

House Energy and Commerce Committee

Subcommittee on Oversight and Investigations

“The State of U.S. Public Health Biopreparedness: Responding to Biological Attacks, Pandemics, and Emerging Infectious Disease Outbreaks”

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Friday, June 15, 2018

The Honorable Gregg Harper

- 1) In the 2017 update to HHS’ Pandemic Influenza Plan, HHS provided benchmarks for manufacturing and distributing vaccines during declared influenza pandemics. HHS stated that it aims to ensure that limited vaccine distribution occurs within 12 weeks of a pandemic being declared, with distribution sufficient to meet overall public demand occurring within 16 weeks. Could you tell us why this process seemingly takes so long, and provide any recommendations for improving it? If the 12 and 16-week benchmarks are HHS’s goals, what are our current capabilities?**

ASPR Response: Domestic manufacturing capacity for pandemic influenza vaccine is a critical component of pandemic preparedness to ensure vaccine is available as soon as possible after emergence of a pandemic virus. ASPR/BARDA has made significant gains in pandemic influenza vaccine preparedness over the last 10 years, including supporting the licensure of faster, more flexible cell-based, recombinant and adjuvanted influenza vaccines and modernizing and expanding domestic manufacturing capabilities. These advancements have dramatically increased the domestic influenza vaccine antigen capacity – increasing from 60 million doses to 600 million doses.

Building on these successes, and to ensure vaccine is available within 12 weeks of pandemic declaration, ASPR/BARDA has a multifaceted approach in place. First ASPR/BARDA is partnering with companies to support the development of novel technologies that rely less on viral growth properties to improve the speed and robustness of vaccine production. For example, ASPR/BARDA supported the first licensed recombinant influenza vaccine (Flublok®), and ASPR/BARDA continues to fund recombinant vaccine-related efforts, moving away from the slow, inflexible production of vaccine in eggs. Second, ASPR/BARDA is supporting the sustainment of domestic production capabilities to ensure vaccines are available when necessary. Third, ASPR/BARDA is supporting further development of recombinant and cell-based vaccines through comparative efficacy clinical studies to expand use indications for a broad range of high-risk and special populations. Fourth, ASPR/BARDA is supporting the addition of currently approved adjuvanted influenza vaccines for all ages into both seasonal and pandemic vaccines, while also developing additional adjuvant options that provide safe and enhanced effectiveness to influenza vaccines that are faster to produce. Lastly, ASPR/BARDA is targeting advancements in vaccine delivery and administration to develop new approaches that would

reduce reliance on needles and syringes supply chain surge capacity and allow faster and more efficient immunization with pandemic vaccine.

2) In general, what is the shelf-life for the H7N9 influenza strain vaccine that is in BARDA's pre-pandemic stockpile that will protect against the 2013 H7N9 strain? When was the last time BARDA performed a potency test on these vaccines?

ASPR Response: The pre-pandemic vaccine made in eggs against the 2013 H7N9 avian influenza virus strain is very stable, with over 80% stability as of the last potency test conducted November, 2017. The most recent potency testing for the egg based vaccine was performed in May 2018 and we are awaiting results of this testing.

3) How serious of a pandemic threat does the BARDA view the 5th wave H7N9 influenza strain, currently circulating in China? If a pandemic were to occur, how severely would it impact public health? Is BARDA currently overseeing the manufacturing of a vaccine for storage in its pre-pandemic stockpile which will match this H7N9 influenza strain?

ASPR Response: BARDA views the 5th wave H7N9 influenza outbreak as a serious concern, as reflected by the high Influenza Risk Assessment Tool (IRAT) score assigned by CDC. Since this assessment system, which assesses the threat of influenza viruses with pandemic potential, was initiated in 2011, the 5th wave H7N9 strain has the highest Potential Impact Risk of any influenza strain evaluated.

Given the human mortality rate seen to date, if the viruses changed to allow them to spread easily between humans, the impact on public health could be catastrophic in the absence of effective medical countermeasures such as vaccines. There is also evidence that some H7N9 influenza viruses may be resistant to most available antiviral drugs.

In response, BARDA produced bulk vaccine, currently held in storage, which matches the 5th wave H7N9 strain. Additionally, the National Institutes of Health (NIH) and BARDA are conducting clinical trials to better understand optimal vaccination approaches in the event mass vaccinations are necessary.

4) How much is BARDA currently spending on CARB-X? Does the agency anticipate maintaining this level of spending over the next five years?

ASPR Response: BARDA established CARB-X in collaboration with the NIH's National Institute of Allergy and Infectious Diseases in 2016. CARB-X, an innovative public-private partnership that addresses the threat of antibiotic resistant bacteria, has received \$85 million in support from BARDA over two years. CARB-X is also funded by the Wellcome Trust. In 2018 the Bill & Melinda Gates Foundation and the United Kingdom Government's Department of Health and Social Care joined as funding partners. BARDA's support for new antibiotics and diagnostics is critical to address 21st century health security threats including genetically engineered bacterial pathogens, complications of bacterial infections as a result of exposure to priority threats such as nuclear and chemical agents, and to quickly identify bacterial pathogens and their susceptibility to antibiotics. BARDA anticipates continued support based on availability of funds.

5) What is the PHEMCE's role in making a material threat determination, and how can the length of time it takes for such a determination be reduced?

ASPR Response: The Public Health and Emergency Medical Countermeasure Enterprise (PHEMCE), a Federal advisory and coordinating body led by ASPR, does have a role in advising on medical countermeasure requirements for national security material threats identified by the Department of Homeland Security (DHS). DHS's newly established Countering Weapons of Mass Destruction Office issues material threat assessments (MTAs) and the Secretary of the Department of Homeland Security (DHS) issues material threat determinations (MTDs). MTAs and MTDs are done in collaboration with other interagency departments, but the responsibility for generating these national, strategic overviews and quantification of the threat is identified by statute (section 319F-2(c)(2) of the Public Health Service Act (42 U.S.C. 247d-6b(c)(2)), added by the Project BioShield Act of 2004") as a DHS authority and responsibility. The PHEMCE benefits from these determinations and uses them to forecast medical countermeasure requirements (type, quantity, special considerations). ASPR is currently working with other PHEMCE interagency partners to evaluate and identify opportunities to streamline and speed up these deliberative steps. We would be pleased to brief the Committee on potential process improvements after the evaluation is completed.

6) After ASPR assumes operational control of the Strategic National Stockpile on October 1, 2018, what role will CDC play in support of the stockpile's mission?

ASPR Response: ASPR recognizes and appreciates the tremendous expertise of CDC subject matter experts including on infectious diseases, other public health threats, epidemiological and laboratory surveillance, as well as understanding of the capabilities of state and local public health departments. CDC is an active partner on the PHEMCE, which is led by ASPR and provides a venue for sharing information across HHS agencies and with interagency partners with a role in medical countermeasures requirement setting, research, development, regulatory review, procurement, stockpiling, distribution and use. CDC will remain an active participant in all PHEMCE workgroups and committees.

In order to ensure a smooth transition of the Strategic National Stockpile with no degradation of operational capability, ASPR and CDC have set up several joint transition workgroups to evaluate all aspects of the program transition. Some of the details involved in the transition have not been finalized. However, we would be pleased to provide a full briefing for Committee staff at any time before the end of the fiscal year. Subsequent to this hearing, the SNS successfully transferred from CDC to ASPR on October 1, 2018.

CDC will maintain its strong working relationships with state and local public health agencies, playing a key role in distribution and dispensing of medical countermeasures. CDC will accomplish this by continuing to provide technical guidance and funding through cooperative agreements and embedding experts in state and local health departments. Coordination with state and local agencies will be enhanced by incorporating ASPR's extensive relationships with health care organizations and emergency management agencies.

Further, to continue to increase collaboration across the Department, ASPR has invited and instituted a new senior CDC liaison who is working within the ASPR Immediate Office.

7) How prepared are the nation's hospitals to respond to biological threats or infectious diseases? What are the most pressing challenges facing non-governmental health systems and what could we do to improve their response capabilities?

ASPR Response: Since the Hospital Preparedness Program (HPP) was established, investments have been made to enhance the overall preparedness of the nation's healthcare infrastructure. Initially, HPP supported the procurement of materials and supplies (e.g., generators, masks, etc.) that would be used should a community be impacted by a public health or medical event. In 2012, HPP shifted its focus from purchasing supplies to investing in health care coalitions (HCCs). HCCs are groups of health care and response organizations that collaborate to prepare for and respond to medical surge events. HCCs incentivize diverse and often competitive health care organizations to work together. During recent events, ranging from mass shootings (e.g., Las Vegas, Florida night club), hurricanes (e.g., Matthew, Harvey, Irma, and Maria), and the most recent tornados in Iowa, we have witnessed the value of the HCCs in enabling communities to quickly assess healthcare capabilities to continue to support communities without requesting assistance from the federal government.

Prior to the 2014 Ebola outbreak in West Africa, the United States did not have an organized, systematic approach to preparing for, and responding to, an outbreak of a highly infectious pathogen. CDC in collaboration with ASPR developed a tiered approach to prepare U.S. health care facilities to safely and rapidly identify, isolate, evaluate, and manage, travelers or patients who have possible or confirmed Ebola. This included providing rapid technical assistance to hospitals strategically located near airports with a large number of travelers returning from Ebola-affected countries and in communities where large numbers of persons from these West African countries reside. To support this, HPP provided awardees with approximately \$214 million of Ebola emergency supplemental funding to establish a nationwide, regional treatment network for Ebola and other infectious diseases. The funding provided through HPP Ebola Preparedness and Response activities is intended to establish the foundation required for the nation's health care system to safely and successfully identify, isolate, assess, transport, and treat patients with Ebola virus disease or under investigation for Ebola (or other highly infectious diseases). Through this mechanism, ASPR awarded cooperative agreements to all 50 states, Washington D.C., all U.S. territories and freely associated states, and select metropolitan jurisdictions, over a five-year project period. Additionally, ASPR competitively awarded funding to 10 regional Ebola and other special pathogen treatment centers (i.e., one in each of the 10 HHS regions).

Additionally, to prepare for, and provide safe and successful care of patients with Ebola, HHS (in a collaboration between ASPR and CDC) awarded funding to establish a National Ebola Training and Education Center (NETEC). The NETEC provides expertise, training, technical assistance, peer review, monitoring, and recognition to state health departments, regional Ebola and other special pathogen treatment centers, state- and jurisdiction-based Ebola treatment centers, and assessment hospitals. NETEC is a consortium of three U.S. health facilities that safely and successfully treated a confirmed Ebola patient – Emory University in Atlanta, Georgia; University of Nebraska Medical Center/Nebraska Medicine (UNMC) in Omaha,

Nebraska; and the New York City Health and Hospitals Corporation/HHC Bellevue Hospital Center in New York, New York.

Going forward and leveraging the best practices from investments made with the Ebola supplemental appropriations, ASPR is developing innovative tiered regional demonstration projects that can serve as a model for building a regional disaster health response system across the country. Subsequent to this hearing, ASPR awarded two grants – Nebraska Medicine in Omaha, Nebraska and Massachusetts General Hospital in Boston, Massachusetts – to conduct pilot projects that show the potential effectiveness and viability of a Regional Disaster Health Response System (RDHDS).

The Honorable Michael C. Burgess

- 1) Dr. Bright, in 2010, BARDA established three centers to develop and manufacture medical countermeasures, such as vaccines and therapeutics, to protect our citizens during public health emergencies. Texas A&M’s Center for Innovation in Advanced Development and Manufacturing is one of these centers, and was intended to focus on surge capacity for flu vaccines. I understand that the initial contract period with the Texas facility expires at the end of this month. How does BARDA plan to utilize these centers in the future? Will BARDA maintain and grow existing partnerships that have the infrastructure to deploy capabilities in the wake of a crisis?**

ASPR Response: BARDA established the Centers for Innovation in Advanced Development and Manufacturing as public private partnerships in 2012. The program has made important investments in the domestic capacity for medical countermeasure production for public health emergencies. Each of the three centers in Texas, Maryland and North Carolina were funded to establish pandemic influenza vaccine manufacturing surge capacity, core service capabilities, and workforce development programs. Program successes include: process updates that resulted in a fourfold increase in yield for the domestically-produced cell based inactivated influenza vaccine; the development of commercially run facilities in Texas and Maryland; and a well-established workforce development program at Texas A&M in College Station, Texas. BARDA recently issued a six month extension to the base period for the Texas A&M center to facilitate additional partnering opportunities.

BARDA is currently evaluating how best to sustain and strengthen the domestic medical countermeasure manufacturing capabilities needed for the nation to be optimally prepared for 21st century health security threats.

- 2) How do you communicate with centers such as Texas A&M about what medical countermeasures they should develop? How involved is BARDA in helping these “centers” identify additional partners with whom they can work?**

ASPR Response: Each Center has a designated federal contracting officer representative and contracting officer. These officials monitor completion of contract requirements and subsequent

task orders that the centers have to meet per the terms of the contract. BARDA also holds frequent site visits and regular status calls with each of the Centers and has encouraged potential partner discussions through those interactions. Lastly, the Centers are required to maintain other commercial business/partnerships to make use of established capacity, to offset costs, and be a shared resource.

The Honorable Frank Pallone, Jr.

- 1) With respect to the three types of threats we often hear about – natural, intentional, and accidental—to what extent do preparedness efforts for the different types of threats overlap?**

ASPR Response: ASPR coordinates with states and local officials before, during, and after emergencies to test existing response capabilities. While each incident, whether naturally occurring, man-made, or accidental, has its own considerations, there are common requirements that spread across all emergencies. Common elements include supporting situational awareness and information sharing between and among all supporting officials, supporting and augmenting local healthcare entities in treating the impacted population, ensuring critical assets are available to communities in need, and supporting the recovery of the community.

Investing in technologies that have the potential to yield multiple diagnostics, vaccines or therapeutics against different pathogens ensures that capabilities are nimble and flexible to support vaccines and therapeutics for future threats. Examples of this type of investment are how BARDA is supporting development of vaccines against the Ebola Zaire virus. Currently, BARDA is supporting two candidates under Project BioShield. There is the potential that same vaccine platform used to develop the Ebola Zaire virus vaccines could be used to develop vaccines against Ebola Sudan or Marburg viruses, by replacing just one element (glycoproteins). In addition, the vaccine platform could be used to express proteins from newly identified pathogens and expedite development of a vaccine for clinical trials.

- 2) How can we plan long-term therapeutics and vaccines in order to respond to outbreaks that we cannot yet anticipate?**

ASPR Response: It often takes 10 or more years and over \$1 billion to develop a new drug or vaccine.

ASPR/BARDA utilizes many of the innovative authorities authorized by amendments made by the Pandemic and All-Hazards Preparedness Act to the Public Health Service Act to support development of medical countermeasures. Authorities like Other Transaction Authorities (OTA) mean ASPR/BARDA can enter into innovative agreements to support development and procurement. As an example, the first BARDA OTA was within the broad spectrum antimicrobial program. Currently three out of six BARDA OTAs are focused on development of antimicrobial products. BARDA has also utilized CARB-X – an innovative public-private partnership conducted under a cooperative agreement – to address the threat of antibiotic resistant bacteria. CARB-X involves seven partners in the U.S. and U.K. and is backed with half a billion dollars in funding. \$85 million in BARDA CARB-X investment resulted in nearly \$500

million in private equity follow on investment. The partnership has 28 different companies making novel antibacterial drugs, vaccines, and diagnostics, including eight new classes of antibiotics.

3) BARDA's CARB-X program is developing many nontraditional products at the preclinical stage. Can you briefly explain why you have supported these products, and what BARDA is doing to make sure that enough products move on to clinical trials?

ASPR Response: Under the National Action Plan for Combating Antibiotic Resistant Bacteria (CARB), published by the White House in 2015, ASPR was directed to establish a biopharmaceutical accelerator in collaboration with NIH. BARDA established CARB-X in collaboration with the NIH's National Institute of Allergy and Infectious Diseases (NIAID), in NIH, in 2016. This was two years ahead of the three year milestone to establish the partnership. CARB-X is an international consortium of funders including BARDA, NIAID, Wellcome Trust, the Bill & Melinda Gates Foundation, and the UK Government's Department of Health and Social Care.

BARDA does not support the product portfolio alone; instead it is a collaborative effort across multiple, international organizations. BARDA funds non-traditional products because antibiotics are a solution but not the only solution for antibiotic resistant bacteria. In addition, all of the candidate products supported under CARB-X can support new treatment options for genetically engineered biothreat pathogens or the secondary bacterial infections that will result from exposures to threat agents, such as ionizing radiation from a nuclear blast or burn injuries resulting from nuclear or chemical agents.

Five products under the CARB-X portfolio have advanced to phase I clinical trials with more expected in the coming years. Candidate products may move into clinical trials when clinical trial proposals and data to support investigational new drug status are submitted to the FDA and data review does not show prohibitive adverse risk-benefit concerns. BARDA, as a funder and as a member CARB-X, works closely with the cooperative agreement awardee's program team to make sure that products are meeting the scientific milestones to advance in development.

4) Can you explain what BARDA is doing to foster public-private partnerships, and why this is important?

ASPR Response: BARDA established and manages the Tech Watch Program (<https://www.phe.gov/about/barda/Pages/BARDA-techwatch-Mtgs.aspx>). Under Tech Watch, companies can come and discuss their technologies with BARDA to determine if the product is appropriate for BARDA to consider funding in the future. If the program does not align with BARDA priorities, we will refer them to other federal agencies that may be able to assist them with development. BARDA holds 150-200 Tech Watches per year.

BARDA also holds an annual BARDA Industry Day (BID), consistent with its authorities under the Public Health Service Act. This meeting brings together BARDA and other PHEMCE partners with industry, academic, and non-government organizations. It provides an opportunity for BARDA to highlight current and future strategic plans and priorities. BID also provides companies the opportunity to discuss their programs and how they might be able to address existing or future requirements.

Lastly, BARDA attends national and international conferences to discuss our portfolio of products, potential additional candidates, and our strategic plans. Numerous stakeholders attend these conferences allowing for another venue for BARDA to meet with potential partners.

BARDA cannot develop countermeasures alone. Public-private partnerships are critical to the continued success of BARDA and all of the ongoing medical countermeasure development initiatives.

5) ASPR has a number of programs in place, including the Hospital Preparedness Program and the Medical Reserve Corps, which are designed to help ensure readiness at the state and local level. How do these programs ensure that our front-line responders are able to respond effectively in a public health emergency situation?

ASPR Response: ASPR’s mission is to save lives and protect Americans from 21st century health security threats. On behalf of the Secretary of HHS, ASPR leads public health and medical preparedness for, response to, and recovery from disasters and public health emergencies.

All of ASPR’s programs and capabilities work together to create “unity of command” by consolidating Federal nonmilitary public health and medical preparedness and response functions. ASPR coordinates across HHS and the Federal interagency to support state, local, territorial, and tribal health partners. ASPR works to enhance medical surge capacity by organizing, training, equipping, and deploying HHS public health and medical personnel, such as National Disaster Medical System (NDMS) teams, and providing logistical support for HHS personnel responding to public health emergencies. ASPR supports readiness at the state and local level by coordinating federal grants and cooperative agreements, such as the Hospital Preparedness Program (HPP), by programs like the Medical Reserve Corps (MRC), and carrying out drills and operational exercises. For example, HPP prepares the nation’s health care system to save lives during emergencies and disasters. It is the only source of federal funding for health care system readiness. HPP prepares the health care system to save lives through the development of health care coalitions (HCCs). HCCs are groups of health care and response organizations that collaborate to prepare for and respond to medical surge events. HCCs incentivize diverse and often competitive health care organizations to work together, allowing them to plan together and respond jointly in emergencies.

Specific to how ASPR supports first responders, ASPR routinely partners with state and local governments, hospitals, and responders to conduct drills and exercises to test various aspects of medical response capabilities. Drills and exercises provide opportunities at all levels to examine

plans, procedures, and capabilities and to work with all government partners to employ resources in response to a specific event or scenario. One recent example is ASPR's Tranquil Terminus Exercise that brought together four regions, seven states, eight cities and three federal departments to test the nation's ability to transport patients with a highly infectious disease. Communities and responders benefitted by having the opportunity to test and rehearse plans with all partners participating. They learned from each other as well as identified best practices for inclusion in their plans and procedures.

6. CDC recently concluded an operational readiness review to assess whether state and local governments and public health services will be able to effectively get medical countermeasures to the appropriate person at the appropriate time. How does BARDA work with CDC and health departments to ensure that we develop countermeasures with this “last mile” of delivery in mind?

ASPR Response: Through its active role in PHEMCE, CDC shares information across HHS agencies, including ASPR/BARDA, who have a role in medical countermeasures requirement setting, research, development, regulatory review, procurement, stockpiling, distribution and use. Through this channel, as well as through established direct program-to-program collaborations with BARDA, CDC provides input on how countermeasure development can better meet end user needs. This includes criteria for how products developed may be stored and packaged to improve/simplify stockpiling and distribution, improved product delivery systems, simplified dosing considerations, etc. These factors assessed by CDC, impact how products are distributed, dispensed/administrated and used.