funds, suspending certain medical regulations, reducing financial impacts on hospitals, using special authorities, and encouraging action in the private sector.

We also recommend that the National Security Council, led by the Homeland Security Advisor, undertake a systematic review of potential legal, social, and financial barriers to action, to determine which might reasonably be ameliorated during the time of the anticipated epidemic and to set plans in motion to reduce or remove such barriers in accord with the observed severity of the epidemic.

Introduction

As discussed in previous chapters, influenza epidemics can be mitigated through medical and non-medical interventions. To achieve their full benefit, such actions require the compliance of individuals and organizations in many sectors, as well as adequate funding. The purpose of this chapter is to identify the potential social, financial, and regulatory barriers to compliance and to recommend ways to lower those barriers. Because the list of barriers and solutions below is likely to be incomplete, it would be valuable for the Administration to undertake a systematic analysis of these issues.

MAIN RECOMMENDATION (CHAPTER 6)

The effectiveness of mitigation efforts can be improved by (a) identifying potential legal, social, and financial barriers to action in the face of an influenza pandemic; (b) developing specific solutions and identifying triggers for implementing these solutions when feasible; and (c) ensuring that relevant actors know about the intentions to deploy the solutions. We describe several potential barriers, propose some solutions, and suggest that barrier-reducing activities be led by the National Security Council and the Homeland Security Advisor.

Emergency Funding for Federal, State and Local Actions

Responding to any widespread health emergency, such as an influenza epidemic, requires substantial resources from public and private sources, and the current economic recession is a potentially limiting factor in the provision of such funds.

The President and Congress have already taken commendable action through the Supplemental Appropriations Act, 2009 (P.L. 111-32), to provide financial support for efforts to control the current 2009-H1N1 pandemic by securing emergency response funds and allocating a substantial portion to support mitigation methods, as described in Chapter 1. We presume that the Office of Management and Budget will continue to closely monitor Federal expenses for influenza mitigation, so that additional emergency appropriations can be sought if necessary.

Using these funds, the Federal Government also has taken an important step to help already overburdened state and local public health organizations respond to the pandemic by providing $350 million from the emergency appropriation, through DHHS, to state and local governments and hospitals.

It is likely that additional funds will be required for various activities. In Chapter 4 we discuss the importance of enhancing surveillance systems—for example, to enlarge the capacity to diagnose 2009-H1N1 infection. In many states, public health laboratories are the only facilities offering this testing. If such laboratories are overwhelmed, key decisions about prophylaxis, treatment, and school closure may be delayed by diagnostic uncertainty. More funds would likely be required for such laboratory expansions.

RECOMMENDATION 6-1: DHHS MONITORING

We recommend that DHHS monitor the financial situation of state and local governments to determine whether they have sufficient financial resources and personnel to carry out necessary surveillance (including monitoring trends in respiratory virus activity and at least a minimal level of viral surveillance) and to respond to the public health situation, which may vary from one jurisdiction to another.

Lowering Barriers to Hospital Care

Hospitals may face regulatory and economic disincentives to care for patients acutely ill with influenza. In large outbreaks, hospitals—and in particular their pediatric wards, emergency departments, and ICUs—may quickly become overwhelmed. This may lead to the need for alternative care sites such as schools, hotels, stadiums, recreation centers, and churches. In addition, as we have already seen in other developed countries coping with influenza outbreaks this year, hospitals may need to reduce the number of beds available for elective surgeries and other activities that provide a major source of revenue. Further, overcrowded ICUs may require hospitals to transport some patients outside of the immediate area. Because rates of hospitalization for 2009-H1N1 are highest in children, hospitals can also anticipate needing more pediatric equipment than is typically available.

To respond appropriately to these pressures, hospitals may require relief from certain regulatory provisions that normally limit the number of severely sick patients who can be seen; require that all patients be subjected to routine tests or procedures that may be irrelevant during a pandemic; or prevent the rapid triaging of patients who are only mildly ill.

Two actions typically are necessary for these usual assurances to be waived. First, the DHHS Secretary must declare a Public Health Emergency. When this action is taken, the Secretary can gain access to a special fund called the Public Health Emergency Fund. (We note, however, that this access is currently since Congress has not appropriated any public monies to the Fund.) Second, the President must make a declaration under the Stafford Act or National Emergencies Act. When both of these actions have been taken, DHHS can waive or modify a number of administrative requirements of the Emergency Medical Treatment and Active Labor Act (EMTALA), Medicare, Medicaid, and the Children's Health Insurance Program (CHIP). For example, the Secretary can waive conditions of participation or certification requirements, allowing health providers to offer care even if not licensed by their state to do so. In addition, an "1135 waiver" of EMATLA could enhance the ability of hospitals to respond to a pandemic by allowing

- Diversion of less ill patients from emergency departments to alternative care sites for triage and treatment without being subject to penalties and fines;
- Provision of emergency care for patients regardless of their ability to pay; and
- Earlier care of patients in emergency departments, by eliminating the requirement for a medical screening exam before evaluation by a health provider.

During the spring 2009-H1N1 outbreak, a Public Health Emergency was declared nationwide but the Stafford Act was not invoked. Because both actions are required for DHHS to issue an 1135 waiver, hospitals were not authorized to divert individuals to off-site alternate care sites, even if their emergency departments were overwhelmed. In addition, the Public Health Emergency Fund, though authorized, is currently unfunded.

RECOMMENDATION 6-2: PUBLIC HEALTH EMERGENCY

We recommend that if the Secretary of DHHS declares a Public Health Emergency, the President consider issuing a Stafford Act declaration so that hospitals can more effectively triage and treat patients.

Alternatively, the Administration could ask Congress to amend the Social Security Act preemptively so that the ability to issue 1135 waivers is linked automatically to the declaration of a Public Health Emergency.

In addition, we recommend that Congress provide funding for the Public Health Emergency Fund.

In addition to regulatory barriers, hospitals face significant financial disincentives for vigorous planning and implementation of appropriate disaster operations. For example, a resurgence of 2009-H1N1 may fill large numbers of hospital beds with individuals who are in need of expensive care but are either

uninsured or have insurance that will reimburse the hospital at unfavorable rates. Moreover, a 2009-H1N1 resurgence could preoccupy hospital personnel; trigger expensive contagion control procedures; and force the postponement of more profitable cases or their diversion to other providers. All of these factors can have a detrimental effect on hospital finances. Hospitals also may need to rely upon alternative care sites and standards, which may not be subject to the usual reimbursement rules, raising the potential for non-reimbursed care.

RECOMMENDATION 6-3: EXAMINATIONS AND REIMBURSEMENT

We recommend that DHHS's Centers for Medicaid and Medicare Services (CMS), which reimburse hospitals for care provided through Medicare, Medicaid, and the Children's Health Insurance Program (CHIP), examine the financial implications for hospitals of actions they might take in responding to the pandemic. Such an analysis should examine the economic implications of hospital reimbursement for the care of 2009-H1N1 patients in conventional and alternative care sites, while also considering the financial losses that hospitals might incur by deferring elective procedures.

Non-medical Mitigation Activities

A key element in mitigating the spread of an epidemic is compliance with social distancing measures—for example, staying home from work or school or avoiding public gatherings such as concerts or sporting events when ill. However, compliance is unlikely when economic or other disincentives punish individuals for these behaviors. It is critical that appropriate Federal officials take the lead in identifying these disincentives and removing or minimizing them. Since immunizing large segments of the population likely cannot be completed before late November or early December, the use of social mitigation measures may represent the most effective means for reducing transmission of virus in the fall when it is spreading most efficiently.

Because crowding in schools is extreme and prolonged and because the risks of infection with 2009-H1N1 to the relevant age groups are high, special consideration should be given to ways to encourage potentially infectious students to remain at home rather than attend school.

RECOMMENDATION 6-4: COMMUNICATING WITH SCHOOLS

We recommend that the Department of Education, working with the Department of Health and Human Services and the Department of Labor, meet with representatives from state and local school districts in August 2009 to identify the financial needs and regulatory barriers that would discourage decisions to close schools when public health conditions warrant such closures and to consider actions that Federal, state, and local authorities could take to reduce those disincentives. Examples of possible actions include waivers on the minimum required number of school days, meals for children who are in school meal programs, access to online or "drop off" educational activities and programs, and childcare options for parents who work. Because actions might need to be taken rapidly, it is important that these plans be well publicized to institutional actors, including school principals.

We also recommend that the Department of Education develop clear and effective 2009-H1N1 contingency plans by October 1, 2009, and designate a health professional who is familiar with public schools to provide guidance to school districts.

Individuals sick with 2009-H1N1, and those who need to care for affected family members, face a loss of income or employment if they stay home from work. Similarly, holders of tickets for travel or sporting events face potentially substantial economic losses from nonrefundable ticket expenses. Such barriers may make them less willing to participate in social mitigation strategies that the government may propose. Both government and private organizations may need to take actions to lower such barriers. For example, the government can encourage businesses to promulgate more flexible sick leave and ticket reimbursement policies in response to an outbreak of influenza.

RECOMMENDATION 6-5: COMMUNICATING WITH BUSINESSES

We recommend that the Domestic Policy Council and the Assistant to the President for Intergovernmental Affairs and Public Liaison meet with leaders of small businesses, industry, and labor to identify mechanisms that might encourage individuals to stay home while sick—for example, by alleviating economic losses employees might otherwise sustain from such responsible actions. These leaders could identify actions the President might advocate to reduce barriers to social mitigation actions, such as more liberal worker leave policies, flexible union rules, and refundable tickets for airlines, trains, or buses or for concerts, athletic, or other public events.

We also recommend that the Federal Government immediately initiate policies that, in the event of increasing spread of influenza virus, would allow Federal employees with respiratory illness (or those caring for a child with same) to stay at home without financial penalty.

VII. Improving Communications

CHAPTER SUMMARY

Communication will be one of the most formidable challenges in managing the anticipated resurgence of 2009-H1N1 this fall, due to the rapidly evolving nature of the outbreak, the number and complexity of the messages, and the myriad channels through which the public will be receiving information.

CDC is the lead Federal agency for communication with state and local health departments, health care providers, and the general public. CDC's communications plans for the first two groups appear to be proceeding well, although we offer some suggestions.

Concerning communications with the general public, the Working Group believes it would be desirable to have well-developed communications plans that cover a variety of contingencies and is concerned that the planning for such communications may be somewhat behind schedule.

We recommend that CDC expand its efforts to develop a full range of communication plans for various contingencies. In view of the fact that 2009-H1N1 particularly affects young people, these plans would ideally include outreach not only to traditional media but also new media and social networking channels.

Introduction

One of the lessons of prior influenza epidemics is the importance of timely, clear, and effective communication among government officials, medical professionals, and the public. In spring 2009, CDC reacted well in terms of communications with both professionals and the public. CDC maintained a steady flow of up-to-date information and admitted the limitations of its knowledge as the situation evolved.

During the expected fall resurgence of 2009-H1N1, communication will again pose a formidable challenge for officials and others trying to manage the pandemic. But the communications challenge will be fundamentally different than in the spring, when the epidemic arrived unexpectedly and CDC's stance was necessarily reactive. For the anticipated fall resurgence, CDC's approach must be pro-active. The fundamental difficulties are that (i) the messages will be more numerous and more complex and (ii) the precise content of the messages is uncertain for now and will depend on the specifics of how the public health situation unfolds. Nonetheless, the existing data give planners enough knowledge to envision different scenarios of how events could play out (see Chapter 3). This makes it possible—and we believe imperative—to have carefully considered communication plans prepared in advance, ready for many contingencies.

For instance, if only limited supplies of vaccine are available initially, it is likely that diverse groups at particularly high risk of severe disease will be prioritized for vaccination and potentially for antiviral medications, as described in Chapter 5. Communication plans need to be developed to reach individuals

who belong to the designated high-risk groups and their health care providers—for example, through patient advocacy groups, provider organizations, radio and TV spots, and social networking. The content and format of the outreach materials should be considered in advance. Contacts should be made in advance with leaders of relevant media or patient organizations so they can prime their networks for rapid delivery of the relevant messages.

CDC clearly is the lead Federal agency for communication with three constituencies: (1) state and local health departments, (2) health care providers, and (3) the general public. The Working Group reviewed CDC's communications plans in these areas for the anticipated epidemic this fall.

The Working Group expressed confidence in CDC's communications plans with the public health departments and health care providers; the Group's primary suggestion for communication with these groups is that CDC work to harmonize recommendations with relevant medical societies. In contrast, the Working Group expressed some concern that CDC's plans for public communications appear to be inadequately developed at present and somewhat behind schedule. In addition, the Group was concerned that CDC had not adequately planned to engage the full range of communications channels. Because 2009-H1N1 will particularly affect young people, there is an opportunity and need to engage new media and social networking channels.

MAIN RECOMMENDATION (CHAPTER 7)

We recommend that CDC accelerate its planning efforts for public communications. Given the limited time frame and the wide range of uncertainties, we recommend that CDC systematically identify the full range of messages that may need to be communicated, particularly messages about actions that may be required of the public under various scenarios; prepare well-developed plans for these communications; and begin outreach to relevant communications channels as soon as possible.

We also recommend that CDC engage not only traditional media, with which CDC has deep experience, but also new media and social networking channels, especially given the propensity of the 2009-H1N1 virus to infect young people. For this purpose we recommend that CDC draw heavily on the expertise of the office of the Federal Chief Technology Officer.

Communication with State and Local Health Departments

CDC deserves high marks for its coordination of information flow to and from state and local health departments during the spring 2009-H1N1 outbreak. It clearly articulated what was known and unknown, provided useful updates in real time, and assimilated large amounts of regional data to provide an evolving picture of what was happening on the national level.

In Chapters 3 and 4, the Working Group recommends that CDC (i) define and disseminate specific scenarios concerning the pandemic and (ii) improve various surveillance systems. These steps should feed into and enhance communications with state and local health departments. In addition, the Working Group urges CDC to prepare materials to help Federal, state, and local health officials deal with potential

misunderstandings relating to adverse events. It is certain that, by chance, some adverse events will occur following vaccination (e.g., on any given day, some elderly individuals will die and pregnant women will miscarry). It is important that CDC has well-developed materials completed in advance to set such events in context, as well as to help experts recognize truly unexpected occurrences.

Communication with Health Care Providers

Medical professionals rightly regard CDC as the authoritative source for public health information, especially during emerging epidemics. In general, CDC has discharged this function well during the present crisis. However, there have been several instances in which its recommendations have been controversial—particularly those regarding hospital infection control, which have sometimes been based on hypothetical concerns rather than epidemiological data. Some of these recommendations generated controversy and even outright opposition from caregivers. For example, CDC's recommendation for use of N95 respirators by those caring for hospitalized 2009-H1N1 patients is at variance with the views of several other expert bodies. Such conflicts can generate confusion and anxiety at many levels in the hospital workplace, impair effective compliance with proper infection control, and undermine physician confidence in CDC and public confidence in local infection control measures at a time when confidence levels need to be maximized.

RECOMMENDATION 7-1: HARMONIZE RECOMMENDATIONS

We recommend that CDC work to harmonize its recommendations with those of relevant professional societies prior to their public release. As discussed in Chapter 5, relevant societies include the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America (IDSA), and, where recommendations concern children, the American Academy of Pediatrics (AAP).

Communication with the General Public

CDC and other Federal agencies must communicate with the public in two broad areas: (1) medical interventions (vaccines and antiviral medications); and (2) non-medical, community-based interventions (e.g., social distancing and isolation of sick individuals). The Working Group has some concerns with the communications plans in both areas. Since they have different origins, the two sets of concerns are considered separately.

Medical Interventions: CDC has a long history educating the public about seasonal influenza and the vaccine that provides protection against it. Despite this experience, efforts to prepare the influenza public information campaign for fall 2009 have been hampered by several factors, including:

- the need to divert staff to communicate urgently with the public regarding the spring 2009-H1N1 outbreak
- uncertainties about the 2009-H1N1 vaccine (including how much will be available, on what schedule it will arrive, how many doses may be needed, and who should receive vaccination); and

- the inherent complexity of a public health message that encompasses two vaccines for two different types of influenza (2009-H1N1 and a seasonal strain), especially if two doses of 2009-H1N1 vaccine are required.

For these and other reasons there is much communications work ahead, and very little time to complete it. CDC's information campaign will need to:

- refocus the public's attention on 2009-H1N1 influenza, which has largely receded from public consciousness (due in part to the media's sporadic attention to the topic), and its relationship to seasonal influenza;
- keep the public updated about the severity of the epidemic;
- educate the public about when to seek medical attention and where to do so;
- inform the public about personal and community-wide action that may be necessary this fall, and steps people can take to be prepared;
- reach groups at particularly high risk; and
- respond effectively to unexpected events, such as reports of adverse events that occur following (but not necessarily because of) vaccination.

To accomplish these missions, it is critical that CDC have well-developed public communications plans that can be launched rapidly. The planning for various contingencies should be completed now, before all the relevant information is available. Contacts with various media should be established soon, and messages and materials should be developed and tested.

We particularly encourage CDC to work with new media and social networking channels. Beyond simply transmitting CDC's own messages, we believe there are opportunities to engage and encourage the creativity of the social networking community to create content and collect information. Members of the Working Group were impressed by a recent paper by researchers at Google and CDC demonstrating that an analysis of Google searches related to influenza-like symptoms was able to identify outbreaks earlier than conventional surveillance systems. Examples could include: 1) websites with information about initial self-diagnosis and treatment, up-to-date information about the epidemic, and perhaps even ways to share personal information that could help inform national surveillance; 2) mobile phone "apps" with similar content; 3) videos that convey messages in unusual ways; and 4) Facebook quizzes on influenza, shared among friends. In support of efforts to fight the influenza virus, we advise the use of communications tools designed to facilitate their "going viral." Such tools are more likely to be created by members of the public than by the government. However, it may be possible to encourage such efforts through contests and other mechanisms.

RECOMMENDATION 7-2: CDC COMMUNICATION EXPANSION

We recommend that CDC expand its efforts to develop a robust communications plan covering the full range of potential public messages about medical and non-medical interventions. We strongly suggest that communications efforts be launched prior to September 1.

- **A.** **With respect to traditional media, we suggest that CDC reach out to major communication channels (e.g., editorial boards and medical reporters at newspapers, TV and radio stations, and magazines) to inform them about issues, to interest them in running stories to promote awareness, and to maintain connections that will facilitate communication when unfolding events demand rapid responses.**
- **B.** **With respect to new media and social networking, we suggest that CDC reach out to key companies (e.g., Facebook, Twitter, Google, Apple) and other innovative entities and individuals (those who maintain prominent websites and blogs related to health in general and influenza in particular). In this outreach, CDC could benefit by working closely with the Federal Chief Technology Officer.**
- **C.** **In addition, we urge CDC to expand its capacity to develop rapid responses to misinformation appearing in traditional media and on the Internet**

Non-medical Interventions: Compared to communications about medical interventions, communications about social actions to mitigate spread of the influenza virus can be crafted in relatively finished form despite uncertainties about details of the epidemic. Public understanding about such personal measures and their public health value are particularly important given the likelihood that vaccine will not be available as rapidly as desirable. The Working Group expressed some concern that public communications plans for such measures appear to be incompletely developed.

Fundamentally, there are two main categories of personal actions to mitigate viral spread, hand hygiene awareness and individual efforts at social distancing, which can be summarized in two simple messages: "Keep your hands clean" and "Stay home when you're sick." Although these messages are simple, the educational campaign is difficult because it involves persuading people to change established patterns of behavior and requires broad adoption to be successful. Campaigns to encourage these actions should strive for clarity and simplicity; use diverse and complementary channels of communication; and incorporate thoughtful policies to mitigate barriers to compliance (see Chapter 7). Importantly, such campaigns will need to educate the public about why the measures are needed as well as how to comply with them.

Hand hygiene awareness is more than just hand washing. It includes minimizing contact of hands with respiratory secretions—by coughing into a sleeve rather than a hand, for example. Communication channels that can transmit graphic visual images (e.g., television and Internet) are likely to be the most effective. The public already has accepted media ads involving more sensitive bodily functions, and major advertising agencies know how to craft effective and acceptable messages in this regard. New media and social networking expertise may also be effective here.

Social distancing campaigns, especially those that go well beyond the simple notion of remaining isolated, generally at home, when ill, must enlist the participation of the general public to be effective. Workers and students will need to know when to stay home and for how long; they will also need guidance about proper infection control in the home. When asking the public to eschew activities that involve crowds at sporting events, concerts, transportation centers, shopping areas, and other gathering places, the messages will need to explain the rationale for such changes in behavior and provide an estimate of the length of time the recommendations will be in place. All channels are useful and efforts should be made to enlist the most effective communicators (e.g., celebrities) to deliver the relevant messages.

Such campaigns also need to enlist the support of those responsible for the venues in which susceptible and infected people are likely to congregate (e.g., employers, school and university administrators, church leaders, sports leagues, and rock concert promoters). Now is the time for the CDC to establish communication channels with corporate human resource professionals, school officials, and others to inform them about the public health issues surrounding 2009-H1N1 and to help them understand that allowing sick individuals to stay home is in their organizations' best interest, as it will minimize large-scale absenteeism. Universities may require special guidance about infection control in dormitory settings.

RECOMMENDATION 7-3: CDC COMMUNICATION QUICK LAUNCH

We recommend that CDC rapidly develop and launch its communications plan concerning personal non-medical interventions.

In particular, we suggest that CDC: a) immediately hire a major advertising organization to help craft ads for non-medical interventions, targeted at various audiences (e.g., employers, the general public, school administrators) and b) work with the Federal Chief Technology Officer to engage new media and social networking channels in support of these goals.

VIII. Planning for More Effective Future Strategies Against Influenza

CHAPTER SUMMARY

The current threat from 2009-H1N1 has highlighted critical shortcomings in public response systems to the emergence of new influenza strains and more generally to outbreaks of infectious diseases.

There are important opportunities to increase national preparedness against future epidemics. These include steps to improve: the design, production, and use of vaccines; the range of antiviral drugs; the availability of rapid diagnostics; and the breadth of health surveillance systems. Some of the steps can be achieved quickly (within the next year), while some will take longer.

We propose that the National Security Council coordinate a government-wide effort to increase national preparedness in response to the lessons learned from the 2009-H1N1 outbreak and provide periodic updates to the President on national progress toward these goals.

The current situation with 2009-H1N1 has highlighted critical shortcomings in public response systems to the emergence of new influenza strains and more generally to outbreaks of infectious diseases. Given the emergence of multiple biological threats during the past decade (including SARS, avian flu, 2009-H1N1, and at least one instance of bioterrorism), it is likely that we will face continued challenges from infectious diseases. While there has been substantial progress in preparedness over the past several years, there is much work that needs to be rapidly completed. Even while we are dealing with 2009-H1N1, the Federal Government should take specific steps to ensure our preparedness for the next event. Some of these steps will also aid our national response to seasonal influenza.

MAIN RECOMMENDATION (CHAPTER 8)

There are important opportunities to increase national preparedness against future epidemics. These include steps to improve: the production and use of vaccines; the range of antiviral drugs; the availability of rapid diagnostics; and the breadth of health surveillance systems. Some of the steps can be achieved quickly (within the next year), while some will take longer.

We propose that the National Security Council coordinate a government-wide effort to increase national preparedness specifically in response to the lessons learned from the 2009-H1N1 outbreak and provide periodic progress updates to the President on national progress toward these goals.

Accelerate Speed and Increase Yield and Effectiveness of Vaccine Production

Current methods for producing influenza vaccine are too slow, cumbersome, and inefficient given the challenge of a rapidly spreading influenza virus epidemic. The predominant design and technologies used to produce influenza vaccines have not fundamentally changed in several decades: Viruses are grown in embryonated chicken eggs, then harvested and processed to create the vaccine. The process typically takes 6 to 9 months, from initial steps to develop a "seed" vaccine virus to completed product. Moreover, when a novel virus is isolated late in an influenza season (as was the case with 2009-H1N1), it is difficult or impossible to prepare and test vaccine before the resurgence in the next influenza season (which, moreover, tends to occur early for novel viruses).

Recently, there has been progress on two new approaches for vaccine production:

- *Cell-based vaccines*, in which viruses are grown in cultured cells rather than eggs. This method obviates the need for large quantities of embryonated eggs and potentially permits increased levels of production beyond those currently achievable. The method, however, does not substantially shorten the timeline between identification of the virus strains to be included in the vaccine and the vaccine's availability. This approach is currently being used by several companies to produce candidate 2009-H1N1 vaccines, but such cell-based vaccines have not yet achieved licensure in the United States.
- *Recombinant vaccines*, in which molecular biology techniques are used to clone influenza virus vaccine proteins into various expression systems. There are several such methods currently under development and evaluation, including some by industry and by the Defense Advanced Research Projects Administration (DARPA). This approach has potential to shorten the time between vaccine strain identification and final vaccine production to as little as a few months, as well as provide a large increase in vaccine production volume. However, considerable additional development and clinical work is required to firmly prove the effectiveness of these technologies and to provide the necessary data for eventual licensure.

In addition to the pursuit of these approaches, greater efforts should be made to take advantage of modern understanding of influenza virus epitopes (the sites on proteins that induce immunity), three-dimensional protein structure, the mechanisms of immune recognition, and the sites on influenza viral proteins at which the most significant variation is observed. By harnessing such information to new methods for protein design and genetic engineering, it is possible to envision influenza vaccines of the future that provide longer-lasting immunity against a wider range of viral isolates. Such vaccines might be produced efficiently as proteins in a variety of expression systems or as attenuated viruses grown in cell culture systems.

In addition to improving vaccine design and technology for vaccine production, efforts need to be undertaken to assess and license adjuvants that are compatible with influenza vaccines. Adjuvants can greatly increase the potency of vaccines and thereby extend the number of people who can be vaccinated with a given supply. None is currently approved for use with influenza vaccines in the United States, although adjuvants have been approved and are being used with influenza vaccines in Europe.

The use of adjuvants thus currently requires Emergency Use Authorization (EUA), a step that regulators may be reluctant to take. Although clinical trials of 2009-H1N1 vaccines with adjuvants are planned for the coming months, it will not be feasible to obtain standard FDA approval in time for use this fall. Nonetheless, it would be desirable to achieve licensure of the currently available adjuvants for use in the near future. Beyond existing adjuvants, recent advances in immunology point the way to powerful new types of adjuvants, the pursuit of which may ultimately enhance the efficacy and lower the costs of influenza vaccines.

Even while these new products are being developed and tested, it is important that the Federal Government ensure that capacity is maintained for influenza production by traditional approaches for the foreseeable future. Capacity was increased in preparation for a potential avian influenza (H5N1) pandemic and is thus available for response to the current 2009-H1N1 pandemic. However, if such high capacity levels are not needed over the coming years, companies may reduce production capacity to bring it more in line with the lower anticipated demand for seasonal influenza vaccine. The prospect of such reduced capacity, which would limit the ability to respond to novel influenza pandemics, provides further incentive for developing more efficient means of production.

RECOMMENDATION 8-1: VACCINES

We recommend that the Federal Government work to:

- **A. ensure that influenza virus vaccines produced in cell culture, as well as vaccines formulated with the currently available adjuvants, proceed expeditiously through the FDA regulatory process for licensure;**
- **B. fully support and encourage development of recombinant influenza vaccines and provide a clear regulatory path for licensure;**
- **C. encourage and support the development of new adjuvants; and**
- **D. ensure that adequate manufacturing capacity is maintained for production of influenza vaccine using currently approved methods.**

Facilitate Development of Additional Antiviral Drugs

There is an urgent need to expand the available range of antiviral drugs that can be used for prophylaxis or treatment of influenza. Currently, there is only a handful of antiviral drugs and only two that are licensed and expected to be effective against 2009-H1N1: the oral drug oseltamivir (Tamiflu) and the inhaled drug zanamivir (Relenza). There currently are no antiviral drugs approved for intravenous use to treat seriously ill patients—although one new drug (peramivir) and the two existing drugs are also being tested in intravenous formulations.

Moreover, these options may narrow further as influenza viruses develop resistance to these drugs. Most seasonal influenza has already developed resistance to oseltamivir, and a handful of cases of oseltamivir-resistance have been reported among 2009-H1N1 isolates (nine as of the end of July), indicating that this virus can also develop resistance.

It will be important to develop new classes of drugs to expand the armamentarium. A particularly promising new approach is to develop drugs that block the virus by acting on a human cellular function ('host target'), rather than a viral protein ('pathogen target'), because such drugs should be less likely to encounter acquired resistance.

RECOMMENDATION 8-2: ANTIVIRALS

We recommend that the Federal Government work to:

- **A. expedite the licensure of intravenous formulations of antivirals, and**
- **B. stimulate the development of new influenza drugs that have novel mechanisms of action in order to reduce the potential for antiviral resistance.**

Facilitate Development of Rapid Point-of-Care Diagnostics

Influenza can be difficult to diagnose because similar symptoms can be caused by agents other than the influenza virus, including adenovirus, respiratory syncytial virus, rhinovirus, parainfluenza viruses, mycoplasma, and other agents. Moreover, it is important to be able to distinguish among different influenza strains, such as seasonal influenza and 2009-H1N1 influenza, because resistance patterns and drug-of-choice may vary. Definitive diagnosis can be important to guide medical decisions for individual patients and to permit accurate epidemiological surveillance.

Accurate diagnostic tests for distinguishing different influenza strains are available, but they (i) require several hours to days to provide results, (ii) are not readily deployed in physicians' offices or even hospital settings, (iii) have limited sensitivity, and (iv) are available in only limited capacity that will be overwhelmed in a serious pandemic. The Nation needs the capability to perform rapid, simple, point-of-care diagnostics. The competence and capability to develop such diagnostics exists in many places, including CDC, NIH, DARPA and DHS, and the importance of this issue warrants strong, mission-driven coordination of efforts across these agencies.

RECOMMENDATION 8-3: DIAGNOSTICS

We recommend that the Federal Government ensure the creation of a national capability to develop, on a rapid basis, accurate point-of-care diagnostics for any novel influenza virus. Such an effort might be led by DHHS, in coordination with DOD and DHS.

Improve Medical Surveillance

As described in detail in Chapter 4, there are substantial gaps in the Nation's medical surveillance systems that limit our ability to obtain accurate, real-time information about epidemics. Some of these gaps can be closed quickly, but a more systematic, long-term effort to eliminate them would substantially improve national preparedness.

Surveillance preparedness to date has emphasized early detection of an outbreak (e.g. early knowledge of an anthrax attack), while underplaying the role of ongoing surveillance once an outbreak of infectious disease is underway. In the case of influenza, while the United States has systems to provide epidemiological and virological data on influenza, we are still not able to make confident estimates each week of the number of people who are infected, seek medical care, are hospitalized, or die of influenza. Notably, the UK measures and publicizes many of these statistics weekly.

Such "situational awareness" is essential for an evaluation of the characteristics of the pandemic, effective allocation of resources to places of greatest need, and appropriate changes in mitigation and other response strategies over the course of a pandemic. Moreover, the ability to make such estimates would improve diagnosis and treatment of respiratory infections in general and of influenza specifically, both in normal and pandemic years, and would provide a basis for greater cost-effectiveness. The estimates could be obtained with a nationally representative electronic reporting system for primary care and emergency visits, hospitalizations, ICU admissions, and deaths for defined respiratory infections, combined with viral testing of a representative subset of these individuals. This would permit public health departments to assess the contribution of various viruses to the disease burden at each level.

A second key shortcoming in our preparedness is the lack of a rapid system for assembling detailed clinical data on severe cases that can provide a statistically adequate and continuously updated picture of risk groups and clinical course. Current systems rely on non-standardized reports from local health departments and on peer-reviewed case series, which are slow to become public.

As the current pandemic continues to unfold, other key gaps in our situational awareness will likely emerge. These revelations should be a basis for improving public health information systems.

RECOMMENDATION 8-4: MEDICAL SURVEILLANCE

We recommend that CDC take steps to improve surveillance systems for use in epidemics. This could include:

- **A. working with state and local authorities to establish a dense, geographically diverse, nationwide, real-time surveillance network that can estimate population rates of primary care and emergency visits, hospitalizations, ICU admissions, deaths from defined respiratory syndromes, and (in a random sample of cases) presence of specific viruses.**
- **B. working with a set of large hospitals, at least one in each of the top 30 metropolitan areas together with the respective local authorities, to establish a system for standardized local and national reporting of demographic, laboratory, and clinical characteristics of hospitalized and more severe cases of defined syndromes, including but not limited to influenza.**

We also recommend that after the current pandemic DHHS undertake a comprehensive review of unmet needs for data, possible solutions to the problems of providing such data under emergency conditions, and the costs of building the necessary surveillance systems.

Enhance Animal Surveillance Measures

Birds and pigs serve as critical intermediate hosts in the evolution of influenza viruses, including the current 2009-H1N1 virus. Methods for monitoring influenza viruses in swine and turkeys are powerful tools for following the appearance, spread, and evolution of viruses, and such surveillance would be valuable for both human public health and agriculture. Currently the United States lacks a reliable system for doing this, but a NIH-funded surveillance program of apparently healthy pigs at a slaughterhouse in Hong Kong has established the benefits of such a system.

RECOMMENDATION 8-5: USDA AND CDC COLLABORATION

We recommend that USDA and CDC collaborate to develop a cooperative program of human and animal public health that includes:

- **A.** **prospective virological and serological surveillance of swine and turkeys, and the workers exposed to them, at permanent sites, to serve as an early warning system of potentially pandemic influenza viruses of humans, swine, and turkeys.**
- **B.** **expanded sharing of influenza viruses, viral sequence information, and reagents.**

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