TESTIMONY

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FACING 21ST CENTURY PUBLIC HEALTH THREATS:

OUR NATION 'S PREPAREDNESS AND RESPONSE CAPABILITIES, PART I

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Introduction

Chairman Alexander, Ranking Member Murray, and members of the committee, thank you for the opportunity to appear today to discuss reauthorization of the Pandemic and All-Hazards Preparedness Act (PAHPA). PAHPA, which was passed in 2006 and reauthorized in 2013, is a key piece of legislation that—along with other significant legislative achievements such as the Project BioShield Act of 2004, the Public Readiness and Emergency Preparedness (PREP) Act (2005), and the 21st Century Cures Act (Cures Act) enacted in 2016—has served to significantly strengthen our country's preparedness for, and response to, public health emergencies involving chemical, biological, radiological, and nuclear (CBRN) threats as well as emerging infectious disease threats, such as the Zika virus and pandemic influenza.

The Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA), in particular, recognized the key role the Food and Drug Administration (FDA or the Agency) plays in emergency preparedness and response, and codified and built on FDA's ongoing efforts to augment review processes and advance regulatory science to enable FDA to better respond to public health emergencies. The provisions in PAHPRA—as well as in the other key pieces of legislation I mentioned—have provided FDA with essential tools that continue to support us in our mission to protect and promote public health.

FDA's Public Health Emergency Preparedness and Response Mission

FDA plays a critical role in facilitating preparedness for and response to CBRN and emerging infectious disease threats. These threats can and often do emerge without warning as was the case with the anthrax attacks of 2001, the 2009 H1N1 influenza pandemic, the 2014 Ebola outbreak in West Africa, as well as in the ongoing Zika virus outbreak.

FDA's role in facilitating preparedness for, and response to, CBRN and emerging infectious disease threats focuses largely on facilitating the development and availability of medical countermeasures—such as vaccines, therapeutics, and diagnostic tests—to respond to these threats. FDA works closely with its HHS and other U.S. government partners through the Public Health

Emergency Medical Countermeasures Enterprise (PHEMCE), as well as with regulated industry and non-governmental organizations (NGOs), to build and sustain the medical countermeasure programs necessary to effectively respond to public health emergencies. FDA is also committed to working closely with the Department of Defense (DoD) to facilitate the development and availability of medical countermeasures to support the unique needs of our Nation's warfighters. The Agency is already actively implementing the legislation enacted at the end of last year to further prioritize this critical work with DoD. Senior leadership at the Agency is leading these efforts, and we look forward to keeping Congress informed of our progress in these critical areas.

FDA's Medical Countermeasures Initiative (MCMi)—established in 2010—brought additional resources to FDA that enabled FDA to hire additional expert staff and to become more deeply and thoroughly engaged in medical countermeasure activities. This program continues to be key to establishing clear regulatory pathways for medical countermeasures, advancing medical countermeasure regulatory science to support regulatory decision making, and advancing important policies and mechanisms to facilitate the timely development and availability of medical countermeasures. FDA's goal is to be modern and efficient in its regulation of safe and effective medical products, and that includes medical countermeasures.

FDA's operations within its medical countermeasures mission cover a broad range of activities vital to facilitating the development of, and access to, safe and effective medical countermeasures, including:

- Reviewing medical countermeasure marketing applications and approving those that meet standards for safety and efficacy;
- Providing regulatory advice, guidance and technical assistance to sponsors developing medical countermeasures, as well as to U.S. government partners, international regulators, and international organizations such as the World Health Organization;
- Supporting efforts to establish and sustain an adequate supply of medical countermeasures, including averting supply disruptions when feasible and, in certain situations, allowing products to be used beyond their expiration dates when supported by appropriate scientific evaluation;

- Enabling access to medical countermeasures that are not yet approved for use—when necessary—through an appropriate mechanism, including through FDA's Emergency Use Authorization (EUA) authority;
- Proactively identifying and resolving regulatory challenges associated with medical countermeasure development and ensuring that FDA regulations and policies adequately support medical countermeasure development and enable preparedness and response activities;
- Fostering the professional development of FDA scientists to ensure that FDA personnel maintain the skills and abilities to support the medical countermeasure mission; and
- Supporting regulatory science to create the tools, standards, and approaches necessary to develop and assess the safety, efficacy, quality, and performance of medical countermeasures.

FDA is also a critical partner in preparing for, and responding to, natural disasters, as demonstrated by its ongoing 2017 hurricane recovery efforts, including its work in Puerto Rico following Hurricane Maria. FDA performs extensive preliminary work in advance of storms to help prepare for potential impacts. For example, FDA utilizes storm prediction data and firm registration databases to prepare maps to identify FDA-regulated firms, including those that manufacture critical products that could be impacted by the storms. Where necessary, FDA may take contingency steps to help ensure a continuous supply of critical medical product manufacturing. The most significant role that FDA plays comes after the storm, as facilities come back on line and may need remediation, and farmers seek to put crops or farmland that were damaged back into commercial use. FDA has supported the many pharmaceutical and medical device manufacturers in Puerto Rico to help address and prioritize recovery operations based on the potential for medical product shortages based on public health needs. Many of the requests FDA received were for infrastructure support, primarily getting a reliable source of power, and FDA worked with partners at the Department of Homeland Security to support getting critical manufacturing back online. Through product registrations and communications with manufacturers, FDA was able to identify the medically necessary products manufactured in Puerto Rico and determine which were the top public health priorities. FDA continues to be focused on storm-related shortage issues, including shortages of saline solution and amino acids,

as well as the cascading increase in demand for other medical products, such as empty IV containers which are now being used in higher quantities for compounded products. FDA has been in direct communication with manufacturers, distributors, hospitals and other health care providers, including the Department of Veterans Affairs (VA), and we are assessing existing product supply, demand trends and manufacturer capacity to increase availability of the empty IV containers.

Fostering Innovation in Medical Countermeasure Development

At FDA, we fully appreciate that the development of medical countermeasures can present complex and unique challenges. For example, it is not ethical to conduct human studies for many of the high-priority threat agents. In these situations, the Animal Rule, which enables animal efficacy studies to substitute for efficacy trials in humans if the results can reasonably be extrapolated to the expected human use, can be used to facilitate the development and availability of medical countermeasures. PAHPRA recognized the importance of the Animal Rule; and in 2015, FDA finalized guidance for product development under the Animal Rule, incorporating the learnings of considerable product development experience and providing scientific and regulatory expectations for animal data intended to support medical countermeasure approval.

To date, 12 medical countermeasures have been approved under the Animal Rule, including inhalational anthrax therapeutics, a botulism antitoxin, antibiotics for the treatment and prophylaxis of plague, and treatments for acute radiation syndrome. These approvals underscore the critical role the Animal Rule and animal studies can play in advancing medical countermeasures for some of the most challenging threats. Of note, through the use of regulatory science, FDA was able to approve the inhalational anthrax therapeutics and the botulism antitoxin for use in children as well as adults, despite the fact that pediatric patients were not actually studied in clinical trials, due to ethical concerns.

However, for many threats there are not yet adequate regulatory science foundation, such as animal models to support medical countermeasure development or sufficient biomarkers to enable

the extrapolation of data generated in animal models to humans. Without such tools, it is difficult to generate the data necessary to support regulatory decision making.

FDA has established a broad and robust portfolio of cutting-edge research under MCMi's Regulatory Science Program to help develop these tools and promote innovation in the development of medical countermeasures. A few examples of projects include: supporting the development of organs-on-chips models to assess radiation damage in lung, gut, and bone marrow, and then using these models to test candidate medical countermeasures; collaborating to establish a publicly available genomic sequence reference database for use by developers seeking to validate candidate multiplex *in vitro* diagnostic tests that could be used to diagnose multiple pathogens simultaneously; developing reference materials for developers to use to validate nucleic acid-based and serological diagnostic tests for Zika virus; supporting a project to identify and correlate biomarkers of host response to Ebola virus infection in animal models and humans to support medical countermeasure development; developing methods for obtaining safety and limited efficacy data from patients who receive medical countermeasures during public health emergencies; and establishing the Animal Model Qualification Program designed to support medical countermeasure development by promoting the development of animal models for use across multiple product applications, thereby minimizing duplication of effort and resources.

PAHPRA also provided authorities to ensure that FDA personnel are well-trained in how to review medical countermeasure applications for approval. Under these authorities, FDA has established a professional development program, including speakers' series and academic certifications, to ensure that FDA scientists are working through the regulatory challenges posed by new areas of science and technology as they relate to medical countermeasure development. FDA also has spent considerable energy and resources establishing an efficient approach to conduct and support training within the agency.

More recently, the Cures Act included several provisions that are intended to advance innovation in medical product development more generally, but will also help to facilitate the development of medical countermeasures, including the provisions to encourage novel trial designs, and to develop new antimicrobial drug products.

Through the Cures Act, Congress also provided a new priority review voucher (PRV) program to help incentivize the development of material threat medical countermeasures. Under this program, FDA will award a PRV upon approval of a material threat medical countermeasure application provided that certain criteria are met. The PRV may in turn be used by the sponsor who receives it, or sold to another sponsor, who may then use it to obtain priority review for a product application that would otherwise not receive that benefit, enabling a developer to potentially bring a product to market sooner than otherwise possible—something that may be of great value to product developers. FDA plans to issue guidance to address medical countermeasure-specific considerations with the intent to implement the program consistently with the other PRV programs, such as the Neglected Tropical Disease Voucher Program.

There are tremendous opportunities to continue to further the development of groundbreaking, innovative medical countermeasures, and the Agency intends to fully seize and build upon these opportunities. Toward that goal, this past July FDA announced the launch of a comprehensive Innovation Initiative aimed at making sure its regulatory processes are modern and efficient so that safe and effective new technologies, including medical countermeasures, can reach patients in a timely fashion.

Facilitating Access to Safe and Effective Medical Countermeasures

Enabling access to medical countermeasures when they are needed is a high priority for FDA. Amended and new authorities provided by Congress have enabled the Agency to further prepare for, and better respond to, emerging public health threats. For example, PAHPRA amended FDA's EUA authority to provide additional flexibility for issuing EUAs. These additional flexibilities have enabled FDA to better support responses to emerging health threats by issuing nearly 40 EUAs to enable the emergency use of *in-vitro* diagnostic devices for H7N9 Influenza virus, Enterovirus D68 (EV-D68), Middle East Respiratory Syndrome Coronavirus (MERS-CoV), Ebola virus, and Zika virus. FDA also issued an EUA to enable the emergency use of an auto- injector medical countermeasure to maintain preparedness for chemical threats, which has been critical for supporting both warfighter and first responder preparedness goals related to an emergency

involving nerve agents. The authority for prepositioning medical countermeasures provided in PAHPRA also proved useful to allow the manufacturer to ship, and the U.S. government stakeholders to receive, certain strengths of the unapproved auto-injectors that were not yet authorized for use under that EUA.

PAHPRA also provided FDA with several new streamlined authorities to facilitate the emergency use of approved medical countermeasures without the need for issuing an EUA. For example, PAHPRA provided FDA with the authority to issue emergency dispensing orders (including mass dispensing at a point of dispensing (POD)) for approved medical countermeasures during an actual CBRN emergency without requiring an individual prescription for each recipient of the medical countermeasure, if permitted by state law or in accordance with an emergency dispensing order issued by FDA. FDA has used this authority to issue emergency dispensing orders to permit emergency dispensing of doxycycline and ciprofloxacin for post-exposure prophylaxis of inhalational anthrax, to ensure government stakeholders can rapidly provide these therapies in the event of an anthrax attack.[1]

Another new FDA authority created by PAHPRA is the explicit ability to extend expiration dating of eligible FDA-approved medical countermeasures stockpiled for use in CBRN emergencies, if the extension is supported by an appropriate scientific evaluation. This authority streamlines FDA's ability to authorize expiration dating extensions without the need to issue an EUA, which will enable faster response, and has been crucial to FDA's ability to support preparedness efforts. For example, when production stopped after quality issues were identified in the manufacturing process of auto-injectors used for the treatment of nerve agent and insecticide poisoning, FDA used this authority to help prevent shortages of auto-injector products to help ensure that the nation's warfighters and first responders continue to have ready access to these products. FDA also used this authority to extend the expiration date of certain lots of doxycycline capsules held in strategic stockpiles by the Centers for Disease Control and Prevention, state and local public health, and other response stakeholders and issued draft guidance to provide recommendations to

1 The term "stakeholder(s)" means the public agency or its delegate that has legal responsibility and authority for responding to an incident, based on political or geographical boundary lines (e.g., city, county, tribal, State, or Federal), or functional (e.g., law enforcement or public health range) or sphere of authority to prescribe, administer, deliver, distribute, or dispense oral doxycycline products in an emergency situation.

government stakeholders on testing that can be conducted to support future extensions, in order to help sustain preparedness levels.

The Cures Act also amended the EUA and related emergency use authorities to clarify their applicability to animal drugs. FDA encourages anyone interested in utilizing these authorities to contact FDA to discuss how to proceed.

Most recently, Congress passed H.R. 4374, legislation that amends FDA's EUA authority to enable FDA to issue EUAs for medical products to reduce deaths and mitigate injuries from agents that may cause imminently life-threatening and specific risks to United States military forces. Prior to the passage of this legislation, the EUA authority was only applicable to medical products to address CBRN threats. In addition, the legislation contains provisions codifying enhanced collaboration between FDA and DoD, in order to facilitate the development of medical products and countermeasures for the warfighter. FDA is working closely with DoD to implement these new and amended authorities as quickly as possible.

Conclusion

At FDA, we have made it a priority to proactively work with our private sector and government partners to help facilitate the translation of breakthrough discoveries in science and technology into innovative, safe, and effective medical countermeasures. FDA takes its responsibility seriously to help drive and foster innovation as part of advancing public health and our national security. Active FDA involvement is essential to encouraging industry engagement in medical countermeasure development. FDA remains deeply committed to working closely with its partners and continuing to use the authorities Congress provides to the fullest extent to help facilitate the development and availability of safe and effective medical countermeasures. We believe that partnership and innovation will continue to be key drivers to success in the medical countermeasure space and are taking steps to further empower FDA's scientific and clinical experts to drive the innovation necessary to help protect the nation from the threats we may face.

FDA appreciates Congress's support in continually delineating, clarifying, expanding, and extending its authorities—and providing resources—to enable FDA to achieve its public health emergency preparedness and response mission. FDA stands ready to work with Congress and stakeholders to enable us to better achieve this critical work.

Thank you for inviting FDA to testify today. I am happy to answer any questions you may have.