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"BARDA's Role in Medical and Public Health Preparedness and Response"

Statement of

Robin A. Robinson, Ph.D.

Deputy Assistant Secretary and BARDA Director
Office of the Assistant Secretary for Preparedness and Response
U.S. Department of Health and Human Services

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Good morning, Senator Burr, Ranking Member Casey, and distinguished Members of the Committee. Thank you for the opportunity to speak with you today about our Government's public health preparedness and response medical countermeasure efforts and challenges. I am Dr. Robin Robinson, Director of the Biomedical Advanced Research and Development Authority (BARDA) and Deputy Assistant Secretary for Preparedness and Response (ASPR). I am happy to testify today with the ASPR, Dr. Nicole Lurie, and my other HHS colleagues.

BARDA is the Federal Government agency, within the Office of the Assistant Secretary for Preparedness and Response (ASPR), created in 2006 by the Pandemic and All-Hazards Preparedness Act (PAHPA) and reauthorized by the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA) to support advanced research and development and procurement of novel and innovative medical countermeasures. These medical countermeasures—vaccines, therapeutics, antiviral and antimicrobial drugs, diagnostics, and medical devices—address the needs of the entire nation to mitigate the medical consequences of man-made chemical, biological, radiological, and nuclear (CBRN) agents of terrorism and naturally-occurring and emerging threats like the 2009 H1N1 pandemic, the 2013 H7N9 influenza outbreak, and the current Ebola epidemic.

Medical countermeasure development is risky, lengthy, and costly with many inexperienced developers failing and many larger pharmaceutical companies avoiding the sector completely. BARDA serves as a bridge over a critical gap in medical countermeasure development. BARDA transitions product candidates from early development into advanced development towards

potential Food and Drug Administration (FDA) approval and stockpile procurement through direct support, public-private partnerships, and technical core service assistance programs.

The Public Health Emergency Medical Countermeasure Enterprise (PHEMCE) establishes product specific requirements for CBRN medical countermeasures based on threat scenarios and Material Threat Assessments performed by the Department of Homeland Security (DHS). The National Institutes of Health (NIH) launch discovery and early stage development of product candidates from academic and industry partners for transition to BARDA. In turn, BARDA supports and assists these product candidates through advanced research and development towards FDA approval, until they are sufficiently mature to be acquired and potentially stockpiled under Project BioShield at the Centers for Disease Control and Prevention's (CDC) Strategic National Stockpile (SNS) or at commercial vendors. Upon FDA approval, the financial responsibility of purchasing medical countermeasures transfers from BARDA under Project BioShield to the CDC/SNS for the stockpile and delivery phases. Finally, in public health emergencies, like we saw in the H1N1 influenza pandemic and today during the Ebola epidemic, BARDA, under the emergency management authorities of ASPR, assumes a response posture, interfacing with other Federal agencies and manufacturers to develop, produce, and test products for FDA review and approval and distribution by CDC to state and local providers.

BARDA is the only Federal Agency that operates in the advanced development space of product development. Advanced development includes critical steps needed to transform a candidate to a product that is ready to use. These steps include: optimizing and validating manufacturing processes such that products can be made at commercial scale; optimizing product formulations,

storage, and product longevity and effectiveness; creating, optimizing, and validating assays to assure product integrity; conducting late-stage clinical safety and efficacy studies; and carrying out pivotal animal efficacy studies that are often required for approval of CBRN medical countermeasures.

PAHPA directed BARDA to promote countermeasure and product advanced research and development. Since its creation, BARDA has built a comprehensive and formidable advanced development product pipeline comprised of more than 160 medical countermeasures for CBRN threats and pandemic influenza. Eight of these products from influenza vaccines to anthrax antitoxins have received FDA approval in the last three years alone; a total of nearly twenty have been approved since 2007. The anthrax and botulinum antitoxin products were the first Project BioShield products approved by FDA under the Animal Rule. Twelve of these products, ranging from anthrax and smallpox vaccines to anti-neutropenia cytokine therapeutics for radiation illness have been procured under Project BioShield with another twelve ready for Project BioShield procurement between now and the end of Fiscal Year (FY) 2018. Many of these Project BioShield medical countermeasures were made possible through use of Advanced and Milestone Payment Authorities designed by PAHPA to provide small companies with greater financial stability. Further BARDA has supported the development and manufacturing of 18 influenza vaccines, antiviral drugs, and diagnostics that were used in the 2009 H1N1 pandemic and stockpiled for avian influenza H5N1 and H7N9 outbreaks; a set of industry and academic partnerships enhanced through our PAHPA authorities (*e.g.*, antitrust exemption). To better serve the needs of special populations, BARDA has led the development of many medical countermeasure candidate formulations for children, like Prussian Blue, a treatment for internal

radiation contamination, and solithromycin, a new antibiotic, as well as a smallpox Modified Vaccinia Ankara vaccine for immunocompromised individuals, which was transitioned from the National Institute of Allergy and Infectious Diseases. BARDA is currently supporting development and manufacturing of several Ebola vaccine and therapeutic candidates destined for clinical trials in West Africa. BARDA's work on Ebola medical countermeasures has marked a milestone, as the medical countermeasure development pipeline now includes at least one product candidate for each of the DHS's Material Threat Determinations and pandemic influenza.

PAHPA directed BARDA to promote innovation to reduce the time and cost of countermeasure and product advanced research and development. BARDA has stimulated innovation in the development and manufacturing of vaccine and therapeutic candidates across the pharmaceutical industry. Innovation investments have transitioned a platform technology using a novel bacterial expression system into a next generation anthrax vaccine candidate by coupling that expression system with rational genetic design technology; the objective of which is an anthrax vaccine with increased stability and production yields, and thus a lower overall product cost. BARDA partnered with industry to use synthetic biology technology to generate influenza vaccine seed strains. In 2013, this technology was pivotal in making pre-pandemic H7N9 bulk vaccine for stockpiling in record time by cutting several weeks off the usual time frame to make influenza vaccines. BARDA began working with industry partners last fall to develop new Ebola monoclonal antibodies rapidly using the latest innovations in monoclonal antibody development; now we are testing these new Ebola antibody candidates in non-human primate challenge studies; if these studies are successful, these products will move into clinical trials later this

year. BARDA has kept a keen eye on and supported innovative technologies that may enhance existing medical countermeasures or generate new transformative medical countermeasures at lower costs and with longer shelf lives.

PAHPA directed BARDA to facilitate collaboration between the Department of Health and Human Services and other Federal agencies, relevant industries, academia, and others, with respect to such advanced research and development. BARDA has established its medical countermeasure development pipeline by collaborating with Federal partners, primarily NIH, CDC, FDA, and the Department of Defense, and by making many public-private partnerships with industry and academia. BARDA partnerships have included nearly 90 pharmaceutical and biotechnology companies, both large and small, and more than 25 academic and other institutions since 2006. BARDA, with vaccine manufacturers, has established the first and largest pre-pandemic influenza vaccine stockpile in the world, one that could, if necessary, vaccinate tens of millions of Americans against potential H5N1 and H7N9 pandemics. BARDA utilized the Other Transaction Authority authorized under PAHPA to create a novel cost-sharing public-private partnership with industry for the simultaneous development of multiple new classes of antibiotics for biothreats and high-priority public health pathogens. Further, BARDA, industry, and academia have entered into partnerships designated as the Centers for Innovation in Advanced Development and Manufacturing (CIADM) to assist inexperienced medical countermeasure developers, expand modernized domestic pandemic influenza vaccine manufacturing capacity, ensure nimble and flexible manufacturing capabilities for emerging infectious threats in public health emergencies, and provide workforce training to the next

generation of vaccine developers and manufacturers. Today the CIADMs are working on anthrax and Ebola medical countermeasures.

Building on the National Strategy for Pandemic Influenza, BARDA has collaborated with industry and Federal partners to: (1) support advanced development of new influenza vaccines, antiviral drugs, and diagnostic devices leading to multiple FDA approvals for the U.S. market; (2) improve influenza vaccine manufacturing resulting in greater vaccine production yields and availability sooner; (3) build and maintain stockpiles of pre-pandemic influenza vaccines for the critical workforce and antiviral drugs at the Federal and State levels; and (4) expand domestic and global pandemic influenza vaccine manufacturing infrastructure and capacity multifold.

To save cost and time in product development and manufacturing, BARDA has established a medical countermeasure infrastructure comprised of core service assistance programs to assist product developers on a daily basis while ensuring rapid and nimble response in a public health emergency. BARDA has employed this medical countermeasure infrastructure for development of CBRN medical countermeasures on a routine basis and is now using them in the current Ebola response by supporting the development and manufacturing of several Ebola therapeutics and vaccines. BARDA's Nonclinical Studies Network (NCSN), which was established in 2010 and is comprised of 17 high-biocontainment laboratories in the United States and the United Kingdom, has developed qualified animal models for CBRN threats, performed animal-challenge studies for CBRN medical countermeasures, and evaluated potential CBRN medical countermeasure candidates in these animal models prior to BARDA investment. Today NCSN is conducting

critical animal challenge studies for promising Ebola monoclonal and antiviral drug therapeutic candidates. BARDA's three CIADMs are helping to develop anthrax vaccines and are expanding the production of new and existing Ebola monoclonal antibodies similar to ZMapp in mammalian cells. BARDA's Fill Finish Manufacturing Network, established in 2013 with four Contract Manufacturing Organizations having aseptic filling capabilities in the United States, is now being used to formulate and fill multiple Ebola antibody and vaccine candidates into vials for clinical efficacy studies in West Africa. Two Contract Research Organizations among the five members of our Clinical Studies Network are working with BARDA scientists and with CDC in-country to conduct Ebola vaccine clinical trials in Sierra Leone. BARDA's modeling unit, which routinely provides medical consequence modeling of CBRN threats to inform medical-countermeasure requirements, generated key models and forecasts on the impacts of medical-countermeasure intervention on the epidemiology of the 2009 H1N1 pandemic, the 2013 H7N9 outbreaks, and the current Ebola epidemic in West Africa. The investments that BARDA has made in our national medical-countermeasure infrastructure since 2010 are playing a major role in the Nation's response to the current Ebola epidemic and will become even more vital for medical-countermeasure responses to public health and national security emergencies in the coming years.

Since PAHPA, FDA and BARDA have greater scientific and regulatory engagement, both in regard to the requirements for Emergency Usage Authorization and Animal Rule, as well all aspects of regulatory approval throughout the medical countermeasure development pipeline. Currently BARDA and FDA are working together to implement a framework for selection of

medical countermeasure candidates needing Regulatory Development Plans as required in PAHPRA.

BARDA has developed multiple opportunities for government, industry, and academic stakeholders to engage us with regard to medical countermeasure research, development, innovation, and stockpiling. The PHEMCE's website,[1] managed by BARDA, serves as a portal for updated information on medical countermeasure goals, priorities, programs, funding opportunities, meetings, and procurement policies and processes. Through this portal, stakeholders can arrange meetings with BARDA and other PHEMCE partners via the BARDA-coordinated Tech Watch program that enables companies and others to discuss product candidates in detail and to understand PHEMCE goals, priorities, and procurement processes. Through the TechWatch program, BARDA has met with an average of more than 150 stakeholders each year on CBRN and pandemic influenza medical countermeasures; in the last year, we've met with an additional 130+ stakeholders on Ebola medical countermeasures. Data have shown that those companies that visit BARDA through the Tech Watch program have a much greater chance of success than those not meeting with BARDA for assistance on technical issues and procurement processes. Additionally, BARDA hosts Industry Day, an annual three-day event in Washington, D.C., where BARDA presents to 700+ stakeholders a status report on the BARDA-funded medical countermeasure portfolio, new programmatic initiatives and funding priorities. Industry Day also offers a concentrated series of TechWatch-like sessions to meet individually with stakeholders. ASPR's contracting office also provides presentations on current procurement policies and processes and provides assistance on contracting issues. BARDA also meets regularly with medical associations, industry alliances, state and local health

[1] medicalcountermeasures.gov

department associations, and first-line end users across the United States to seek their input on BARDA medical countermeasure programs and initiatives. BARDA's stakeholder outreach demonstrates further our commitment to partnerships with many different sectors and fulfills PAHPA's directive to facilitate collaboration on medical countermeasure development.

PAHPRA extended, reauthorized, or amended many of the authorities that were initially enacted in PAHPA and that BARDA has utilized successfully to establish an advance-development medical-countermeasure pipeline, invigorate Project BioShield with new products, and enable BARDA to meet pandemic influenza medical countermeasure goals. More importantly, PAHPRA reauthorized funding for BARDA Advanced Research and Development programs and the Special Reserve Fund for Project BioShield through FY 2018. The recently-released PHEMCE Multi-Year budget details BARDA's plan for utilizing these resources. However, substantial returns on investment seen already in medical countermeasure candidate development and innovative technologies are leading to mature and FDA-approved products and national medical countermeasure infrastructure assets are becoming mature. Major new initiatives in the coming years will include development of products that address our core mission space – man-made and emerging infectious-disease threats – that also will pay dividends in everyday public healthcare. Specifically, BARDA's focus will expand towards development of new classes of antibiotics and new diagnostics to combat antimicrobial drug resistance primarily for biothreats but also public health pathogens, as appropriate; universal influenza vaccines to afford more effective control of seasonal influenza and better preparedness for pandemic influenza; influenza immunotherapeutics to mitigate the emergence of drug resistance to the present classes of influenza antiviral drugs; and continuous manufacturing of pharmaceutical products that may

transform where and how we make medical countermeasures in the next twenty years. These new initiatives and the lessons learned from Ebola coupled with BARDA's medical countermeasure advances provide a compelling argument for BARDA to create a new Emerging Infectious Disease program in the coming year.

Conclusions

State- or terrorist-sponsored actors using chemical, biological, nuclear and radiological agents of mass destruction, and recurring natural events including pandemic influenza and emerging infectious diseases like Ebola present real and present health threats to the nation. BARDA has made significant progress in developing and acquiring medical countermeasures that can address the catastrophic medical consequences of many of these threats. BARDA's progress has been not just in medical countermeasure preparedness, but in the establishment of a rapid and nimble response national infrastructure to develop, manufacture, and test in animals and humans new medical countermeasures for known and unknown emerging infectious diseases. Authorities and responsibilities created by the Project BioShield Act, PAHPA, and PAHPRA including the establishment of BARDA have demonstrated a successful model to address market failures and high priority USG needs.

Going forward, it is important that we maintain our medical countermeasure preparedness in areas where we have succeeded against key threats, continue medical countermeasure development and manufacturing where we are not yet finished, and reach forward towards transformational medical countermeasure innovations that may bring both more rapid and better preparedness and response capabilities at less expense to these threats. Advancing BARDA's mission will help ensure that we are prepared to face the next Ebola epidemic, influenza

pandemic, anthrax attack, or unknown pathogen. BARDA is prepared to meet those challenges and provide resources, expertise, and technical assistance for promising and transforming vaccine, therapeutic and diagnostic candidates.