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

Examining U.S. Public Health Preparedness for and Response Efforts to Seasonal Influenza

Statement of

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Introduction

Chairman Harper, Ranking Member DeGette, and distinguished members of the committee, thank you for the opportunity to testify on behalf of the Assistant Secretary for Preparedness and Response (ASPR) to discuss the current influenza season and efforts to develop appropriate and effective medical countermeasures. I am Dr. Rick Bright, Director of the Biomedical Advanced Research and Development Authority (BARDA) and Deputy Assistant Secretary for Preparedness and Response within ASPR.

Today, I will provide background on the unique role of ASPR and BARDA in influenza preparedness, describe the progress made in preparing for an influenza pandemic, discuss the steps we can take now to support better and faster vaccine technologies, and highlight advancements in other medical products needed to mount an effective influenza response.

The Influenza Threat – Seasonal and Pandemic

Influenza has long posed a serious threat to human health. Seasonal influenza occurs every year, leading to hospitalizations and deaths. Because influenza viruses mutate as they traffic and reassort among birds, swine, and humans, achieving protection against seasonal influenza viruses is a significant challenge. In addition, because of the quickly changing nature of the virus and the potential for a pandemic, we have to act swiftly to develop effective medical countermeasures and make products available to limit spread. In the last decade, we have been reminded how complex the management of seasonal and pandemic influenza is. Challenges include supporting preparedness efforts across our healthcare system, developing and

manufacturing effective vaccines quickly, and mitigating the impact of the virus through development of diagnostics and antivirals. As a reminder, recent novel influenza outbreaks of significance include:

- The H1N1 pandemic of 2009-2010;
- The emergence of seasonal H3N2 virus variants in 2012 in the Midwest primarily affecting children; and,
- The emergence of H7N9 avian influenza viruses in China in 2013 that were highly virulent for humans, causing repeated outbreaks including the largest outbreak in 2017 of a new variant of the H7N9 virus that required development of a new vaccine.

It is important to note that our approaches to seasonal and pandemic influenza are inextricably interwoven; what we do in one area directly impacts the other. This holds true for preparedness efforts as well as medical countermeasure development and manufacturing capabilities. For example, expanding the domestic manufacturing capacity for pandemic response enabled manufacturers to have the capacity to include an additional strain in the seasonal vaccine—moving from three strain (trivalent) to four strain (quadrivalent) seasonal vaccines for better coverage. This increased production capacity and also supported the U.S. policy to expand influenza vaccination recommendations to include all age groups, ensuring sufficient supply of vaccine would be available to everyone who needs it.

What is ASPR?

ASPR has a central role in influenza preparedness. When ASPR was originally established by Congress a decade ago, the objective was to create "unity of command" by consolidating all federal public health and medical preparedness and response functions under the HHS Secretary, and by establishing the ASPR as the Secretary's principal advisor on these matters. This approach was modeled on the Goldwater-Nichols Act that created the Department of Defense (DoD) combatant commands; the impetus was the fragmented response to Hurricane Katrina in 2005 and concerns about an H5N1 influenza pandemic.

ASPR's mission is to save lives and protect Americans from 21st century health security threats. ASPR is, in effect, the national security mission manager for HHS. As such, on behalf of the Secretary of HHS, ASPR leads the federal public health and medical, preparedness, response and recovery to disasters and public health emergencies, in accordance with the National Response Framework (NRF) and Emergency Support Function (ESF) No. 8, Public Health and Medical Support. It is ASPR's responsibility to coordinate the nation's medical and public health capabilities to help Americans during such events, whatever their cause. ASPR also coordinates with other components of HHS with respect to HHS's role in ESF No. 6, Health and Social Services, and HHS's lead role as the coordinating agency with respect to the Health and Social Services Recovery Support Function.

ASPR, in partnership with other HHS agencies, works to enhance medical surge capacity when needed during disasters by organizing, training, equipping, and deploying federal public health and medical personnel and providing logistical support for federal responses to public health emergencies. ASPR also supports readiness and preparedness efforts at the state and local level

by coordinating grants to support capabilities across the nation's healthcare infrastructure and carrying out drills and operational exercises. ASPR oversees advanced research, development, and procurement of medical countermeasures (e.g., vaccines, medicines, diagnostics, and other necessary medical supplies) against biomedical, chemical, radiological and nuclear agents and pandemic or epidemic diseases and coordinates the stockpiling of such countermeasures.

What is BARDA?

BARDA is a component of ASPR. Congress established BARDA to bridge the so-called "valley of death" in late-stage development of medical countermeasures where many products historically languished or failed due to a limited commercial market incentive. Generally, the development of an effective medical countermeasure can take over 10 years and cost over $1 billion. By using flexible, nimble authorities, multi-year advanced funding, strong public-private partnerships, and cutting edge expertise, BARDA has successfully pushed innovative medical countermeasures, such as vaccines, drugs, and diagnostics, through advanced development to stockpiling and Food and Drug Administration (FDA) approval or licensing.

In the last decade, BARDA's strong partnerships with 190 biotechnology and pharmaceutical companies, U.S. government partners, and academic institutions have led to 34 medical countermeasures approved or licensed by the FDA. BARDA has supported the development of 27 medical countermeasures against Department of Homeland Security (DHS)-identified national security threats through Project BioShield, including products for smallpox, anthrax, botulinum, radiologic/nuclear emergencies, and chemical events. Fourteen of these products

have been placed in the Strategic National Stockpile and are ready to be used in an emergency. BARDA has also supported the development and production of 23 influenza vaccines, antiviral drugs, and diagnostics; some of these were used in the 2009 H1N1 pandemic, stockpiled to enhance preparedness for H5N1and H7N9 influenza outbreaks or pandemics, and some were licensed for seasonal influenza and are entering the marketplace.

BARDA focuses on advanced development, which includes critical steps needed to transform a promising candidate into a product that is ready to use safely when a crisis hits. These steps include: optimizing and validating commercial scale manufacturing processes; optimizing product formulations, storage, product longevity and effectiveness; creating, optimizing, and validating assays to assure product integrity; and, conducting late-stage clinical safety and efficacy studies.

Better and Faster Influenza Vaccines Right Now

BARDA has always been driven by the strategy to make more, safer, faster, and better influenza vaccines. With benefits to both pandemic and seasonal influenza preparedness and response, BARDA has prioritized partnering with industry partners to build domestic vaccine manufacturing infrastructure, and develop and license better and faster manufactured influenza vaccines. With supplemental funding from Congress over the last decade, BARDA has invested heavily in increasing the domestic capacity for monovalent vaccine antigen production—from approximately 60 million doses to 600 million doses.

BARDA also established the first and largest pre-pandemic influenza vaccine stockpile in the world, one that could, if necessary, vaccinate tens of millions in the event of H5N1 and has advanced the science of antigens and adjuvants through unique programs. The stockpile and rapid response capability is a true national asset that not only provides vaccine to America's first responders and critical workforce, but also provides each vaccine manufacturer that holds a US license with valuable lead time to develop vaccines against influenza viruses that pose the greatest risk to becoming a pandemic virus. This asset also allows for BARDA, industry and HHS partners to develop reagents and conduct clinical studies to understand the science about each of these vaccines. This lead time and advance work saves a tremendous amount of time during the start of a pandemic, therefore leading to the more rapid availability of vaccine and ultimately to saving lives. While this represents a significant accomplishment, and a success of the BARDA public-private partnership model, there is more to be done to ensure that the most effective vaccines are available when and where we need them.

Since the 2009 influenza pandemic, BARDA has made significant progress in partnering with cutting edge companies to develop novel manufacturing technologies that offer the potential to provide more effective influenza vaccines.

The traditional technology for manufacturing influenza vaccines is egg-based. Although this method has been optimized for efficiency, it has not fundamentally changed since the 1940's, and it is still the predominant method of vaccine production for the commercial market today. Recognizing the need to improve the robustness and responsiveness of our vaccine manufacturing technology, BARDA first 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 (Flucelvax®) was developed. Flucevlax was licensed by the FDA in 2012, and is now produced by Seqirus in Holly Springs, NC and can now be administered to individuals four years and older. In 2013, the FDA licensed the first recombinant influenza vaccine (Flublok®) that can be given to people over 18 years of age. This vaccine was developed by Protein Sciences Corporation which was recently acquired by Sanofi Pasteur. BARDA also supported several companies to develop influenze vaccine adjuvanted to enhance the effectiveness of the seasonal vaccine and to reduce the overall amount of vaccine antigen needed in a dose as a way of stretching a limited supply to protect more people faster during a pandemic. The first pre-pandemic vaccine adjuvanted was developed by GSK, which was soon followed by achieving licensure of a season influenza vaccine adjuvant for adults over age 65.

These cell-based and recombinant technologies offer the potential to provide more effective vaccines than those produced in eggs, more quickly, and with flexibility to rapidly shift to keep pace with changes in the virus. However, due to marketplace competition, such as a current inability to differentiate cell-based and recombinant technologies in the market, and limited domestic production capacity, during the 2017/2018 influenza season these vaccine technologies represent only 18 percent and 3 percent, respectively, of the total vaccine available. Investments in next-generation manufacturing processes to maximize the scale, efficiency and speed of cell-based and recombinant technologies, as well as investments in clinical studies needed to expand age indications and validate potential benefits of these vaccines, including the potential to have more effective vaccines that are not vulnerable to adapting human vaccine viruses to grow

efficiently in chicken eggs will help improve preparedness and response for both seasonal and pandemic influenza. In addition, utilizing these flexible manufacturing technologies domestically also improves our capability to rapidly produce other critical medical countermeasures for other threats.

There are significant strides that can be made to improve the effectiveness of our existing vaccines in preparation for the long-term vision of an ultimate universal influenza vaccine. Leveraging the successful development and licensure of both recombinant and cell-based influenza vaccines, we should:

1) Continue to expand the domestic capacity of cell-based and recombinant influenza vaccines;
2) Explore ways to enhance their effectiveness, such as through the addition of adjuvants and higher doses of vaccine;
3) Conduct clinical trials in support of applications to expand their licensed indications for all age groups; and,
4) Fully integrate manufacturing process improvements to realize efficiencies to increase flexibility and robustness while reducing response time and establishing a 21st century foundation for next generation vaccines.

Moreover, to improve influenza vaccines now, we must modernize and harmonize the end-to-end process of vaccine production, to completely incorporate new technologies to decrease the time needed to produce vaccines that are ready for administration, and increase efficiency and flexibility. We must also work closely with our partners in industry and at the FDA to continue

to explore modern methods of continuous manufacturing of vaccine that will provide added flexibility and response capabilities matched to the rapid changes we know so well with influenza. BARDA will continue to invest in sustaining the overall domestic influenza vaccine manufacturing capacity to ensure vaccines can be produced and accessed quickly when needed to protect health in a pandemic. Emergency supplemental funding supported the work to increase this domestic resource, in recognition of the urgent need to have U.S.-based response capabilities, and we must sustain these hard-won gains.

Advancing Other Medical Products Needed for Effective Influenza Response

While vaccination is the best way to prevent influenza infection, every year, and especially in the event of a pandemic, a large number of individuals will nevertheless become ill and will need urgent treatment. There is an ample supply of antiviral drugs, including pediatric formulations, for this influenza season. However, continued development of novel antivirals is essential to provide additional treatment options if drug resistance emerges to our only class of currently FDA-approved and CDC-recommended influenza drugs. BARDA is committed to the development of novel treatments for people infected with influenza. Last year, BARDA utilized Other Transactional Authority to forge flexible, portfolio-based public-partnerships with Janssen, and Regeneron to address this critical need.

Early information on influenza infection is critical for proper treatment, and can help reduce the spread of disease. The time needed to effectively access, administer, and receive results from current diagnostic tests often exceeds the window of opportunity for optimal treatment; current influenza drugs are most effective when taken within the first 48 hours of symptom onset.

Therefore, BARDA is partnering with companies and researchers to develop new influenza diagnostics. Our goal is to develop 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 their illness, reduce the spread of disease, reduce overall health care costs and to save lives. An in-home or wearable diagnostic would have a positive impact by providing early, actionable information to the patient.

Conclusion

Influenza and other emerging infectious diseases with pandemic potential continue to mutate, evolve, and infect animals and humans, posing continued significant threats to global public health and to the security of the United States. Together with our Federal and industry partners, ASPR and BARDA have made huge progress towards pandemic influenza preparedness. Our Nation must continue to invest in domestic pandemic preparedness efforts and work with key global partners to prepare for, prevent, detect, and respond to emerging pandemic threats. Building on a decade's worth of progress, partnered with industry, the time is right to make better seasonal and pandemic influenza vaccines, antivirals, and diagnostics widely available. BARDA has a unique responsibility in supporting advanced research, development, and procurement of pandemic influenza medical countermeasures. While the promise and advantages of universal influenza vaccines is an elusive but highly worthy goal, led by our colleagues at NIH, the near term threat of influenza demands that we work right now to make influenza vaccines better and faster, and we ensure that diagnostic tools and antiviral treatments are also available to save lives. Now is the time to act. Thank you for your time, and I look forward to your questions.