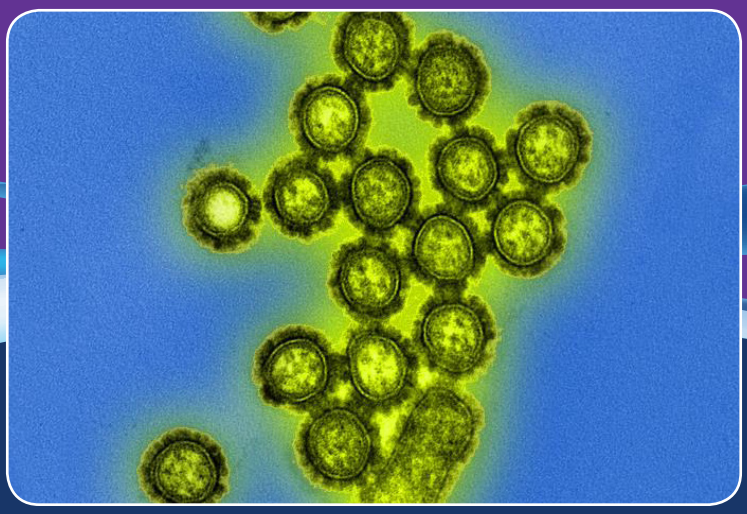
Pandemic Influenza Plan

2017 UPDATE



U.S. Department of Health and Human Services

Contents

FOREWORD

The last Pandemic Influenza Plan for the Department of Health and Human Services Update was issued in 2009. Since that time, our nation has experienced, and learned from, the 2009 Influenza A(H1N1) pandemic and the emergence of other influenza viruses of concern, such as H7N9 that emerged in 2013 in China and continues to cause periodic outbreaks. We have also responded to other serious disease outbreaks, including Ebola and Zika virus. Each instance has highlighted the need to be as prepared as we can be—because a fast, effective public health response demands it.

The original 2005 Plan was audacious in its goals—for domestic pandemic vaccine production capacity, for stockpiling of antiviral drugs and pre-pandemic vaccines, and for using community mitigation measures to slow spread of disease. At the time of the Plan's writing, the Nation was wholly unprepared to address the significant medical and health needs that a severe pandemic might present. Challenges included limited domestic vaccine manufacturing capacity, a very low supply of antiviral drugs, and lack of community planning for responding to an infectious disease outbreak. More than ten years later, we have many successes to celebrate—but we must not become complacent, because so many challenges remain.

Today, with a domestic vaccine manufacturing capacity well-established, stockpiles maintained, and evidence-based guidance on prevention, mitigation and treatment available for state and local governments, the private sector, individuals, and families, we face different challenges—how to sustain the advances we have made, to keep up with the changes in how people live and work, and to close in on those goals that have proved more elusive.

Pandemic influenza is different from other outbreaks we have faced because the characteristics of influenza viruses – their propensity to change, the ability to spread easily among people, and the routes of transmission – make the disease challenging to contain. Throughout history, influenza pandemics have led to widespread illness and death. Pandemic influenza is not a theoretical threat; rather, it is a recurring threat. Even so, we don't know when the next pandemic will occur, or how severe it will be.

The 2005 Pandemic Influenza Plan and subsequent updates focused planning for a severe pandemic with effects that would extend beyond health consequences to include social and economic disruption. By preparing exclusively for a very severe pandemic, the Plan did not include specific guidance for the type of pandemic we experienced in 2009, which was comparatively less severe. However, the capabilities that were developed through the HHS Plan, the National Strategy for Pandemic Influenza, and its companion 2006 Implementation Plan, were effectively adapted and used to respond to the pandemic that emerged. Lessons learned were captured to inform future responses.

We issue this 2017 Update to the HHS Pandemic Influenza Plan with the aim of highlighting and building upon the successes of the last decade, and making clear the

additional efforts that are needed to improve pandemic preparedness. These efforts are described in the seven domains that form the basis for this update.

However, scientific progress in the last decade compels us not only to articulate what is possible, but what is needed to truly transform our pandemic preparedness—to be more visionary. Innovation and new approaches should be considered to augment planning and response. With this in mind, HHS is exploring:

The development of innovative diagnostic testing and disease monitoring, building on the emerging technologies used for personalized health, including the potential for home diagnostic testing and on-line access to health care services.

Re-conceptualizing respiratory protection to limit transmission of disease from those who are infected to those who are well and protect caregivers and other responders by redesigning respiratory protective devices so they provide better protection and are easy and practical to use.

Accelerating vaccine and antiviral development, with a goal of having vaccine ready for administration within 3 months of the emergence of a pandemic strain, and approved broad spectrum antiviral therapies suitable for a range of influenza and other viral pathogens.

Modernizing medical countermeasure distribution and administration by linking information technology and modern supply chain science to patterns of human behavior and care seeking.

Ensuring people get the right care at the right place and at the right time, beginning with tools to aid individuals in their care seeking and decision making, and implementing surge strategies so that people receive care that is safe and appropriate to their level of need, thereby conserving higher levels of care for those who need it.

These goals are attainable, but achieving them will require dedication in terms of resources, innovation, education and outreach, and commitment. Although pandemic influenza threats are one of the greatest public health challenges of our time, other emerging infectious diseases can also have a devastating impact on human health. Balancing the need to respond to threats as they emerge with the long-term preparedness activities needed to mitigate them represents a significant challenge. However, the capacity and capabilities developed for pandemic influenza preparedness will enable HHS to respond more effectively to other emerging infectious diseases.

EXECUTIVE SUMMARY

In 2005, the U.S. Department of Health and Human Services (HHS) developed the HHS Pandemic Influenza Plan to prevent, control, and mitigate the effects of influenza viruses that pose high risk to humans. Influenza viruses, of which there are many types, can cause rapid, widespread disease and death. Pandemic influenza outbreaks in the 20th Century alone left tens of millions of people dead in their wake and cost hundreds of billions of dollars in lost lives, wages, productivity and economic devastation. Influenza viruses with pandemic potential require the rapid development, production and availability of medical countermeasures (MCMs) such as vaccines, diagnostics and antiviral drugs to mitigate the impact of the pandemic, as well as additional preparedness and response efforts beyond medical countermeasures.

HHS has made substantial progress in pandemic influenza preparedness since the 2005 Plan was released. In the current document, HHS reviews that progress, highlighting both the successes and remaining gaps in our preparedness and response activities for pandemic influenza. Most significantly, HHS efforts in pandemic influenza preparedness now are closely aligned with seasonal influenza activities, harnessing expanded surveillance, laboratory, vaccine, and antiviral drug resistance monitoring capacity. These activities are linked to efforts to communicate protective measures to the public and to help the health care system manage the demands of seasonal and potential pandemic influenza. Research across all these areas, and increased global capacity to diagnose and type the influenza viruses encountered outside the United States, contribute to domestic preparedness against pandemic influenza.

The original 2005 Plan consisted of four key pandemic response elements. This 2017 Update builds upon goals elaborated in the 2005 Plan and, using evolving science and budget priorities, identifies domains, goals, objectives, and key actions to serve as planning guides for the next decade. The seven domains for 2017-2027 are:

1. **Surveillance, Epidemiology, and Laboratory Activities** - Better detection and monitoring of seasonal and emerging novel influenza viruses are critical to assuring a rapid recognition and response to a pandemic. Over the next decade, HHS will increase use of new gene sequencing technologies for detecting and characterizing influenza viruses in the U.S. and globally. Candidate vaccine viruses will be more rapidly developed and synthesized when needed, to speed manufacturing of vaccines. Greater use of ‘big data’, analytics, and forecasting will enhance surveillance and planning.

2. **Community Mitigation Measures** - Incorporating actions and response measures people and communities can take to help slow the spread of novel influenza virus. Community mitigation measures may be used from the earliest stages of an influenza pandemic, including the initial months when the most effective countermeasure—a vaccine against the new pandemic virus—might not yet be broadly available.

3. **Medical Countermeasures: Diagnostic Devices, Vaccines, Therapeutics, and**

Respiratory Devices - Aggressive translation of applied research in diagnostics, therapeutics, and vaccines may yield breakthrough MCMs to mitigate the next influenza pandemic. Building on existing systems for product logistics, as well as advances in technology and regulatory science, can increase access to and use of critical countermeasures to inform response activities.

4. **Health Care System Preparedness and Response Activities** - Delivery system reform efforts of the past decade have made today's health care system dramatically different from 2005. The next 10 years will bring even more changes to delivery settings, provider types, reimbursement models, the sharing of electronic health information, referral patterns, business relationships, and expanded individual choice. Despite these changes, health care systems must be prepared to respond to a pandemic, recognizing that potentially large numbers of people with symptoms of influenza, as well as those concerned about the pandemic will present for care. Systems must implement surge strategies so people receive care that is appropriate to their level of need, thereby conserving higher levels of care for those who need them. HHS must keep abreast of these changes and adapt tools and strategies accordingly.

5. **Communications and Public Outreach** - Communications planning is integral to early and effective messaging when a pandemic threatens, establishes itself, and expands. Accurate, consistent, timely, and actionable communication is enhanced by the use of plain language and accessible formats. Testing messages and using appropriate channels and spokespeople will enhance our ability to deliver consistent and accurate information to multiple audiences.

6. **Scientific Infrastructure and Preparedness** - A strong scientific infrastructure underpins everything HHS does to prepare for, and respond to, pandemic influenza and other emerging infectious diseases. Strong scientific foundations are needed to develop new vaccines and therapeutics, and to determine how well other control efforts are working. Rigorous scientific methods applied during a pandemic response yield information to improve both ongoing and future responses.

7. **Domestic and International Response Policy, Incident Management, and Global Partnerships and Capacity Building** - HHS will continue to coordinate both domestic and international pandemic preparedness and response activities. This will include having clearly defined mechanisms for rapid exchange of information, data, reagents and other resources needed domestically and globally, to prepare for and respond to an influenza pandemic outbreak.

These domains reflect an end-to-end systems approach to improving the way preparedness and response are integrated across sectors and disciplines, while remaining flexible for the conditions surrounding a specific pandemic. This will allow HHS to respond more quickly to a future influenza pandemic and, at the same time, strengthen our response to seasonal influenza to mitigate the next influenza pandemic.

INTRODUCTION

Influenza viruses have been shown to be capable of causing rapid, widespread morbidity and mortality among infected humans. Pandemics happen when new (novel) influenza A viruses emerge which are able to infect people easily and spread from person to person in an efficient and sustained way. Historically, pandemic outbreaks of influenza viruses have left tens of millions of people dead in their wake and have cost hundreds of billions of dollars in lost lives, wages, productivity and economic devastation. In 1997, highly pathogenic avian influenza (HPAI) A(H5N1) viruses jumped from birds to humans in Hong Kong; six of 18 people with confirmed infections from H5N1 influenza virus died. In 2003, avian influenza A(H5N1) viruses emerged in humans again, this time in Southeast Asia, leading to severe illness and further deaths caused by this virus. Since 1997, over 1826 confirmed human infections and 784 deaths have been caused by avian influenza A(H5N1) around the world. The continual evolution and spillover of avian influenza viruses from birds into humans, coupled with their potential to rapidly spread and cause severe illness and death in people who are immunologically naïve triggered a global assessment of preparedness and response capabilities for a pandemic outbreak caused by influenza.

In 2005, the U.S. Department of Health and Human Services (HHS) developed the HHS Pandemic Influenza Plan to prevent, control, and mitigate the effects of influenza A(H5N1) and other influenza viruses assessed to pose high risk to humans. Since their emergence in 1997, A(H5N1) viruses have become enzootic among poultry in many parts of the world, causing sporadic human infections and deaths. Influenza A(H5N1) is not the only animal influenza virus to infect humans. Mammalian influenza viruses (e.g., swine variant viruses H1N1v, H1N2v, H3N2v) and other avian influenza viruses (H5N2, H5N6, H5N8, H7N9) pose threats to humans. For example, since 2013 over one thousand human infections caused by avian influenza A(H7N9) virus have been reported, predominantly in China. In late 2014 and 2015, highly pathogenic avian influenza (HPAI) A(H5N8) viruses spread to birds in the United States from Asia and mixed with North American viruses. The resulting A(H5Nx) virus caused outbreaks in poultry in 15 states (predominantly A/H5N2), affecting 50.4 million birds. An aggressive animal response plan curtailed the outbreak but resulted in the slaughter of 7.5 million turkeys and 42.1 million egg-layer and pullet chickens, costing federal taxpayers more than $950 million.[1] An aggressive public health response that emphasized monitoring of exposed responders and the general public found no human infections with these avian viruses.

Over the past decade, the global public health community ramped up pandemic influenza preparedness efforts with an eye toward the emergence of HPAI influenza A(H5N1) viruses in Asia; however the real-life test of pandemic planning came in 2009 following the emergence of a novel H1N1 virus in North America. The 2009 pandemic was caused by a novel reassortant virus designated A(H1N1)pdm09. This pandemic illustrated that pandemic influenza viruses can originate anywhere, vary in severity and

[1] Animal and Plant Health Inspection Service. “2016 HPAI Preparedness and Response Plan.” Washington, DC: US Department of Agriculture, 2016. Accessed 7/31/2016.

population penetration, and each pandemic will differ in its range and impact. It also highlighted the speed with which a novel influenza A virus can be transmitted among people, respecting no geographic or jurisdictional boundaries, and the need for rapid development, production and availability of MCMs such as vaccines, diagnostics and antiviral drugs to mitigate the impact of the pandemic. Lessons learned from the 2009 H1N1 influenza pandemic were published in 2012 as the 2009 H1N1 Influenza Improvement Plan, and the World Health Organization (WHO) released its Pandemic Influenza Risk Management Interim Guidance in 2013. In 2016-2017, HHS reviewed the progress made since the 2009 H1N1 Influenza Improvement Plan.

This document highlights both the progress and remaining gaps in our preparedness and response capabilities for pandemic influenza. It serves as an Update of the 2005 HHS Pandemic Influenza Plan and its interim updates issued in June 2006, November 2006, and January 2009, and sets the course for the next decade.

Accomplishments over the past decade reflect significant HHS effort and investments in pandemic preparedness and are described in the following sections. Expanded global influenza surveillance and laboratory capacity provide a clearer picture of evolving influenza A viruses and the occurrence of novel viruses with pandemic potential. Forecasting, modeling and planning tools now facilitate dynamic estimates of pandemic virus spread, burden and impact. The National Pre-Pandemic Influenza Vaccine Stockpile (NPIVS) has been established and satisfies requirements for vaccine and adjuvants to address influenza viruses that are assessed to be the highest risk for human infection. Modifications made to respiratory devices—both respirators and ventilators—should ensure better availability and improved technology in a future pandemic. Influenza vaccines can be produced more rapidly, and there is now sufficient domestic manufacturing capacity to make influenza vaccine for every person in the United States. The goal of a 12-week time frame for first doses of vaccine is now within reach, compared with the typical six to nine month time for seasonal vaccine production, though challenges may still persist in ensuring enough supply of pandemic vaccine is immediately available for the entire population. Influenza antiviral drugs are available in many formulations, including some specifically for children. Federal stockpiles of antiviral drugs have increased to levels projected to meet treatment needs across multiple pandemic scenarios. Vaccines are now more broadly available in many settings, including pharmacies and retail clinics, to improve access to these countermeasures and reduce the surge on hospital and emergency care centers during a pandemic. Social media messaging channels now reach millions of Americans directly, and expanded partnerships with an array of nongovernmental organizations can deliver influenza pandemic-related messages through those channels. The health care and public health systems have begun to plan for implementation of principles articulated in Crisis Standards of Care: Systems Framework for Catastrophic Disaster Response, if needed during a severe pandemic. Robust population-based surveillance and evaluation networks capture influenza-associated hospitalizations and monitor the effectiveness of influenza antivirals and vaccines. Finally, State, Local, Tribal, and Territorial governments (SLTT) have developed, and many have exercised, pandemic influenza preparedness plans, supporting global commitments made by the United States to pandemic preparedness planning.

Complementing progress on the domestic front, HHS has made significant improvements in strengthening global capacities to prevent, detect, and respond to an influenza pandemic. A robust international surveillance network has been established by partnering with more than fifty countries to build capacity to detect novel influenza viruses wherever they emerge. HHS participated in the development and adoption in 2011 of the WHO Pandemic Influenza Preparedness (PIP) Framework for the Sharing of Influenza Viruses and Access to Vaccines and Other Benefits. In addition, expanded international coordination on pandemic preparedness and response has been facilitated by HHS's continued support to the WHO Global Influenza Surveillance and Response System (GISRS). This system not only allows for the capture of more viruses from more places for greater ability to detect an emerging pandemic threat, but also to produce timely seasonal and pandemic vaccine candidates. HHS also supported the development of influenza vaccine manufacturing capacity in developing countries, creating a rapid response capability of over 500 million doses of pandemic influenza vaccine in remote regions where previously there was none. Finally, HHS has integrated its domestic and international pandemic response policies and operations to minimize duplication of effort. HHS led the development of the North American Plan for Animal and Pandemic Influenza (NAPAPI), which launched in 2012 as the primary framework for pandemic influenza preparedness and response through collaboration among the United States, Canada, and Mexico. The Global Health Security Agenda, which officially launched in 2014, and the continued efforts to implement the International Health Regulations (IHR), published in 2005 by the WHO, both highlight the ongoing need to establish or improve the global capacity to prevent, detect, and respond to biological threats such as pandemic influenza.

All of these international activities serve to directly improve national security as they enable rapid communications, surveillance, and mitigation of emerging novel influenza viruses with other countries to ensure a better national response.

Today, domestic and global public health preparedness and response benefit from improved products, responsive manufacturing, and broader disease surveillance. However, much remains to be done even as these critical efforts must be sustained. This 2017 Update describes HHS's progress over the past decade of influenza response activities and the critical objectives for the decade ahead.

SCOPE, AUDIENCE, AND PURPOSE

Pandemic preparedness planning has become more sophisticated and has grown in breadth and depth across all levels of government, stakeholders, private entities, and sectors over the past ten years. Today, every state, four major metropolitan areas, and eight U.S. territories and freely associated states have their own pandemic influenza plan. HHS support has expanded public health and health care preparedness capabilities domestically and abroad, improved laboratory diagnostics, and enhanced development and manufacturing of MCMs.

This 2016 Update describes the HHS approach to protecting human health before, during, and after an influenza pandemic. To sustain the momentum of the past decade, the pandemic preparedness work that lies ahead must take advantage of new or emerging opportunities posed by improvements in technology, detection and assessment of viruses, and enhanced response capacities both domestically and internationally.

Stakeholders in this effort comprise an array of public and private entities: SLTT policymakers; critical infrastructure sectors such as public health, health care, social services, research, manufacturing, and education and child care; employers; international and multilateral partners in these areas; and the general public, who need to know not only how HHS fulfills its mission, but also how they can take actions to help reduce the spread of influenza, whether in a pandemic or every year during the influenza season.

Finally, whereas this 2017 Update primarily addresses pandemic influenza, the continually changing nature of influenza viruses that can lead to mismatches between vaccine strains and circulating viruses, as seen during the 2014–2015 influenza season, remind us that pandemic and seasonal influenza planning and improvement efforts are interdependent. Both rely on a strong and sustainable public health system infrastructure that can rapidly detect, and respond to, changes in circulating influenza viruses. Many of the activities that HHS and its partners undertake each year to understand and mitigate the impact of seasonal influenza are critical to a pandemic response both domestically and globally, so this 2016 Update reinforces critical connections between seasonal and pandemic influenza preparedness and response.

INFLUENZA RESPONSE ACTIVITIES

Year-round seasonal influenza activities provide the foundation for any influenza pandemic response. Surveillance and monitoring, research and development, delivery of MCMs (for example, vaccines and therapeutics, diagnostics, and respiratory protective devices) and non-pharmaceutical interventions (NPIs), health care system response, and communications are integral to the domains and objectives described in detail later in this Update. Public health preparedness work on seasonal influenza continues throughout the year because influenza viruses circle the globe in a constant state of evolution and emergence that necessitates annual updates to the vaccine formulation for both the Northern and Southern Hemispheres. Detecting unpredictable outbreaks of novel influenza viruses with human pandemic potential might prompt a sudden change in this mode of operation, which must be addressed by accelerating and amplifying this work specifically with the new virus. It also affects incident response activities, which prioritize and coordinate public health efforts to address a potential pandemic, sometimes even as the seasonal influenza efforts must continue. Shortly after a novel influenza virus has been detected and transmitted among humans, HHS will have determined if vaccines in the NPIVS are likely to offer protection, begun to develop a safe and effective vaccine against the novel influenza virus, determined its susceptibility to antiviral drugs, and triggered a series of domestic and international response activities to mitigate the potential risk of further spread of the virus. A comprehensive U.S. government (USG)-coordinated pandemic response will consider an array of non-pharmaceutical and pharmaceutical intervention options to mitigate pandemic impact on public health.

Despite uncertainty in future pandemic influenza scenarios, developing and implementing a set of planning principles and parameters encompassing a range of potential pandemic impacts will be critical to ensure a prompt and flexible response. Therefore, HHS has developed a process to assess various risk scenarios that estimate illness, outpatient medical care, hospitalizations, intensive care unit care, and deaths for low, moderate, high, and very high severity pandemics. Appendix A contains more information about pandemic influenza scenarios and planning assumptions.

PLANNING TOOLS FOR PREPARATION AND RESPONSE

At the onset of an outbreak with pandemic potential, the uncertainty and complexity of the situation demand ways to assess the risk and potential public health impact posed by the emerging virus, understand the possible progression of the event, and evaluate its severity and transmissibility to enable informed public health interventions. HHS has developed and refined three tools over the past decade to help guide different aspects of planning and response: the Pandemic Intervals Framework (PIF), the Influenza Risk Assessment Tool (IRAT), and the Pandemic Severity Assessment Framework (PSAF). Details about these tools are included in Appendix B. These tools align with the WHO initiative for all nations to develop response plans within the WHO's global framework of pandemic phases and risk-assessment activities for preparedness, response, and recovery.

The PIF defines and describes six time intervals of an influenza pandemic, including indicators signaling each interval and recommended interventions. There are two pre-pandemic intervals, investigation and recognition, and four pandemic intervals that include initiation, acceleration, deceleration, and preparation. The PSAF is a systematic framework for assessing the public health effects of an emerging pandemic. It helps to identify the type and timing of actions needed for effective intervention, thus informing the development of operational plans and guiding response efforts.

The IRAT assesses the potential human pandemic risk of novel influenza A viruses to inform decisions regarding the development, manufacturing, use, and stockpiling of diagnostics, vaccines, and therapeutics. The IRAT process is continual among HHS pandemic influenza stakeholders to monitor for, and assess when, a novel influenza A virus in animals or humans has been identified. Experts assess the potential for emergence and human health risk of the virus to anticipate the risk that the virus will 1) develop efficient and sustained human-to-human transmission (emergence), and 2) significantly affect public health (impact). The IRAT and PSAF are complementary tools. Should widespread human disease occur, the PSAF is the companion tool for estimating a pandemic's potential impact; the PSAF uses two sets of measures to score viral transmissibility and clinical severity of new influenza A viruses as they circulate among humans.

THE 2017 UPDATE TO THE HHS PANDEMIC INFLUENZA PLAN

This 2017 Update to the HHS Pandemic Influenza Plan builds upon goals elaborated in the 2005 plan, describes ongoing work toward those goals, and identifies key actions for the next decade. Based on experience drawn over the past decade, it presents the current best thinking about how to address pandemic influenza challenges and builds upon the four domains featured in the 2005 plan:

1. Surveillance, Investigation, and Protective Public Health Measures
2. Vaccines and Antiviral Drugs
3. Health Care and Emergency Response
4. Communications and Outreach

In the 2017 Update, seven domains describe how HHS and its partners have added to the evidence base or applied lessons learned, and areas in which capabilities can be optimized:

1. Surveillance, Epidemiology, and Laboratory Activities
2. Community Mitigation Measures
3. Medical Countermeasures: Diagnostic Devices, Vaccines, Therapeutics, and Respiratory Devices
4. Health Care System Preparedness and Response Activities
5. Communications and Public Outreach
6. Scientific Infrastructure and Preparedness
7. Domestic and International Response Policy, Incident Management, and Global Partnerships and Capacity Building

Taken together, the updated domains reflect an end-to-end systems approach to improving the way preparedness and response are integrated across sectors and disciplines, while remaining flexible for the conditions surrounding a specific pandemic. This more-nuanced and contemporary approach recognizes the interdependence of domain areas, which should lead to a better understanding of how the system functions as a whole.

By necessity, these domains have some overlapping content, reflecting the fact that this work is intimately integrated with other aspects of domestic and international pandemic preparedness and response. Within each domain, the Update summarizes the relevance to pandemic influenza, an accompanying goal, and a list of objectives for sustaining momentum that address ongoing work, challenges, and opportunities for the next decade. Evolving science and budget priorities will influence the direction and scope of progress that is critical to mitigating the next influenza pandemic.

HHS cannot and does not undertake this work alone. This 2017 Update reflects the work already under way, and it builds a vision together with many partners. State and local governments; a range of public health and health care professionals and institutions; and other federal agencies and nongovernmental organizations, academic centers, international partners, manufacturers, suppliers, and businesses in the United States and worldwide are vital to successful global pandemic preparedness and response. For all these entities, budgetary, legal, and other administrative actions pose opportunities and operational challenges. Identifying and addressing such practices as staffing, contracting, procurement, and statutory authorities that can be used during an emergency are critical to efficient and effective response activities even when funding is limited. The domains and efforts described here for HHS can and should complement other areas of planning for infectious disease pandemics or outbreaks. These synergies must be identified and aligned to optimize investments in public health and scientific infrastructure, protecting the health of all.

Domain 1 – Surveillance, Epidemiology, and Laboratory Activities

Goal 1: Increase capability to gather better, timelier data through surveillance, epidemiology, and laboratory activities.

Objective 1.1 – Expand global capacity to monitor and characterize seasonal and novel influenza viruses and infections.

Objective 1.2 – Accelerate the timeline for the development and delivery of candidate vaccine viruses and assess effectiveness of MCMs against circulating viruses.

Objective 1.3 – Improve the ability to describe influenza disease and conduct epidemiologic studies to inform pandemic response efforts.

Fundamental to pandemic preparedness is the continual surveillance, epidemiologic, and laboratory activities of HHS to monitor and characterize seasonal and emerging influenza threats. Existing influenza surveillance networks rely on data from domestic and international public health partners to monitor seasonal, novel, and animal influenza infections. HHS collaborates with SLTT health departments; public health, clinical, and academic laboratories; vital statistics offices; health care providers, clinics, and emergency departments; federal partners, such as the Departments of Agriculture and Defense; and international partners to collect, compile, and analyze information on year-round domestic and international influenza activity.

Global and domestic disease surveillance systems, integrated with virologic surveillance, provide the basis for risk assessments and recommendations regarding the composition of seasonal and pre-pandemic vaccines. The systems' year-round operation also provides a standing capability to monitor and characterize circulating viruses with respect to contemporary vaccine formulations, assess the potential for viruses resistant to antiviral drugs to emerge and spread, and provide early warning of emerging influenza viruses with pandemic potential. Although global and domestic systems have improved over the past two decades—including the establishment of more networks in the northern and southern hemispheres to estimate vaccine

effectiveness (VE)—HHS must sustain and amplify efforts to optimize their geographic coverage and timeliness of data and specimen sharing. HHS investments over the past decade have yielded technological, scientific, and public health advances that enable more precise characterization of viruses, their geographic spread, and population impact. As a result, public health officials gain an earlier understanding of possible changes in seasonal and zoonotic viruses. This information further supports better targeting of risk assessments and preparations for seasonal and potential pandemic outbreaks. Notable progress over the past 10 years and key actions for the next decade include the following:

- Advances in sequencing speed and cost reductions. Such technologic advances have enabled more complete and simultaneous characterization of hundreds of co-circulating viruses. Whole genome, next-generation sequencing of thousands of specimens per year enables more accurate monitoring of viruses and improves vaccine virus selection. A public database of thousands of human and animal influenza virus genomes is available for public health officials, researchers, and developers of vaccines, antiviral drugs, and diagnostic tests.
- Vast expansion of global capacity for influenza detection and surveillance due in large part to HHS support. This has produced clearer data, leading to better surveillance and enabling earlier responses as pandemic influenza strains emerge with increasing frequency around the world. This better global capacity helps the U.S. respond to threats that emerge abroad to mitigate their impact at home. Maintaining these gains while filling remaining surveillance gaps is critical.
- Developing and implementing right-sizing of surveillance. States now use new specimen submission calculators to determine the optimal number of influenza-positive specimens that state public health laboratories should send to one of the three Centers for Disease Control and Prevention (CDC) supported National Influenza Reference Center Laboratories, to detect emerging seasonal influenza antigenic variants or novel influenza virus infections. This improves the efficiency of situational assessments.
- Establishing the International Reagent Resource (IRR). This biotechnology resource provides public health laboratories with on-line access to reagents, tools, and information for detecting and characterizing influenza virus activity. Through this tool, HHS now distributes diagnostic test reagents and materials to all qualified state and local public health laboratories in the United States and to National Influenza Centers around the globe engaged in virologic surveillance. This dissemination significantly improves the timely availability of appropriate reagents, and enhances global disease detection. In 2016, the IRR was expanded to include reagents for other respiratory and emerging pathogens, including Middle East Respiratory Syndrome (MERS) and Zika virus.
- Uptake of health information technology in the United States. Increased use of technology has enabled monitoring of infectious disease outbreaks and integrating geographic information systems with other sources of data on hospitalization and illness to generate a national picture of influenza activity. It has also promoted the

use of social media to relay significant developments.

- Implementing automated electronic laboratory reporting. Since implementing automated reporting from all U.S. public health laboratories in 2010,[2] real-time reporting of about 80,000 influenza tests per year is now available using standard electronic health information messages.

- Improving and expanding diagnostic capabilities**.** Such improvements promote detection and differentiation of seasonal and novel influenza viruses, as well as other respiratory viruses. This helps guide earlier, appropriate treatment and infection control measures in health care settings.

- Expanding the ongoing monitoring of VE and safety. The U.S. Flu VE Network[3] monitors annual influenza vaccine effectiveness and confirms the value of vaccination as a public health intervention. This enables mid- and post-season estimates, including age-specific and some product- specific measurements. These data have been instrumental in refining vaccine policies and improving virus selection to update the composition of seasonal vaccines.

Key action: HHS will increase U.S. and global capacity to use genetic sequencing for better and timelier surveillance and development of MCMs. HHS will more broadly implement whole-genome, next-generation sequencing, with its unprecedented throughput, to provide more genetic information to more rapidly detect and characterize viruses and select viruses for vaccines. Data generated from these capabilities will be available to HHS stakeholders to rapidly inform vaccine and therapeutic development.

Key action: HHS, through the IRR, will further improve the time from reagent production to distribution to domestic and international laboratories to improve the time for development of MCMs.

Key action: HHS will further enhance the capacity of global surveillance and response by bolstering laboratory and epidemiologic resources. In particular, HHS will continue to collaborate with international partners to assess and build national sentinel and laboratory-based surveillance capabilities, including developing interoperable, interconnected electronic reporting systems.

Key action: HHS will leverage "Big Data" to improve its ability to monitor and describe influenza disease and conduct epidemiologic studies. HHS will use supplemental data sources (such as electronic health records, social media, or big-data repositories) to better monitor and characterize potential pandemic influenza activity in as close to real time as possible. It will utilize innovative data sources and models to better forecast disease emergence and patterns.

[2] Lamb E, et al. Update on Progress in Electronic Reporting of Laboratory Results to Public Health Agencies — United States, 2014. MMWR Morb Mortal Wkly Rep 2015; 64(12):328-330.
[3] See Centers for Disease Control and Prevention. Seasonal Influenza Vaccine Effectiveness, 2005–2016. Atlanta, GA: CDC, 2016. Accessed 7/31/2016.

Key action: HHS will validate and fully implement Right Size tools in all state public health labs to ensure efficiency in specimen processing and reduce bottlenecks of testing for improved surveillance systems.

Key action: HHS will improve laboratory identification of novel influenza viruses by supporting development of innovative detection tools and methods, as well as distributing diagnostic reagents using the IRR.

Key action: HHS will leverage trends in personal health monitoring, including possibilities of at-home diagnosis and treatment, to prevent and control further spread of disease during a pandemic.

Key action: HHS will develop and implement systems to track effectiveness of pandemic influenza vaccines, alone or in combination with seasonal influenza vaccines.

Key action: HHS will double the number of domestic sentinel sites used for annual VE determination and coordinate data and processes for VE determination with international VE processes to improve the alignment of VE data. HHS will also implement an annual process for VE determination by vaccine manufacturers to inform vaccine development and optimization.

Key action: HHS will work closely with partners in agriculture to improve surveillance of influenza viruses in birds, swine, and other animals, and will improve tools and processes for monitoring workers engaged in responding to influenza outbreaks in animals.

Leveraging progress in Surveillance, Epidemiology, and Laboratory Activities, and applying lessons learned from other recent responses to novel influenza virus infections, yield areas for improvements for the U.S. response to pandemic influenza. Over the next decade, the goal of HHS will be to sustain momentum and continue to improve upon its surveillance, epidemiology, and laboratory activities domestically and globally.

Domain 2 – Community Mitigation Measures

Goal 2: Sustain momentum and improve implementation of community mitigation measures.

Objective 2.1 – Improve public awareness and implementation of non-pharmaceutical interventions to slow the spread of influenza.

Objective 2.2 – Provide updated guidance for public health officials on the use of non-pharmaceutical interventions (NPIs) by the general public and in key community settings (schools, child care settings, workplaces, mass gatherings), and improve communication to these key community settings.

Objective 2.3 – Maintain support of state and local public health officials preparing for, and utilizing non-pharmaceutical interventions during, a pandemic influenza response.

Objective 2.4 – Ensure that travelers' health messages and border health measures taken at US ports of entry to slow the introduction or exportation of influenza are based on best available data and aligned to the severity and stage of the influenza pandemic.

Community mitigation aims to slow the spread of a novel influenza virus in communities through the use of NPIs and threat-appropriate travel and border health measures. Community mitigation measures are the first line of defense against pandemic influenza, and may help reduce the spread of other respiratory infectious diseases. They can be used from the earliest stages of an influenza pandemic, including the initial months when the most effective countermeasure—a vaccine against the new pandemic virus—might not yet be broadly available.

NPIs are readily available behaviors or actions and response measures people and communities can take to help slow the spread of respiratory viruses such as influenza. Enhanced understanding of such interventions, and the capacity to implement them in a timely way, can increase community resilience during a pandemic. Using multiple NPIs simultaneously, also referred to as layering, can reduce influenza transmission in communities even before vaccination is available.

NPIs that all people should practice at all times are particularly important during a pandemic. These everyday preventive actions include staying home when sick, covering coughs and sneezes, frequent and appropriate hand-washing, and routine cleaning of frequently touched surfaces. Community-level interventions can be added during pandemics and implemented in a graded fashion depending on the severity of the pandemic; these include measures aimed to reduce social contacts between people in schools, workplaces, and other community settings.

HHS is investing in evaluating the effectiveness and timing of implementing NPIs. Scientists already understand a great deal about which interventions are effective and when to implement them; ongoing research will augment the science base for NPIs. Using the best available science, HHS continues to develop and disseminate public health communication and educational materials on the use of NPIs, for the general public, such as websites, posters, checklists, and fact sheets. In accordance with cultural and health literacy best practices, all communication materials use plain

language. Clear communication helps deliver easy-to-understand and actionable messages to the public. These materials can quickly be updated and disseminated electronically when a pandemic alert, or even a severe seasonal influenza epidemic, occurs.

Pre-pandemic planning guidelines and related planning tools can also assist SLTT public health officials prepare for a potential influenza pandemic and take action to slow the spread of the influenza virus throughout their communities.

Before a pandemic strikes, clear communication, ongoing coordination and collaboration among public health officials and key community planners (for example, schools and child care settings, institutions of higher education, and businesses) can lay the groundwork for optimal pandemic response. Timely and strong lines of communication will ensure the consistency and effectiveness of information and local decision making before and during a pandemic. Travel and border health measures may be considered to slow the introduction or export of pandemic influenza between the United States and other countries, but they should be carefully evaluated based on their effectiveness and potential economic and social impacts.

HHS's efforts to evaluate NPIs and form strategic collaborations with partners over the past decade have generated progress across a range of community settings, although continued work is needed to understand how changes in messages and ways of delivering them can improve public response to a pandemic. Notable examples and key actions for the future include the following:

- Increasing knowledge and research on the feasibility, public acceptability, and effects of a range of NPIs, including school and child care closures.
- Establishing partnerships among HHS, U.S. Customs and Border Protection, and the Coast Guard at more than 300 U.S. ports of entry. These partnerships were critical in the response to the risk of importation and potential domestic spread of Ebola, as they also provide notifications from emergency medical services and state and local health departments. Procedures are in place for conducting contact investigations among passengers and crews of aircraft and cruise ships, scalable by disease and situation. This experience strengthens future responses to pandemic influenza, even with potentially limited application of travel and border health measures.
- Creating and maintaining a public website to provide helpful plain language information about the different types of NPIs and how they can be used at home, school and child care settings, work, and large gatherings.

Key action: HHS will continue to collect data on the effectiveness of specific or combination NPIs in reducing the spread of influenza virus. These data will be published in public health journals, and clear communication materials will be developed to assist in community implementation of effective NPIs.

Key action: HHS will continue to update and translate into multiple languages the public information on NPIs as new data are generated on NPI effectiveness.

Key Action: HHS will integrate behavioral health, organizational and resilience research in communications about NPI and community resilience.

Incorporating behavioral, organizational, and health literacy research and using community-driven channels to communicate about NPIs are relatively new aspects of community mitigation. Fully engaging diverse stakeholders in problem-solving before a pandemic contributes to community resilience and can help slow disease transmission in communities if vaccines are not readily available or until vaccines or other MCMs arrive. Leveraging progress in Community Mitigation, and applying lessons learned from the 2009 influenza pandemic and other recent responses to novel influenza viruses will yield areas for potential breakthroughs for the next influenza pandemic.

Domain 3 – Medical Countermeasures: Diagnostic Devices, Vaccines, Therapeutics, and Respiratory Devices

Goal 3: Improve effectiveness, timeliness, availability and accessibility to medical countermeasures (diagnostics, vaccines, therapeutics, and respiratory devices).

Objective 3.1 – Develop new and improved medical countermeasures for influenza: vaccines that are more effective for all ages than currently available; novel broad-spectrum therapeutics for high-risk, severely ill, and hospitalized patients and pediatric populations; rapid point-of-care and in-home diagnostics; and effective and reusable respirators.

Objective 3.2 – Augment and sustain sufficient domestic influenza vaccine manufacturing and fill/finish capacity to deliver finished doses of pandemic vaccine within 12 weeks of the declaration of a pandemic.

Objective 3.3 – Secure raw materials and sustain supply chain integrity to meet the production needs of vaccines and other MCMs.

Objective 3.4 – Re-assess requirements and maintain pre-pandemic vaccine and adjuvant stockpiles and other MCMs needed to combat pandemic influenza while strengthening the underlying pandemic risk-assessment infrastructure in collaboration with United States Government (USG) and global partners.

Objective 3.5 – Expedite access to vaccines and other MCMs, and enhance the ability to monitor demand, product distribution, and dispensing and administration.

Objective 3.6 – Monitor the clinical safety and effectiveness of vaccines and other MCMs through enhanced data collection and analysis capabilities.

Objective 3.7 – Develop and update guidance on the clinical use of, and the prioritization of access to vaccines and other MCMs.

MCMs are central to the public health response to mitigate the impact of influenza epidemics and pandemics. Diagnostic devices, antiviral drugs and other therapeutics, vaccines, respiratory protective devices, and ventilators provide the means to detect, prevent, or treat influenza. The most effective MCMs cannot be identified until the characteristics of the pandemic virus are known: its transmissibility, virulence, antigenic properties, and susceptibility and clinical responsiveness to antiviral drugs. Vaccination is the most effective medical intervention for mitigating the potentially devastating impact of an evolving pandemic. This requires developing a well-matched, safe, and effective vaccine in the shortest time possible, and promptly making it available to the public. Shortening the time between detection of pandemic influenza viruses and widespread distribution of vaccine to cover the U.S. population (currently within about six months) is a priority for HHS and its partners.

Planning efforts for implementing MCMs in the event of an influenza pandemic are a part of the USG-wide Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) process to increase public health preparedness. HHS leads the federal departments and agencies involved in use of MCMs to protect the civilian population. PHEMCE's mission areas include describing and defining the characteristics of MCMs identified through basic research; discovery and early product development; advanced

development; regulatory science; procurement and stockpiling; response planning, which includes distributing, administering, and dispensing vaccines and other MCMs; and performance monitoring, evaluation, and assessment. To ensure that priorities reflect current scientific progress and fiscal capabilities, the PHEMCE annually assesses and updates a PHEMCE Strategy and Implementation Plan, to ensure optimal allocation of resources to address high-priority threats, including influenza. The content here is consistent with, and complementary to, the 2016 PHEMCE Strategy and Implementation Plan and is expected to align with subsequent annual updates.

An influenza risk assessment before an influenza pandemic using the IRAT focuses on rapidly characterizing newly emerging animal influenza viruses with human pandemic potential. The analysis includes available epidemiologic, virologic, and immunologic data to determine the relative risk for human health. It should account for factors that contribute to person-to-person transmission and virulence in humans and/or animals. The IRAT score is linked to triggers for specific activities associated with the NPIVS to inform decisions for the development, evaluation, storage, and/or distribution of vaccines against influenza viruses that have high pandemic potential. Stockpiled vaccines and adjuvants could be used for early vaccination efforts among those who are at increased risk of exposure. Individuals would include those who play critical roles in the response, are critical to maintaining essential society functions, and those at increased risk of severe disease because of age or underlying medical conditions. Early in a response to an emerging influenza pandemic, and before a vaccine well matched to the pandemic influenza virus is developed, produced, and distributed for use among the broader U.S. population, this strategy could be useful in protecting higher risk populations.

The long-term strategy for pandemic vaccine preparedness focuses on developing more effective influenza vaccines that would provide longer-lasting protection against antigenically diverse influenza viruses. Continued progress in characterizing and understanding influenza virus immunology and pathogenesis are essential to future success in new approaches toward a vaccine that provides long-term protection from influenza viruses of human or animal origin.

In their Report to the President on Reengineering the Influenza Vaccine Production Enterprise to Meet the Challenges of Pandemic Influenza, members of the President's Council of Advisors on Science and Technology noted with concern in 2010 that, in the 2009 influenza pandemic, first doses of vaccine became available only after about 26 weeks from the initial decision to begin vaccine development and manufacturing and initially only in small quantities; most vaccination occurred after the peak in illness had occurred. A supply adequate to protect the entire nation (with a single dose) would have taken about 48 weeks to produce. These time frames did not include the time required to then immunize the susceptible population. The Report concluded this time frame was far too slow to protect the U.S. population.

Successful development and licensure of adjuvanted seasonal and pandemic influenza vaccines has substantially increased options for vaccination during a pandemic. The HHS-supported expansion of domestic vaccine manufacturing capacity, the use of adjuvanted vaccines, and the licensure of recombinant influenza vaccines are

expected to substantially shorten timelines to make vaccines available to immunize the U.S. population.

Whereas vaccines are the most effective MCMs to reduce the overall public health impact of influenza pandemics, other MCMs are critically important to mitigate emerging pandemics before effective vaccines become available. Such other measures are an essential part of a comprehensive mitigation response at different stages of the pandemic to protect diverse at-risk populations. These countermeasures include antiviral drugs and other therapeutics, diagnostic tests to determine whether someone has been infected with influenza (and the influenza subtype) or has a secondary bacterial infection, personal protective equipment (including respiratory protective devices, face shields, gowns, and gloves) to protect those in direct contact with infected individuals, and mechanical ventilators to provide respiratory support to those who are severely ill. Global surveillance to determine the susceptibility of influenza viruses to licensed and approved antiviral drugs is conducted to inform clinical guidance for treatment. Because influenza viruses change constantly, they can become resistant to one or more of the antiviral drugs used to treat or prevent influenza. A pandemic caused by drug-resistant viruses would pose an unprecedented challenge to the public health system. Development of new, broad-spectrum therapeutics with different mechanisms of action from currently approved antiviral drugs, as well as host-targeted therapeutic approaches, may mitigate the emergence of antiviral drug resistance that could rapidly reduce the effectiveness of single drug approaches.

HHS has made significant strides in developing, manufacturing, and distributing influenza MCMs, and in monitoring their use, safety, and effectiveness. Notable progress over the past decade and key actions for the next 10 years include the following:

- Developing and clearing a diagnostic test that can identify an influenza subtype in 20 minutes.
- Developing and licensing new cell-based, recombinant, and adjuvanted vaccines for seasonal and pandemic influenza.
- Evolving and diversifying vaccine production processes from solely egg-based technology to cell- and recombinant-based vaccines, increasing domestic seasonal influenza vaccine production capacity that can be leveraged for pandemic response. The number of manufacturers that can supply vaccine to the United States has expanded from two in the 2004–2005 influenza season to six in the 2016–2017 season.
- Expanding the pre-pandemic vaccine stockpile subtype diversity comprising monovalent bulk product from subtype A(H5N1) representing various antigenically distinct H5 viruses from different clades, as well as bulks from the most recent subtype A(H7N9).
- Establishing AS03 and MF-59 adjuvant stockpiles to permit antigen-sparing approaches, thus increasing the number of people who can be vaccinated with adjuvanted vaccine.

- Assessing the safety and immunogenicity of various combinations of stockpiled adjuvants and vaccines in clinical trials to meet regulatory requirements for use in mitigating an emerging pandemic.
- Expanding types of vaccinators and settings to include pharmacists and retail clinic settings, more than tripling the number of U.S. adults who report receiving seasonal influenza vaccine at a pharmacy or retail setting, from 6% in 2007 to almost 25% in 2015.
- Improving capability of electronic health records (EHR) to directly populate immunization information systems, to improve vaccine order.
- Modernizing HHS's ability to manage vaccine orders and distribution logistics through implementation of CDC's Vaccine Tracking System, across the United States through the 64 CDC-funded state and local immunization programs.
- Developing and applying epidemiological modeling tools developed for use in public health emergencies, including influenza pandemics, to inform policy, clinical guidance, and response strategies involving the use of MCMs.
- Analyzing and modeling product needs and gaps through interagency collaboration, through the PHEMCE, and establishing stockpiling goals across pandemic influenza countermeasures through the PHEMCE requirements-setting process.
- Discovering broad-spectrum monoclonal antibodies, host-targeted therapeutic drug candidates, and small molecule antivirals with novel mechanisms of action. Some of these candidates have shown preliminary activity against wild-type and drug-resistant influenza viruses and are currently under evaluation in Phase 2 and Phase 3 clinical trials.
- Approaching full FDA approval for a next-generation ventilator for all populations, which will mean a more affordable ventilator with increased neonatal capability. In addition, HHS is leading efforts to determine the feasibility of standardized and interchangeable ventilator components.
- Developing technology and processes that allow for rapid production of N95 respirators, to significantly increase respirator supply during an influenza pandemic. At the same time, HHS supports development and use considerations for effective reusable respirators that will reduce the burden to produce and dispense large volumes of disposable respirators during an outbreak.
- Improving the understanding of respirator and other PPE use practices. Areas of research have evolved to include effectiveness, availability, selection, and use to better inform decisions and guidance during a pandemic response.
- Procuring millions of courses of antiviral drugs, including pediatric formulations, to achieve national stockpiling goals and sustaining products through extended product shelf life and stability testing.
- Deploying vaccine internationally through the WHO Pandemic Influenza A(H1N1) Vaccine Deployment Initiative, and antiviral drugs to Mexico and the Pan American

Health Organization as part of the global response to the 2009 H1N1 influenza.

- Developing novel methods and approaches that might help to assess therapeutic safety and effectiveness in seriously ill and hospitalized patients by using alternative clinical endpoints to facilitate regulatory approval of novel therapeutics.

- Engaging partners to improve capacity to monitor the distribution, effectiveness, and safety of MCMs throughout an influenza pandemic.

Key action: HHS will lead innovation in influenza diagnostics through supporting: (1) the development of low-cost molecular point-of-care (physician's office or pharmacy) diagnostic tests that yield results in under 15 minutes and provide subtype information, thereby enabling early detection of potentially pandemic viruses; (2) the development and use of simple, low-cost, accurate in-home diagnostics that will inform patients who have been infected with influenza viruses and allow them to obtain rapid care and treatment by telemedicine approaches without requiring an in-person visit to the physician for prescription; and (3) diagnostics that are incorporated into wearable technology, such as patches or smart watches, to assess an algorithm of pre-symptomatic biological markers of virus infection and trigger patient action to seek more definitive diagnosis (home- or pharmacy-based).

Key action: HHS will support the development and licensure of influenza vaccines that are more effective than currently licensed influenza vaccines. These vaccines will show transformative improvements in the breadth and duration of immunity while providing greater protection against a wide diversity of antigenically divergent influenza viruses. At a minimum, phase 3 clinical trials will be initiated to demonstrate field efficacy of these transformative vaccine candidates.

Key action: HHS will further support innovation in influenza vaccine production for improved efficiencies to enable the production and distribution of final presentation vaccines for pandemic response within 12 weeks from the declaration of an influenza pandemic. Such innovation will lead to improvements in manufacturing processes, platforms, formulation and filling quantities of sufficient vaccine for an effective domestic pandemic response and to meet the public demand for vaccine will be available within four months of a pandemic declaration with first doses available in 12 weeks.

Key action: HHS will engage with private sector partners to develop and share strategies and priorities for MCM supply chain preparedness, as well as discuss capabilities and challenges faced by manufacturers and distributors and other elements critical to maintaining a resilient supply chain during a pandemic influenza event.

Key action: HHS will continue to work with state and local governments, hospitals networks, and the private sector (including manufacturers, distributors, pharmacies and professional societies) to improve operational plans for rapid and widespread distribution, dispensing, and administration of vaccines and other medical countermeasures. In addition, advancing efforts in monitoring MCM and vaccine use, safety, and effectiveness during a public health emergency will be a priority using

existing and new tools, technologies and systems.

Key action: HHS will complete a full assessment of requirements for vaccine and therapeutics and determine the most effective approach to impacting the spread of an influenza pandemic.

Key action: HHS will support development of multiple, safe and broad-spectrum therapeutics for use in seriously ill and/or hospitalized patients, including pediatric patients. HHS intends to continue supporting informative clinical trials until at least two new influenza therapeutics are found to have sufficient evidence of safety and effectiveness to support approval.

Key action: HHS will support the development and effectiveness evaluation of reusable respiratory protective devices for the reduction of transmission of influenza viruses to and/or from patient and health care provider.

Key action: HHS will update the prioritization of vaccine recipients to have the greatest impact on health, community resilience and risk mitigation during an influenza pandemic.

Advances in developing and strategically sourcing vaccines and other MCMs in the past decade have provided a variety of effective and rapidly available options for a pandemic. Still, the time required between identification of a pandemic influenza virus and full production capacity and distribution of vaccines limits their availability. To achieve the goal of vaccine delivery within weeks, rapidly developing, licensing, and producing a sensitive and specific test for the pandemic influenza virus is critical. Supporting end-user engagement for all new MCM development to ensure alignment with current practices or to update and/or shape practices to align with new medical products is critical to ensure products developed may be optimally used. In the long term, aggressive translation of applied research in diagnostics, therapeutics, and vaccines may yield breakthrough MCMs to mitigate the next influenza pandemic.

Domain 4 – Health Care System Preparedness and Response Activities

Goal 4: Continue improving the health care system's preparedness and response capacity.

Objective 4.1 – Ensure access to appropriate care, including behavioral health care, during an influenza pandemic.

Objective 4.2 – Increase the day-to-day resilience of the U.S. health care system before a pandemic event.

Objective 4.3 – Support the ability of health care facilities and community health care providers to remain operational and deliver care during a pandemic influenza event.

Objective 4.4 – Develop policies, practices, and resources to keep health care professionals safe, healthy, and willing to work during an influenza pandemic.

Pandemic influenza has the potential to place unprecedented strain on the U.S. health care system. True pandemic preparedness will require engaging the entire health care community, and health care assets from across the spectrum of care will have to be prepared to meet the increased demands. Over the past decade, HHS has made significant investments to assist the health care sector in identifying gaps in preparedness, determining specific priorities, and developing plans for building and sustaining health care delivery. HHS will continue to support and encourage a comprehensive response by the health care system to pandemic influenza and other threats. In parallel, the delivery system reform initiatives of the past 10 years have changed the structure and incentives of the health care system to encourage quality and efficiency, reward care coordination among various health care providers through the sharing of information, and improve patients' and consumers' engagement. These underlying changes to the health care system have provided unique opportunities to build upon the preparedness and response activities of the past decade and further integrate preparedness activities into the U.S. health care system.

Because private sector entities deliver the overwhelming majority of health care in the United States, all health care organizations[4] must exhibit day-to-day resilience and be prepared to respond when an influenza pandemic arises. An effective health care response to a pandemic event requires an overall awareness of the system's capabilities, capacity, and stress to form a common operating picture. Individual health care facilities must be prepared to adjust to varying stressors on the system over time through collaboration with diverse partners, effective sharing of information, and coordinated response activities. The use of parallel and interoperable communication systems to share plans, information, and statuses can facilitate this goal. Facilities may also wish to form agreements that enable sharing of resources, supplies, and personnel

[4] For the purposes of this document, the broad term "health care organization" is defined as a hospital, ambulatory care center, emergency medical service (EMS), primary care center, physician office, urgent care center, health care clinic in a retail setting, long-term care facility, behavioral health care system, home health care provider, specialty care service (for example, dialysis, pediatrics, women's health care, or freestanding surgery facility), or associated health care support service (for example, laboratory, pharmacy, blood bank, or poison control center).

to ensure access to appropriate care, including behavioral health care, with special attention to planning for at-risk or vulnerable individuals. To remain operational, facilities must ensure the effective use of infection control practices; ensure health care professionals are safe, healthy, and willing to work; and plan to accommodate a sudden influx of patients.

As a result of lessons learned after the 2009 influenza pandemic, HHS recognizes the importance of a comprehensive and inclusive approach to health care system preparedness. The agency also encourages the involvement of a wide variety of health care organizations and providers—not only hospitals—in preparedness efforts. Accordingly, HHS has promoted and facilitated the development of health care coalitions (HCCs) to plan a coordinated regional health care response. HCCs—groups of individual health care and response organizations (such as hospitals, emergency medical services, emergency management organizations, public health agencies, and many others) in a defined geographic location—play a critical role in developing preparedness and response capabilities in the health care delivery system. They promote collaborative partnerships among traditional partners in health care preparedness, such as hospitals and emergency departments, long-term care and dialysis facilities, ambulatory care centers, emergency medical services, other health care providers, SLTT health departments, emergency management officials, and other community partners.

HHS has provided guidance to HCCs and other health care organizations regarding their roles and responsibilities during an influenza pandemic. HCCs facilitate community planning, communications, the sharing of resources (supplies and personnel), and planning for vulnerable and at-risk individuals and those with special health care needs. HHS has published tools and resources to facilitate planning and response (for example, checklists or best practices that emphasize infection control procedures to limit spread in diverse health care settings), and offered technical assistance services before, during, and after a pandemic response. HHS also has developed and updated policies that facilitate health care preparedness and response activities, and has provided funding and reimbursement opportunities to support this aim.

Notable areas of progress over the past 10 years, and key actions for the next decade, include the following:

- Connecting more than 28,000 members as part of HCCs formed among states, localities, and various provider settings to help coordinate a regional health care response.
- Developing and testing Flu on Call™, a network of telephone triage lines staffed by information specialists and medical professionals, and a service that builds on existing infrastructure to support state and local entities in their efforts to improve access to antiviral medications. Flu on Call™ reduces both the need for face-to-face provider encounters, and surge on medical facilities during a severe pandemic event.
- Providing, at the local or state level, almost 50,000 Medical Reserve Corps

volunteers for 2009 A(H1N1) pandemic activities, including surveillance, vaccination, mitigation measures, communications, and education. These local volunteers respond to public health crises and would supplement community efforts in a pandemic.

- Training respiratory therapists, physicians, and other clinicians on the ventilator models available through the Strategic National Stockpile (SNS).
- Promoting key capabilities for health system preparedness that build an interdisciplinary approach to emergency response, including operational coordination, continuity of service delivery, and the ability to deliver medical care.
- Developing plans to implement Crisis Standards of Care: Systems Framework for Catastrophic Disaster Response, by the National Academies of Science, Engineering, and Medicine, defined as the ethical alteration of health care service delivery during pervasive or catastrophic disaster.
- Finalizing a rule, establishing emergency preparedness standards which will promote increased patient safety during emergencies, for participating Medicare and Medicaid providers and suppliers.

Key action: HHS will leverage HCCs, including behavioral health stakeholders, to serve as a hub for common communication and coordination of a public health response. Health care systems at all levels (federal, state, local) will be able to share equipment and resources.

Key action: HHS will work to expand and improve the reach of health care systems to be able to keep people at home during a public health emergency, while providing them with full care through the duration of the public health event. This includes strategies for home health care, as appropriate, and investigating alternative or remote care strategies (including the use of nurse triage phone lines, and telehealth).

Key action: HHS will improve access to necessary behavioral health programs.

Key action: HHS will focus on supporting health care infrastructure to augment infection control training and capacity, promote workforce resilience, increase system capabilities through changes to scope of practice, volunteerism and credentialing.

Health delivery system reform efforts of the past decade have made today's health care system dramatically different from 2005, when the HHS Pandemic Influenza Plan was released. The next 10 years will bring even more changes to delivery settings, provider types, reimbursement models, the sharing of electronic health information, referral patterns, business relationships, and expanded individual choice. HHS must keep abreast of these changes and adapt tools and strategies accordingly.

Domain 5 – Communications and Public Outreach

Goal 5: Assess and improve communication and public outreach activities.

Objective 5.1 – Develop, evaluate, and deploy a national pandemic influenza communications strategy and expand it to global partners as circumstances warrant, building on lessons learned from other national or global outbreaks of significance.

Objective 5.2 – Increase the resources and capacity of core program staff devoted to seasonal influenza communications efforts – including plain language communications – that could be used during an influenza pandemic.

Objective 5.3 – Enhance and expand communications channels critical to disseminating seasonal influenza messages that could be leveraged and used during an influenza pandemic.

Objective 5.4 – Develop, test, and refine risk communication and plain language messaging relevant to an influenza pandemic.

Objective 5.5 – Formalize and expand a government-wide influenza communications task force to better coordinate risk communications related to seasonal and pandemic influenza.

Significant uncertainty accompanies any public health emergency, presenting dynamic challenges to communication efforts. An influenza pandemic will be no less challenging. An influenza pandemic is not a singular event: it is a series of outbreaks that occur at different times in communities over a sustained period of time. Messaging must be grounded in risk communication principles and based on time and location of the outbreaks. The public must be informed about the potential threat, kept informed in an environment of uncertainty, and provided a solid foundation of relevant and usable information upon which people can base current and future actions. Similarly, health care providers and response personnel must be kept informed about best practices, availability of resources, and methods to ensure appropriate care. As a pandemic evolves, and even after it abates, effective use of scientifically derived crisis and emergency risk communication principles can help instill and maintain public confidence in the nation's public health system. Success relies upon open, honest, transparent, and clear communications grounded in those principles.

Throughout a pandemic, the public, news media, health care providers, international partners, and other groups will demand easy-to-understand information on how to respond appropriately to reduce the risk of getting or spreading influenza. Early in the pandemic, prevention and mitigation messages—with an emphasis on NPIs—will have to be conveyed despite incomplete information. Subsequent, ongoing communications amid rapidly expanding knowledge about the particular threat will challenge even the most highly skilled communications efforts. Messages will have to evolve with the pandemic, as vaccines and other MCMs become available, and as the case numbers and geographic spread expand. Messages will also need to be conveyed regarding counterfeit products and fraudulent or exaggerated product claims, particularly for products advertised or made available over the internet. Furthermore, behavioral health and stress reactions are health risks in a pandemic that must be integrated into

messages to mitigate individual psychological harm, increase compliance with public health directives, and promote the resilience of communities.

A major lesson learned from the 2009 A(H1N1) pandemic response is that the programmatic and communications platforms for seasonal and pandemic influenza are strongly correlated. Pandemic communications cannot be successful in the absence of strong, ongoing, seasonal influenza communications activities. During the 2009 A(H1N1) pandemic, staff with subject matter knowledge and long-term experience with influenza and influenza-related topic areas provided the greatest efficiency and effectiveness in pandemic influenza communications. Longstanding relationships among program communicators, subject matter experts, and outreach channels were critical to a rapid, credible, and science-based communications response. These relationships continue to be critical for future pandemic response capabilities.

The 2009 A (H1N1) pandemic also informed the development and fine- tuning of plain-language risk communication and prevention messaging. New channels of message dissemination were exploited, and community partnerships were invaluable in spreading information about at-risk and priority groups, surveillance and epidemiological data, community mitigation measures, and medical countermeasure guidance to health care providers and the general public. Many of these community partners continued to be engaged after the pandemic, promoting the importance of seasonal influenza vaccination. Maintaining and expanding HHS's reach to a diverse group of community partners will be vital to our ability to disseminate risk communication messages to multiple audiences through trusted sources.

Notable areas of progress over the past 10 years and key actions for the next decade include the following:

- Developing an HHS-wide communications plan that details roles, responsibilities, and procedures related to communications during an influenza pandemic, and ensuring messages are clear and consistent across HHS and to the general public.
- Using digital media as an integrated platform for HHS's influenza communications and increasing the number of mobile device-accessible flu web pages to complement briefer social media messages.
- Consolidating seasonal and pandemic influenza information and planning resources to one website: https://www.cdc.gov/flu/.
- Conducting communication research, including messages and concepts, to inform a communication strategy for the development of new seasonal influenza campaign products that target specific audience groups with a high disease burden. Establishing the National Influenza Vaccination Disparities Partnership, and corresponding Facebook page, and listserv to quickly notify and mobilize grassroots partners with critical information for disparate populations.
- Partnering Digital Ambassadors since the 2013–2014 influenza season, which expanded visibility of credible science-based and user-friendly plain language

seasonal influenza prevention messages, through blogs, websites, and social media posts.

- Ongoing development of resources and distribution channels so health care professionals can more readily obtain the most up-to-date guidance.

Key action: HHS will continue to strengthen communication mechanisms and platforms that prepare for and surround influenza public health emergencies. HHS will assess communications efficiencies and gaps in existing communication platforms. HHS will target these gaps for improvement across federal, state, and local communication mechanisms to build effective communication bridges that will be used during a public health emergency.

Key action: HHS will establish flexible and sustainable communications capabilities by conducting annual exercises that evaluate the effectiveness of various communications functions (e.g. clearance, planning, message testing, staffing surge) and by leveraging partnerships and adopting innovative communication platforms to reach multiple target audiences.

Communications planning is integral to early and effective messaging when a pandemic threatens, establishes itself, and expands. Accurate, consistent, timely, and actionable communication is enhanced by the use of plain language and accessible formats. Using appropriate channels and spokespeople will enhance consistent and accurate messages.

Domain 6 – Scientific Infrastructure and Preparedness

Goal 6: Strengthen preparedness throughout the scientific infrastructure.

Objective 6.1 – Support scientific infrastructure preparedness with capacity to conduct clinical, behavioral and epidemiological research; facilitate its safety oversight and monitoring; and simplify collaboration, ethical practices, and evaluation activities to provide evidence-based findings to inform pre-pandemic planning.

Objective 6.2 – Support basic and translational research to improve MCMs and strategies to prevent, diagnose, treat, and respond to pandemic influenza through collaboration among government agencies, the private sector, and academic institutions.

Objective 6.3 – Establish and sustain a scientific preparedness framework that can align and integrate public health practice and scientific research during an influenza pandemic.

A strong scientific infrastructure underpins everything HHS does to prepare for and respond to pandemic influenza and other emerging infectious diseases. HHS's scientific infrastructure includes its own laboratories, data systems, and investigators, as well as research institutions in the United States and abroad that receive HHS funding. Science reveals how influenza viruses evolve, spread, and cause disease, as well as how a host's immune system responds to the infection. Strong scientific foundations are needed to develop new vaccines and therapeutics, and to determine how well other control efforts are working. Rigorous scientific methods applied during pandemic response yield information to improve both ongoing and future responses.

HHS has established a scientific preparedness infrastructure that informs sound public health practices and incident response efforts. This system is meant to be nimble, taking advantage of the rare opportunities when these events arise so that scientists can quickly mobilize to identify research needs, collect and analyze critical and time-sensitive data, and share and build upon their findings. HHS learns something different from each outbreak of influenza with pandemic potential, addressing scientific questions about the characteristics of the virus, effects of existing mitigation measures on the spread and severity of the disease, and the effectiveness and safety of MCMs that will be needed. A robust scientific preparedness infrastructure also provides decision makers with the best evidence available to plan for the appropriate path forward, which is critical for response and recovery during a pandemic. This infrastructure also can support data collection and sharing before a pandemic and address immediate questions decision makers ask during the pandemic. For example, HHS-supported Centers of Excellence for Influenza Research and Surveillance provide ongoing genomic analysis of animal-origin influenza viruses and rapid *in vitro* and *in vivo* characterizations to evaluate their pandemic potential. These Centers provided key information on the 2009 H1N1 virus's origin and transmission, and they continue to assess emerging viruses. These types of investments position public health experts to design additional analyses to understand the longer-term implications of actions taken to mitigate a pandemic, then translate research outcomes into more effective interventions.

The 2009 A(H1N1) pandemic provided the impetus for HHS's science preparedness infrastructure. These efforts provided significant insight into influenza virus pathology, epidemiology, and antigenic drift. Science has elucidated mechanisms of resistance to MCMs and has sought to improve the fit and performance of PPE. Notable progress and key actions for the next decade include the following:

- Implementing authorities under Section 564 of the Federal Food, Drug, and Cosmetic Act, United States Code, Title 21 (FD&C Act), as amended by the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013, Public Law No. 113-5.
- Establishing and expanding the clinical studies networks that provide a full range of services required to plan, perform, monitor, and interpret clinical studies. Specifically, science preparedness has resulted in performing clinical studies required for the approval of a product for human use, comparing the properties of multiple products, or evaluating the potency of products stored in the SNS.
- Applying basic research studies to determine how influenza viruses emerge, transmit, and cause disease, and applying systems biology approaches to better understand host–virus interactions. These efforts have helped to identify the role of neuraminidase mutations in viral resistance to antiviral medications and broadly neutralizing antibodies against influenza viruses. Scientists also use them to develop antiviral drugs and antigenically advanced vaccines for further development and vaccination strategies.
- Expanding a population-based surveillance system[5] (FluSurv-NET) in the United

[5] See Chaves SS, et al. The US Influenza Hospitalization Surveillance Network. Emerg Infect Dis. 2015 Sep.

States for laboratory-confirmed influenza in hospitalized patients. Data have helped determine risk factors, document severity, and guide recommendations for treatment and vaccination programs.

- Collaborating with the WHO and other global partners to develop a manual for estimating disease burden associated with seasonal influenza.[6] HHS field staff who are stationed overseas have worked with countries to develop burden estimates for use in guiding evidence-based decisions on introducing vaccines in low- and middle-income countries.
- Providing research resources such as animal models, reagents, and full genome sequencing of more than 20,000 influenza viruses from avian, swine, human, and other mammalian sources to researchers and diagnostics developers.
- Developing performance criteria for a respirator with improved comfort and fit, based on research on filtering face piece respirator designs; manufacturers are evaluating and optimizing prototype devices in anticipation of submitting to the National Institute of Occupational Safety and Health for certification and/or the FDA for clearance.
- Improving our knowledge of respirator use by quantifying reasons for poor compliance, and applying this knowledge to design and administer more effective respiratory protection programs.
- Working to quickly obtain institutional review board approval for clinical research needs in the event of a pandemic.

Key action: HHS will establish and validate sets of tools (protocols, templates, agreements, and procedures) that will permit the smooth initiation of critical scientific response before and during an influenza pandemic. These tools include: (1) pre-approved clinical protocols to conduct dynamic clinical trials of multiple candidates for rapid assessment of clinical utility during the pandemic and for rapid assessment of safety of countermeasures used under emergency regulatory mechanisms; (2) clinical networks, with agreements in place, to enable rapid clinical evaluation of medical countermeasures; and (3) databases to permit data sharing as a common resource for HHS stakeholders to access and review data simultaneously to inform planning and decisions made pre, during and post pandemic outbreak.

Key action: HHS will expand and improve clinical trial evaluation networks, regulatory processes, databases, and systems needed to rapidly evaluate the safety and effectiveness of multiple influenza vaccines and therapeutics, for study and use during seasonal influenza outbreaks or during a pandemic response. This key action may include products that are investigational, licensed, approved, or used under emergency use authorization.

Key action: HHS will improve understanding of reasons for low seasonal vaccination rates among health care workers in some high risk populations, and investigate ways to improve vaccine uptake in a variety of health care settings to reach Healthy People 2020 targets and beyond.

[6] See WHO Global Influenza Programme. A Manual for Estimating Disease Burden Associated With Seasonal Influenza. Washington, DC: WHO, 2016.

HHS's fundamental investments in science infrastructure and preparedness have delivered critical knowledge to understand both seasonal influenza viruses and those with pandemic potential. Establishing and sustaining scientific research frameworks, addressing the full spectrum from basic discovery through patient intervention, will dramatically improve comprehensive pandemic outbreak preparedness, response and recovery. As influenza viruses with pandemic potential emerge, we will use our science infrastructure to characterize strains, and identify and develop MCMs and NPIs to combat spread of a pandemic.

Domain 7 – Domestic and International Response Policy, Incident Management, and Global Partnerships and Capacity Building

Goal 7: Develop and enhance domestic and international response coordination policies, incident management, and global partnerships and capacity building.

Objective 7.1 – Build out and implement the requirements of the Biological Incident Annex to the Federal Interagency Operations Plan—Response and Recovery and lead the operational coordination for domestic incident support in a federal response to an influenza pandemic.

Objective 7.2 – Develop, implement, and coordinate domestic and international policies and processes to mitigate an influenza pandemic domestically or globally within national and international legal authorities, regulations, agreements, and frameworks.

The emergence of influenza viruses with pandemic potential, as well as other emerging infectious diseases, poses a threat to national and global health security. HHS recognizes the critical connection between the health of the global community and the health and well-being of the American people and, thus, supports international preparedness efforts for pandemic influenza. As such, there is a growing need to align domestic and international response policies and incident management systems. In addition, partnerships are essential for global capacity building and international pandemic influenza preparedness. Thus, in past years, HHS has supported activities involving more than 165 countries and the WHO to build international capacities in the areas of surveillance, laboratory, human resources, response, research, and vaccine manufacturing, as well as to align efforts worldwide.

Domestic

The Public Health Service Act; the FD&C Act; and The Social Security Act, among others, provide HHS with the legal authority to respond to public health emergencies and infectious disease threats (including pandemic influenza). For all hazards (including pandemic influenza), HHS conducts incident support consistent with the National Incident Management System, in effect since 2004, and the National Response Framework (NRF), established in 2008. The NRF is one of five frameworks under the National Preparedness System and provides a national preparedness and operational coordinating structure and doctrine for responding to incidents and emergencies, with or without an emergency declaration. The NRF also allows for the coordination of multiple federal agencies and emergency support functions involved in a response in support of state and local efforts in a consistent, national approach integrating all critical stakeholders, including public and private partners. The Biological Incident Annex to the Response and Recovery Federal Interagency Operational Plans, describes the whole-of-government operational approach for a pandemic response and recovery. Under the NRF, HHS is the lead federal agency in a federal interagency response to a pandemic. From a response policy coordination standpoint, HHS convenes its Disaster Leadership Group (DLG) to develop and coordinate Department-wide policy, limit duplication of operational efforts, and ensure that HHS speaks as a single voice. The DLG has responded to multiple disease outbreaks and disasters, including the 2009 influenza pandemic, the Deep Water Horizon oil spill (in the Gulf of Mexico), and the Ebola and Zika virus outbreaks. Notable progress over the past decade includes the following:

- Committing to the National Preparedness System organizing structure whenever a public health threat or emergency demands nationwide mitigation, response, and recovery.
- Clarifying roles, responsibilities, and required resources for federal partners in an HHS-led, federal government-wide response to a pandemic through interagency planning and coordination efforts, in response to recent outbreaks that threatened the United States, such as MERS, 2013 A(H7N9), Ebola virus, and Zika virus.
- Identifying and improving fiscal and administrative practices that govern funding, procurement, contracting, grants management, and hiring. These improvements should accelerate, streamline, and accountably manage responses at all levels of government touched by HHS's efforts.
- Leveraging state and local health departments' incorporation of administrative and fiscal processes into their emergency response plans. These processes include emergency procurement, contracting, and hiring. Health departments must define how these processes differ from normal operations. Further, state-level grantees of HHS public health emergency preparedness and response funds are required to establish procedures for efficiently allocating those funds to local health departments. Grantees also must develop reporting and monitoring methods to ensure accountability.
- Increasing attention to the depletion of human resources supporting the services integral to emergency response. For example, laboratory services and the staff to

conduct them; health care providers to administer vaccine and to care for critically ill patients; mental health and behavioral health providers to address the needs of the general public and the stress and mental health needs of the health care workforce; public health staff for all aspects of response; and services such as transportation, supply chain management, and logistics, all of which could be overwhelmed during a pandemic. Developing and exercising contingency plans is essential to seamless provision of these capabilities.

- Supporting the development of a pandemic influenza plan in every state, four major metropolitan areas, and eight U.S. territories and freely associated states since 2006. Subsequent to the 2009 A(H1N1) pandemic, many states also developed robust administrative preparedness plans, testing them in a 2015 Table Top Exercise to examine processes associated with HHS's ability to secure, disburse, and manage funds accountably during a public health emergency, especially when a disaster has not been declared under the Stafford Act.
- Supporting the Emergency System for Advance Registration of Volunteer Health Professionals and resultant increased use of volunteers in response activities. In addition, Medical Reserve Corps volunteers provide support to activities such as surveillance, vaccination, mitigation measures, communications, and education, including during the 2009 A(H1N1) pandemic.

International

By leading the integration of domestic and global pandemic influenza preparedness and response capabilities, partnerships, and policies, HHS aims to rapidly detect outbreaks of influenza virus, characterize the virus, and communicate effectively with U.S. and international stakeholders to promote a faster, more efficient response domestically and abroad. Recognizing this, the *National Health Security Strategy 2015–2018* [7] states that "by working together with international partners to develop global capacities and operational capabilities to prevent epidemics, detect threats early, rapidly respond to incidents, and support integrated recovery efforts, the United States will also protect the health of the American people from global health security threats." Notable progress over the past decade includes the following:

- Adopting the IHR (2005), establishing the U.S. National Focal Point within HHS, and developing processes for assessment and notification of potential public health emergencies of international concern, which have resulted in 41 notifications to the WHO about novel influenza events since 2005.
- Enhancing the capability of the WHO's GISRS to support global pandemic influenza preparedness, especially related to surveillance, laboratory diagnostics, vaccines, antiviral drug susceptibility, and risk assessment.
- Supporting the global adoption of the WHO Pandemic Influenza Preparedness Framework for the sharing of influenza viruses and access to vaccines and other benefits in 2011, which provides a platform for greater collaboration between WHO

[7] US Department of Health and Human Services (HHS). National Health Security Strategy (NHSS) and Implementation Plan 2015–2018. Washington, DC: 2014.

Member States, industry, civil society, and stakeholders. The WHO conducted its first five-year review in 2016.

- Fostering international partnerships such as the Global Health Security Initiative and the Global Health Security Agenda to enhance coordination and support capacity building to prevent, detect, and respond to, international public health emergencies.
- Establishing and maintaining cooperative agreements to build or strengthen capacities in partner countries to prevent, detect, and respond to, pandemic influenza and other global health threats, which have resulted in the establishment of critical infrastructure components, including evaluation of preparedness plans, establishment of sentinel surveillance networks and national influenza centers, in several partner countries in Africa, Latin America, and South East Asia.
- Leading the development and implementation of the NAPAPI in 2012, a comprehensive cross-sectoral regional health security framework developed mainly with the input of the health, agriculture, security, and foreign affairs sectors to protect against, control, and provide a public health response to, animal and pandemic influenza in North America, while avoiding unnecessary interference with international travel and trade.
- Supporting 13 influenza vaccine manufacturers in 12 low- to middle-income countries through the WHO's Global Action Plan for Influenza Vaccines to develop capacity to produce influenza vaccine to expand global vaccine availability and access. This effort has led to the production capacity of over 500 million doses of pandemic influenza vaccines, compared to less than one million doses produced in 2006.
- Establishing a USG framework to receive, consider, communicate about, decide upon, and respond to international requests for public health and medical assistance, including provision of MCMs, during influenza pandemics, based on lessons learned from the 2009 A(H1N1) pandemic.
- Continuing to develop and implement policies and processes to facilitate international assistance, when appropriate, including the 2013 USG Policy Framework for Responding to International Requests for Public Health and Medical Assistance during an Influenza Pandemic, which provides a basis for USG-wide coordinated response when multiple requests are received or anticipated.

Key action: HHS will continue to coordinate both domestic and international pandemic preparedness and response partnerships and activities. This will include having clearly defined mechanisms for rapid exchange of information, data, reagents and other resources needed domestically and globally to prepare for and response to an influenza pandemic outbreak.

Key action: HHS will continue to lead a unified and coordinated operational and policy structure and process for preparedness and response to public health emergencies, and maintain a system of response exercises and improvements based on lessons learned. HHS will achieve this by working both within HHS and externally with federal, SLTT, and international partners.

Strengthening global preparedness and incident response capacities for pandemic influenza is a complex effort that requires significant efforts in policy, planning, and technical areas within each partner country and internationally. Although HHS has made significant investments in international pandemic influenza preparedness activities in every region of the world, additional work with public and private partners spanning multiples sectors is still needed. Given the complexity of this enterprise, HHS is committed to establish priorities and leverage resources to coordinate policies, partnerships, and programs focused on strengthening USG policies, plans, and structures to ensure they address the international aspects of an influenza pandemic; collaborating with partner countries and multilateral organizations to harmonize policies, plans, and initiatives that support pandemic influenza preparedness and response in alignment with current USG foreign policy and national security priorities and goals; developing collaborations with countries in regions with the highest risk of pandemic emergence or with a potential to develop regional resources for pandemic influenza preparedness and response; and focusing investments on resource-limited countries to increase their response capacities, ultimately protecting the health security of the American population.

CONCLUSIONS

As this 2017 Update demonstrates, HHS has made progress in pandemic influenza preparedness over the past decade. Ongoing work enables HHS to respond more quickly to a future influenza pandemic and, at the same time, strengthens our response to seasonal influenza. That work encompasses supporting domestic and international influenza response capacity building; enhancing the science preparedness infrastructure; communicating across all sectors of society; bolstering the health care system; developing, delivering, and monitoring MCMs; helping communities protect themselves against influenza; and sustaining vigilance through core public health functions of surveillance and epidemiology with laboratory support. The seven domains and associated objectives and key actions in this 2017 Update may seem daunting, given the competing demands for limited resources. However, one major achievement of the past decade is that HHS now leverages its seasonal influenza monitoring and response mechanism as a platform to address influenza viruses with pandemic potential.

HHS's success in responding to, and containing, a potential pandemic relies on collaborations across federal departments and agencies, but the role of nonfederal partners is critical. Those partners include SLTT health departments; medical, public health, and social services professionals in non-governmental sectors such as academia, clinical practice, and industry; schools and childcare settings; employers in all these sectors and beyond; and voluntary and professional organizations trusted by the public for actionable health information. International partners, from the WHO to non-governmental organizations and individual nations, also contribute essential information about influenza that helps inform U.S. preparedness.

Potential pandemic influenza viruses can be unpredictable, characterized by significant uncertainty of their place of emergence, timing, and severity. Flexibility is essential to any pandemic influenza planning effort, as plans will need to be easily and quickly adapted to the circumstances. HHS must be prepared to respond to the specific needs of an evolving pandemic, as epidemiologic and laboratory data emerge. Each response is different, even if the same basic principles apply. A nimble and effective pandemic response with flexible, sustainable capabilities will save lives and mitigate social and economic disruption.

Finally, this 2017 Update illustrates the status of work as of April 2017. While the threat of pandemic influenza remains constant, the time needed to mount an effective response will not. Pandemic preparedness must be twofold—maintaining the gains that HHS has achieved over the last decade while improving scientific understanding of influenza and the tools to best fight it. As new scientific knowledge and applications evolve, the information linked to this Update will reflect that progress, and concrete strategies and measures for future progress can be developed. Given the continuous threat of an influenza pandemic, HHS will revisit the goals, objectives, and strategies as knowledge expands about preparing for, responding to, and recovering from an influenza pandemic.

APPENDIX A

PLANNING SCENARIOS

An emerging influenza pandemic virus can place extraordinary and sustained demands on public health and health care systems and on providers of essential community services across the United States and throughout the world. By some estimates, and based on experience with past pandemics, 20 to 30 percent of the global population could develop clinical disease; a substantial proportion of these people could develop severe disease, and even die. Although the 1918 pandemic resulted in an estimated 500,000 deaths in the United States (out of a total population then of about 105 million), the 1968 pandemic caused an estimated 34,000 US deaths (out of a total population then of about 201 million), and the 2009 A(H1N1) pandemic resulted in approximately 12,500 US deaths (out of a total population then of about 305 million). [8] The direct and indirect health costs alone (not including disruptions in trade and other costs to business and industry) have been estimated to approach $181 billion for a moderate pandemic (similar to those in 1957 and 1968) with no interventions. Faced with such a threat, the United States and its global partners will have to respond quickly and decisively to protect human health and preserve community functioning.

Planning Assumptions

Given the difficulty associated with estimating timing or impact, pandemic planning is based on the following assumptions about viral epidemiology and human susceptibility:

- Delays in availability of vaccines and shortages of antiviral drugs are likely, particularly early in the pandemic.
- The seasonality of a pandemic cannot be predicted with certainty. With seasonal influenza, peak disease usually occurs during December through March in the United States. During the 2009 A(H1N1) pandemic, the first cases were identified in April, and widespread US community outbreaks first began in August, with illness peaking in October 2009, months earlier than is routinely seen with seasonal influenza.
- The novel virus will have the ability to spread rapidly worldwide.
- If the pandemic is characterized by severe disease, it will have the potential to disrupt national and community infrastructures (including health care, transportation, commerce, utilities, and public safety) due to widespread illness, absenteeism, and death among workers and their families, as well as concern about ongoing exposure to the virus.
- Not all jurisdictions will experience clusters of disease simultaneously; however, near-simultaneous clusters likely will occur in many communities across the United States, thereby limiting the ability of any jurisdiction to support and assist other jurisdictions.
- During a pandemic, infection in a localized area can last about six to eight weeks. At least two pandemic disease waves will occur. Following the pandemic, the newly

[8] Shrestha SS, Swerdlow DL, Borse RH, Prabhu VS, Finelli L, Atkins CY, Owusu-Edusei K, Bell B, Mead PS, Biggerstaff M, Brammer L, Davidson H, Jernigan D, Jhung MA, Kamimoto LA, Merlin TL, Nowell M, Redd SC, Reed C, Schuchat A, Meltzer MI. Estimating the burden of 2009 pandemic influenza A (H1N1) in the United States. (April 2009-April 2010). Clin Infect Dis 2011;52 (Suppl 1):S75-82.

circulating virus is likely to become a regularly occurring seasonal influenza.

- Immunity to the novel pandemic influenza subtype will vary based on the strain of the virus, but most people will likely be susceptible, depending on whether a similar strain has circulated in previous seasons.
- The clinical disease attack rate could range from 20% to 30% of the overall population. Illness rates will likely vary by age group (and other epidemiologic characteristics) and could create selective pressures on segments of the community, such as nursing homes or schools.
- The typical incubation period (the time between acquiring the infection and becoming ill) for influenza averages two days (range is one to four days).
- Of those who become ill with influenza, up to 50% will seek outpatient medical care.
- The number of hospitalizations and deaths will depend on the severity of the disease and the success of steps to mitigate its transmission. Nonetheless, estimates could differ by as much as a factor of 10 between more and less severe scenarios.
- Risk groups for severe and fatal infections cannot be predicted with certainty. During annual fall and winter influenza seasons, infants and the elderly, people with certain chronic illnesses, people with morbid obesity, and pregnant women are usually at higher risk of complications from influenza infections than other groups. In contrast, in the 1918 pandemic, deaths were notably evident among young, previously healthy adults; in 2009, elderly people were disproportionately spared severe illness and death.
- People who become infected will shed virus and transmit infection for up to one day before the onset of illness.
- Viral shedding and the risk for transmission will be greatest during the first two days of illness and may persist for five to seven days.
- Children will shed the greatest amount of virus and, therefore, are likely to pose the greatest risk for transmission.
- The most severely ill people with influenza will shed the most virus for the longest period of time.
- One or two secondary infections will occur as a result of transmission from someone who is ill. In contrast, some estimates from past pandemics have been higher, with up to three secondary infections per primary case.

Because the precise impact of a future pandemic is unpredictable, national, state, and local planners need multiple scenarios for pandemic planning to implement rapid response efforts. The timing and progression of a pandemic, as well as its severity and transmissibility, will determine the mitigation measures selected. HHS will use several possible scenarios for pandemic planning, including a future pandemic that is moderate in severity, a pandemic that is severe, and one that is very severe in its effects on human health. These scenarios will provide a way to plan for use of response measures scaled to different levels of pandemic severity.

Table A.1 provides estimates of illness; outpatient medical care; hospitalizations; intensive care unit care; and deaths for moderate, severe, and very severe influenza pandemics. These estimates are based on scenarios that are unmitigated, meaning that they do not account for public health interventions that would likely be implemented during a pandemic. For comparison, the 2014–2015 season was at the high end of severity for seasonal influenza, with an estimated 974,206 hospitalizations, due to a significantly drifted influenza A(H3N2) virus for which the vaccine was not effective.

Table A.1. Estimated Illness, Types of Medical Care, and Deaths from a Moderate to Very Severe Influenza Pandemic

Pandemic Severity (based on multiple factors[a]	Transmissibility (% of US population[b] with clinical illness)	Illness	Outpatient medical care	Hospitali-zation	ICU care	Deaths
Moderate	20%	64,000,000	32,000,000	800,000	160,000	48,000
	30%	96,000,000	48,000,000	1,200,000	240,000	72,000
Severe	20%	64,000,000	32,000,000	3,800,000	1,200,000	510,000
	30%	96,000,000	48,000,000	5,800,000	1,700,000	770,000
Very Severe	20%	64,000,000	32,000,000	7,700,000	2,300,000	1,300,000
	30%	96,000,000	48,000,000	11,500,000	3,500,000	1,930,000

[a] Adapted from Reed C, Biggerstaff M, Finelli L, Koonin LM, Beauvais D, Uzicanin A, Plummer A, Bresee J, Redd SC, Jernigan DB. Novel framework for assessing epidemiologic effects of influenza epidemics and pandemics. Emerg Inf Dis 2013; 19:85-91.

[b] 2015 US Population estimate used for calculation.

APPENDIX B

PLANNING TOOLS

At the onset of a potential pandemic, much will be unknown about how infectious and transmissible the influenza virus is until cases emerge and the virus's characteristics are better described. As the outbreak spreads, continued assessment of the virus and its impact on the human population will inform the nature and scope of the response. Mitigation actions will vary based on the virus characteristics and might have to change over the course of the pandemic.

The uncertainty and complexity surrounding the onset of an outbreak with pandemic potential emphasize the need for establishing an organizing framework to identify influenza viruses with pandemic potential; to weigh the risk of widespread human disease and potential public health impact; to describe the progression of the event and evaluate severity and transmissibility; and to consider the potential to mitigate impact with public health measures and MCMs that are available early in the pandemic's evolution. Together, these are the elements that will inform decisions related to public health interventions. HHS has developed three tools to guide planning and response:

1. Pandemic Intervals Framework (PIF)
2. Influenza Risk Assessment Tool (IRAT)
3. Pandemic Severity Assessment Framework (PSAF)

These tools align with a request from the World Health Organization (WHO) for Member States to establish national plans for response within the WHO's global framework of pandemic phases and risk assessment activities for preparedness, response, and recovery.[9] The United States has developed a more refined operational framework to respond to a pandemic (Table B.1), providing guidance for coordinated actions among federal, state, local, tribal, and territorial entities involved in pandemic response.

Pandemic Intervals Framework

The framework describes the progression of an influenza pandemic using six intervals (two pre-pandemic and four pandemic). This framework can be used for influenza pandemic planning and provides recommendations for risk assessment, decision making, and action in the United States. The Pandemic Intervals Framework replaces the stages from the 2006 federal implementation plan for the National Strategy for Pandemic Influenza.[10] The framework has six intervals:

1. Investigation of cases of novel influenza
2. Recognition of increased potential for ongoing transmission
3. Initiation of a pandemic wave
4. Acceleration of a pandemic wave

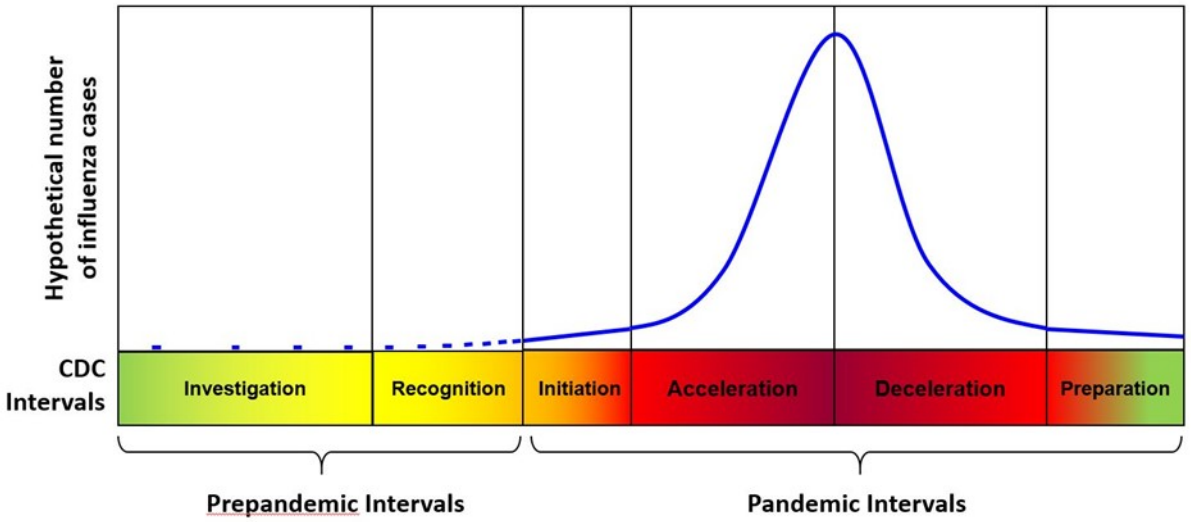
[9] Pandemic Influenza Risk Management – WHO Interim Guidance, 2013.

[10] US Homeland Security Council. National Strategy for Pandemic Influenza - Implementation Plan. Washington, DC: US Homeland Security Council; 2006.

5. Deceleration of a pandemic wave
6. Preparation for future pandemic waves (described later)

Figure B.1 includes a hypothetical influenza outbreak curve and the corresponding preparedness and response framework for novel influenza A virus pandemics with the CDC intervals.

Figure B.1. Preparedness and response framework for novel influenza A virus pandemics: CDC intervals



CDC = Centers for Disease Control and Prevention

Progression through the intervals is not exclusively linear and is meant to enable jurisdictions to respond with actions that are appropriate for the level of activity occurring in their regions. These intervals, described in the publication Updated Preparedness and Response Framework for Influenza Pandemics, provide a common orientation and epidemiological picture of pandemic activity that can inform interventions. The intervals are flexible enough to accommodate the variable spread of a pandemic in different areas, allowing appropriate local, state, and federal actions for jurisdiction-specific conditions (for example, a jurisdiction with cases versus a jurisdiction with no cases but that is close to an area with cases). In addition, state and local health authorities could elect to implement interventions at different times within their jurisdictions, starting with communities that are first affected and then progressing to others. The state–local initiation, acceleration, deceleration, and preparation indicators can be out of step with the federal indicators. The published document provides additional details.

Table B.1. Preparedness and response framework[11] for novel influenza A virus pandemics: World Health Organization phases and CDC intervals, with federal and state/local indicators

World Health Organization phases	CDC intervals	Federal indicators for CDC intervals	State/Local indicators for CDC intervals
Interpandemic phase: Period between influenza pandemics	**Investigation:** Investigation of novel influenza A infection in humans or animal	Identification of novel influenza A infection in humans or animals anywhere in the world with potential implications for human health	Identification of novel influenza A infection in humans or animals in the United States with potential implications for human health
Alert phase: Influenza caused by a new subtype has been identified in humans	--	--	--
--	**Recognition:** Recognition of increased potential for ongoing transmission of a novel influenza A virus	Increasing number of human cases or clusters of novel influenza A infection anywhere in the world with virus characteristics, indicating increased potential for ongoing human-to-human transmission	Increasing number of human cases or clusters of novel influenza A infection in the United States with virus characteristics indicating increased potential for ongoing human-to-human transmission

[11] Updated Preparedness and Response Framework for Influenza Pandemics

World Health Organization phases	CDC intervals	Federal indicators for CDC intervals	State/Local indicators for CDC intervals
Pandemic phase: Global spread of human influenza caused by a new subtype	**Initiation:** Initiation of a pandemic wave	Confirmation of human cases of a pandemic influenza virus anywhere in the world with demonstrated efficient and sustained human-to-human -- transmission	Confirmation of human cases of a pandemic influenza virus in the United States with demonstrated efficient and sustained human-to-human transmission
	Acceleration: Acceleration of a pandemic wave	Consistently increasing rate of pandemic influenza cases identified in the United States, indicating established transmission	Consistently increasing rate of pandemic influenza cases identified in the state, indicating established transmission
	Deceleration: Deceleration of a pandemic wave	Consistently decreasing rate of pandemic influenza cases in the United States	Consistently decreasing rate of pandemic influenza cases in the state
Transition phase: Reduction in global risk, reduction in response activities, or progression toward recovery actions	**Preparation:** Preparation for future pandemic waves	Low pandemic influenza activity but continued outbreaks possible in some jurisdictions	Low pandemic influenza activity but continued outbreaks possible in the state

It is important to note that routine activities monitoring the onset and severity of seasonal influenza provide the baseline surveillance, epidemiology, and laboratory data that would detect the appearance of a novel influenza A virus with pandemic potential. Even with that identification, however, this does not ensure progression to the next interval (the recognition interval): the virus might not demonstrate the potential for increased numbers of human illnesses, nor increased potential for ongoing human-to-human transmission. Further, after the preparation interval, subsequent waves of outbreaks likely will occur, prompting federal, state, and local public health officials to respond to subsequent acceleration, deceleration, and preparation intervals. The duration of each pandemic interval might vary from weeks to months depending on the characteristics of the virus and the public health response.

Influenza Risk Assessment Tool (IRAT)

When a novel influenza A virus is identified in the human population, but not yet circulating widely, it is important to evaluate 1) the risk that the virus will develop efficient and sustained human-to-human transmission (emergence) and 2) the risk that the virus will significantly affect public health (impact). The IRAT assesses potential pandemic risk based on these two scenarios, emergence and impact.[12] The initial trigger to use the IRAT is a newly identified influenza A virus in animals or identification of a novel influenza A virus in humans. The U.S. Department of Health and Human Services (HHS) uses the IRAT during a risk assessment process that includes data gathering and discussion among subject matter experts that culminates in an IRAT score. Scoring uses 10 predefined criteria that fall into three categories:

1. Attributes that pertain to the biologic properties of the virus (four elements)
2. Attributes of the population (three elements)
3. Attributes of the ecology and epidemiology of the virus (three elements)

HHS uses the results of this process to decide whether and how to act and to communicate concerns regarding both emergence of the virus and the potential public health impact. As new information becomes available, the scoring process is repeated to adjust or validate the risk assessment, providing a baseline and context for assessment of newly emerging viral strains. This risk assessment process informs vaccine development, manufacturing, and stockpile decisions. Recently, the World Health Organization (WHO) launched another tool (the Tool for Influenza Pandemic Risk Assessment) that focuses on genetic predisposition and transmission in animals. This tool is expected to assist other countries with risk assessment in a similar approach to how HHS uses the IRAT, but applied less frequently.

[12] Influenza Risk Assessment Tool (IRAT), 2014.

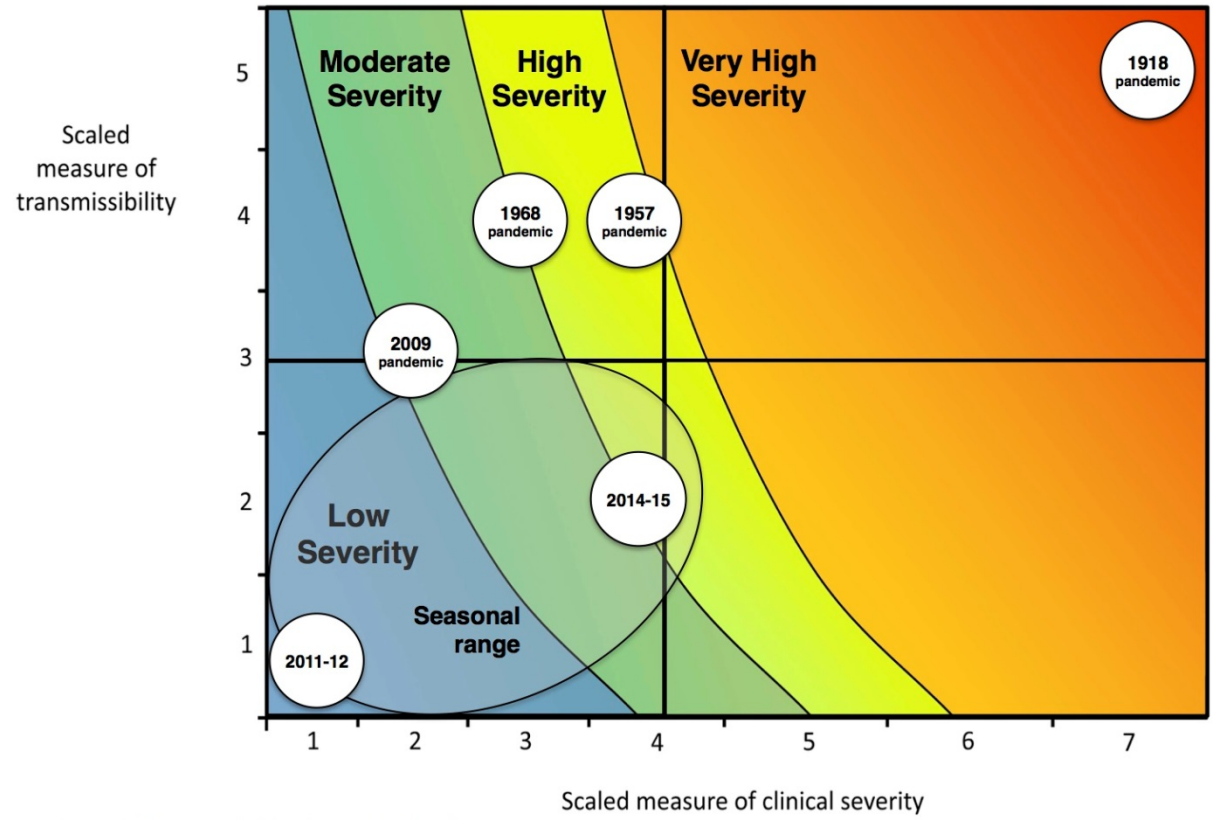
Pandemic Severity Assessment Framework (PSAF)

When a novel influenza virus has emerged and circulates in human populations with efficient and sustained transmission, the public health impact posed by the pandemic can begin to be assessed. The PSAF uses information available from surveillance, investigations, initial case series, and other sources to help predict how severe the impact of the pandemic will be compared with past seasonal and pandemic experiences. Although the IRAT focuses on the risk of emergence and potential for impact before a pandemic begins, the PSAF focuses instead on epidemiologic parameters of transmissibility and severity after the virus emerges with efficient and sustained transmission in humans. The PSAF can be used early in a pandemic, with assessments repeated as information evolves, but determination of an initial assessment requires a sufficient number of human cases and clusters of illness to be identified and characterized. Depending on the number of cases, size of clusters, and the geographic locations of outbreaks, the trigger for using PSAF is likely to occur during the early initiation interval when a pandemic is beginning. The PSAF can be updated regularly as the pandemic progresses.

The PSAF is based on transmissibility and clinical severity parameters and uses different scales for 1) initial assessments and 2) more refined assessments when more data become available. The initial assessment, performed early in the outbreak when there might be uncertainty about viral characteristics resulting from limited epidemiologic data, uses a dichotomous scale of low-to-moderate versus moderate-to-high transmissibility and severity. The refined assessment, performed when more reliable data are available, uses a 5-point scale for transmissibility and a 7-point scale for clinical severity. After available data are assessed on these scales, the overall results are plotted as a two-dimensional chart, with the measures of transmissibility along the y-axis and the measures of severity along the x-axis. The PSAF results can be compared with referent points, such as previous pandemics or particularly severe influenza seasons.[13]

[13] Reed C, Biggerstaff M, Finelli L, Koonin LM, Beauvais D, Uzicanin A, et al. Novel framework for assessing epidemiologic effect of influenza epidemics and pandemics. Emerg Infect Dis 2013 Jan;19(1):85-91.

Figure B.2. Two-dimensional chart used to plot results of assessment using the Pandemic Severity Assessment Framework (PSAF)



Adapted from: Reed C, Biggerstaff M, Finelli L, Koonin LM, et al. Novel framework for assessing epidemiologic effect of influenza epidemics and pandemics. Emerg Infect Dis 2013;19(1):85–91.