Written Testimony
House Committee on Energy and Commerce, Subcommittee on Oversight and Investigations

Flu Season: U.S. Public Health Preparedness and Response

Statement of

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Introduction

Chairwoman DeGette, Ranking Member Guthrie, and distinguished Members of the Subcommittee, thank you for the opportunity to testify on our efforts to develop appropriate and effective medical countermeasures to mitigate a future pandemic influenza event. I am Dr. Bob Kadlec, the Assistant Secretary for Preparedness and Response (ASPR) at the Department of Health and Human Services (HHS).

Today, I will provide background about how ASPR is partnering with the private sector to develop influenza vaccines, antivirals, and diagnostics to ensure we are as prepared for both seasonal as well as pandemic influenza. I will also provide an overview of the current challenges we face in preparedness due to dependence on active pharmaceutical ingredients (API) and other raw materials manufactured in other countries.

Pandemic Influenza: a Costly National Security Threat

Influenza has long posed a serious threat to human health. Seasonal influenza epidemics occur every year, leading to hundreds of thousands of hospitalizations and tens of thousands of deaths,1 and billions of dollars in economic loss. In the simplest of terms, the difference between seasonal influenza and a flu pandemic is that a pandemic occurs when a new flu virus emerges that humans have little or no immunity against, allowing the virus to spread easily from person to person worldwide. A pandemic influenza event could occur at any time, potentially claiming hundreds of thousands of lives. Containing a pandemic will require an end-to-end solution: better diagnostics to detect the new virus, improved therapeutics, especially for hospitalized patients, and, perhaps most importantly, better vaccines, produced faster, and made in the United States. As noted in the White House Council of Economic Advisors' report, *Mitigating the Impact*

[1] https://www.cdc.gov/flu/about/burden/index.html

of Pandemic Influenza through Vaccine Innovation, "in a pandemic year, depending on the transmission efficiency and virulence of the particular pandemic virus, the economic damage would range from $413 billion to $3.79 trillion. Fatalities in the most serious scenario would exceed half a million people in the United States. Millions more would be sick, with between approximately 670,000 to 4.3 million requiring hospitalization."[2]

In the last decade, we have been reminded of how complex the management of seasonal and pandemic influenza is. We all remember:

- The H1N1 pandemic of 2009-2010, with severe and fatal cases among children, pregnant women, and other vulnerable populations;
- The emergence of avian influenza A(H7N9) in China in 2013, with high mortality rates in older adults, and the ensuing drifted H7N9 virus in 2017 that caused the largest recorded avian influenza outbreak and required development of a new pre-pandemic vaccine; and
- The severe H3N2 seasonal influenza virus that caused over 61,000 deaths in the United States and hospitalized hundreds of thousands more during the 2017-2018 influenza season.

ASPR's Role in Pandemic Preparedness

ASPR's mission is to save lives and protect Americans from 21st century health security threats. In addition to carrying out preparedness, response, and recovery activities within the National Response Framework (NRF) (Emergency Support Function (ESF) # 8, Public Health and Medical Services), as well as the National Disaster Recovery Framework (Health and Social Services Recovery Support Function), ASPR

[2] The Council of Economic Advisers. (2019), Mitigating the Impact of Pandemic Influenza through Vaccine Innovation, October 30, 2019, pp. 1 https://www.whitehouse.gov/wp-content/uploads/2019/09/Mitigating-the-Impact-of-Pandemic-Influenza-through-Vaccine-Innovation.pdf

also oversees advanced research, development, manufacturing capacity improvements, and procurement of medical countermeasures (MCM) against pandemics and other public health threats (e.g., vaccines, medicines, diagnostics, and other necessary medical supplies), and coordinates the manufacturing, supply chain, and stockpiling of such countermeasures. Through the Biomedical Advanced Research and Development Authority (BARDA), ASPR has supported a number of investments over the last decade to move the preparedness needle forward for protection and response to an influenza pandemic. Utilizing the supplemental funds Congress appropriated in 2005-2006 and 2009, ASPR has supported the development and production of 23 new or improved influenza vaccines, antiviral drugs, and diagnostics. Several of these products, such as cell and recombinant-based vaccines, new diagnostics, and therapeutics, are used every year to prevent, diagnose and treat seasonal influenza (or commonly known as "flu"). Other products have been licensed, and in some cases stockpiled, as pre-pandemic vaccines, ready to be rapidly formulated and distributed in the event of a pandemic.

I want to take a moment to thank all the members and their staff who worked to pass the Pandemic and All-Hazards Preparedness and Advancing Innovation Act of 2019 (PAHPAIA). The new law strengthens public health and healthcare readiness, bolsters response and recovery programs, and increases transparency. In particular, there is now a formal authorization for annual funding for programs to develop medical countermeasures for pandemic influenza and other emerging infectious diseases. In the past, this funding came partly from annual appropriations in the absence of a formal authorization, and largely from supplemental appropriations after public health emergencies occurred, such as the H5N1 outbreaks in many countries in 2005, the H1N1 pandemic in 2009, the Ebola responses in 2014-2015, and the Zika response in 2016. Having an authorization of appropriations shows Congressional support for this initiative and gives private partners more confidence to research and develop products and enhance their manufacturing capacities before a disease spreads within the U.S. When an outbreak occurs, every minute counts. Developing, testing, and obtaining approval for medical countermeasures as quickly as possible, equates to saving lives; to make medical countermeasures available rapidly, we must complete these steps, to the

maximum extent possible, before the emergence of an infectious disease.

ASPR's Accomplishments to Date

President Trump signed the Executive Order on Modernizing Influenza Vaccines in the United States to Promote National Security and Public Health on September 19, 2019. This the Executive Order (EO) directs ASPR, and three specific agencies within HHS – the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), and the Food and Drug Administration (FDA) – to accelerate the adoption of improved influenza vaccine technologies. Specific to ASPR, the EO directs HHS to: estimate the cost of expanding and diversifying domestic vaccine-manufacturing capacity using innovative, faster, and more scalable technologies; estimate the cost of expanding domestic productions capacity of adjuvants; estimate the cost of expanding domestic fill-and-finish capacity; estimate the cost of developing, evaluating, and implementing delivery systems; evaluate incentives for the deployment and production of vaccines by private manufacturers and public-private partnerships; support, in coordination with the Departments of Defense, and Veterans Affairs, as well as with NIH a suite of clinical studies featuring different adjuvants; and, in coordination with other relevant public health agencies, research agenda to dramatically improve the effectiveness, efficiency, and reliability of influenza vaccine production. Utilizing the supplemental appropriations in 2005-2006 and 2009, ASPR has supported many efforts to build capacity and enhance overall preparedness for pandemic influenza. With the EO in place, ASPR will push forward to continue to move preparedness forward and meet the intent of the requirements included in the EO.

The traditional technology for manufacturing influenza vaccines has been egg-based. Although this method has been optimized for efficiency, it has not fundamentally changed since the 1940s – almost 80 years ago – and requires strain selection many months in advance as well as millions of eggs, which may be a

vulnerability in a pandemic. In an effort to improve the robustness and responsiveness of our vaccine manufacturing technology, ASPR began supporting the development of six different cell-based manufacturing technologies in 2006 and three different recombinant manufacturing technologies in 2009. As a result of these investments, a cell-based influenza vaccine was developed and licensed by the FDA in 2012 that can be administered to individuals four years and older. In addition, in 2013, the FDA licensed the first recombinant influenza vaccine that can be given to people 18 years of age and older.

ASPR also supported several companies in developing influenza vaccine adjuvant to enhance the effectiveness of vaccine and to reduce the overall amount of antigen needed in a dose. Adjuvant enhances the immune response, inversely limiting the amount of vaccine needed; reducing the vaccine antigen stretches supply and ultimately allows more people to be protected. The first pre-pandemic vaccine adjuvant was developed and approved by FDA in 2013. Through ASPR's efforts, the domestic capacity for both seasonal and pandemic vaccine production rose from approximately 60 million doses to over 600 million doses. Advances like this save lives and reduce costs while bolstering our domestic manufacturing capacity.

Supporting the treatment of persons infected with pandemic influenza, ASPR is working to advance development of antiviral drugs with novel mechanisms of action to reduce viral resistance, expand treatment windows, and allow for co-administration with other influenza antivirals. ASPR has funded six novel antiviral advanced development projects since 2007. One of the earliest projects supported development of intravenous (IV) peramivir, which received Emergency Use Authorization during the 2009 H1N1 pandemic. This product recently received FDA approval in 2014 as a single-dose influenza antiviral drug for treatment of uncomplicated influenza. In 2015, BARDA awarded contracts to support two new novel influenza therapeutics that have novel mechanisms of action compared to existing approved antivirals. Novel antiviral drugs, especially when used in conjunction with early identification through diagnostics, can strengthen preparedness and response levels by enabling medical and health care

professionals to effectively treat influenza disease in patients, reducing morbidity and mortality and potentially limiting the spread of disease in communities.

Lastly, to better detect the emergence of influenza, ASPR is supporting the development of in-home and wearable diagnostics to inform and empower patients to take responsible actions towards earlier treatment and non-pharmaceutical approaches to reduce the severity of illness and spread of disease. These wearable diagnostic devices will leverage advanced data analytics and algorithms coupled with innovative detection modalities to accurately and quickly diagnose patients who have been exposed to pathogens and prognosticate outcomes. The de-identified data from these individual signals will create real-time information for public health officials about outbreaks in communities. ASPR's Division of Research, Innovation, and Ventures (DRIVe) has made three awards towards this effort to date. Rapid diagnostics are a cornerstone of our strategy to protect Americans from many bacterial and viral infections; earlier diagnosis can empower patients to take action to reduce disease transmission.

While medical countermeasures will aid in the response and potentially limit the spread of an infectious disease, it is important that the health care system be as prepared as possible to treat an influx of patients. ASPR's Hospital Preparedness Program (HPP) is critical to State, local, tribal, territorial, and regional health care preparedness and response efforts. As the only source of Federal funding to prepare the nation's mostly private health care system to respond to emergencies, ASPR supports health care system readiness. With HPP grant funding, ASPR encourages diverse organizations to work together through health care coalitions (HCCs) to make sure their communities are ready to respond during emergencies. Through these investments, communities are more prepared than ever for threats to public health. Since 2002, investments administered through HPP have improved individual health care entities' preparedness and have built a system for coordinated health care system readiness.

In 2018, ASPR began supporting Regional Disaster Health Response System (RDHRS) pilot projects. These pilot projects provide funding directly to hospitals and health systems to establish multi-state regional partnerships that increase preparedness and response capability and capacity for hospitals and health care facilities in advance of, during, or immediately following incidents, including emerging infectious diseases. Two sites were selected in September 2018 to pilot the RDHRS model. In addition, in 2019 two new grants were awarded to support pilots focused on regional pediatric care. The RDHRS and pediatric cooperative agreement requirements are intentionally aligned to ensure synergy between the programs and collaboration between all sites and facilities. The lessons learned from these pilots will help health care delivery systems prepare for and respond to disasters and emergencies and aide help limit the impact of disaster.

Gaps in Preparedness

To identify potential gaps in preparedness and, where possible, make improvements, ASPR manages a robust exercise and evaluation process. Related to pandemic influenza, August 13-16, 2019, ASPR led the Crimson Contagion 2019 Functional Exercise (Crimson Contagion). Crimson Contagion exercised a nationwide pandemic influenza response, testing current plans, policies, and procedures, as well as the nation's core capability to respond. This exercise was the largest pandemic exercise to date and included 12 Federal departments/agencies, 12 states, 96 local jurisdictions, 24 Native American Tribes, 87 hospitals, and more than 100 private sector partners. The exercise found that, in the event of a pandemic:

- If vaccine development and procurement for medical countermeasures is needed above current capacity, additional funding would likely be required.
- The U.S. lacks sufficient domestic manufacturing capacity and/or raw materials for almost all pandemic influenza medical countermeasures, including vaccines and therapeutics, the needles and syringes needed to administer them, and personal protective equipment, including masks, needles, and syringes. Further, in a pandemic, global manufacturing capacity will likely not be sufficient to

meet demand, resulting in an inability to import adequate quantities of medial countermeasures.

To that point, supply chain issues are among the most significant challenges to preparing for an influenza pandemic as well as other infectious diseases. Today, we are dependent on receipt of active ingredients in America's pharmaceutical and over the counter drugs come from China and India; this dependency also extends beyond pharmaceuticals and includes auxiliary medical supplies such as syringes and gloves[3]. This dramatic shift in the manufacture of medicines is very recent in origin. In the 1990s the U.S., Europe, and Japan manufactured ninety percent of the global supply of the key ingredients for the world's medicines and vitamins. Now, China is the largest global supplier. In a pandemic environment, this dependence could become a matter of national security, as we witnessed during the H1N1 pandemic of 2009. Countries with influenza vaccine manufacturing facilities restricted exports to satisfy their domestic requirements first.

ASPR's DRIVe program and the TechWatch effort allow ASPR to partner with industry to develop innovative technologies that can help mitigate some of these concerns. The accelerator network under DRIVe improves BARDA's outreach to non-traditional partners, attracting entrepreneurs, innovators, and researchers and providing insight into working with DRIVe. The network actively identifies promising candidate technologies and introduces them to DRIVe solicitations for potential funding consideration. One current DRIVe initiative is examining the possibility of shifting vaccine delivery from needles and syringes to wearable patches. ASPR will continue to examine other alternatives in medical countermeasure development, manufacturing, distribution, and administration to continue to reduce our reliance on foreign partners.

Conclusion

[3] Gibson, Rosemary and Singh, Janardan Prasad. (2018), China Rx: Exposing the Risks of America's Dependence on China for Medicine

This committee and Congress at large have been very supportive of ASPR and our mission. Again, thank you for reauthorizing the PAHPAIA and for all the hard work that went into realizing the vision of this legislation. We could not do our job without your partnership and support.

An influenza pandemic poses a significant threat to global public health and to the security of the United States. Together with our Federal, Congressional, and our industry partners, ASPR has made major progress towards pandemic influenza preparedness. Our nation must continue to invest in domestically-based pandemic preparedness efforts and work with key global partners to prepare for, prevent, detect, and respond to emerging pandemic threats.

Thank you for your time. I look forward to discussing how we can continue to work together on this important issue.