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BEFORE THE
SUBCOMMITTEE ON HEALTH
COMMITTEE ON ENERGY AND COMMERCE
U.S. HOUSE OF REPRESENTATIVES

STRENGTHENING PUBLIC HEALTH EMERGENCY RESPONSE ACT OF 2015

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INTRODUCTION

Good morning Chairman Pitts, Ranking Member Green, and members of the Subcommittee. I am Michael Mair, Director of Strategic Operations in the Office of Counterterrorism and Emerging Threats (OCET) at the Food and Drug Administration (FDA). Thank you for the opportunity to appear today to discuss H.R. 3299, the Strengthening Public Health Emergency Response Act of 2015, which contains provisions intended to help improve preparedness for and response to chemical, biological, radiological, and nuclear (CBRN) threats.

FDA Role in the CBRN Mission

FDA plays a critical role in protecting the United States from deliberate CBRN threats and naturally occurring infectious diseases, such as Zika virus and pandemic influenza. FDA is responsible for ensuring that medical countermeasures—including drugs, vaccines, and diagnostic tests—against these threats are safe, effective, and secure. It is the mission of OCET to facilitate the development and availability of these life-saving products.

FDA works closely with interagency partners—including the Office of the Assistant Secretary for Preparedness and Response (ASPR) and its Biomedical Advanced Research and Development Authority (BARDA), the National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), and Department of Defense (DoD)—as well as with medical countermeasure developers and international partners to facilitate the development and availability of the medical countermeasures necessary to respond effectively to public health emergencies and to support the unique needs of the warfighter. FDA supports medical countermeasure development and availability by providing subject matter expertise and technical assistance in medical countermeasure development, as well as by providing scientific and regulatory input to inform medical countermeasure stockpiling and deployment decisions. In

addition, FDA employs its authorities, such as Emergency Use Authorization (EUA), to facilitate access to available medical countermeasures to respond to public health and military emergencies, even when products are investigational or not yet approved for that particular use provided certain criteria are met.

In 2010, FDA launched its Medical Countermeasures initiative (MCMi), focusing increased resources on identifying and resolving regulatory challenges to medical countermeasure development and availability. The MCMi mission is to promote the development of medical countermeasures by establishing clear regulatory pathways for the development of medical countermeasures, instituting effective regulatory policies and mechanisms to facilitate timely access to available medical countermeasures, and advancing medical countermeasure regulatory science to create the tools that support regulatory decision making.

This interagency collaboration has been extremely successful in facilitating the development and availability of medical countermeasures to respond to CBRN and emerging infectious disease threats. For example, since 2000, FDA has approved 89 medical countermeasures for CBRN threats and pandemic influenza, as well as 17 supplemental changes to already approved applications and 71 modifications to diagnostic devices. This success is in part due to the continuing support provided by Congress in establishing the programs and authorities necessary—as well as providing the funding needed—to create and sustain a robust medical countermeasure enterprise.

The Tropical Disease Priority Review Voucher Program

In 2007, in an effort to incentivize the development of new drug and biological products for the prevention and treatment of tropical diseases that affect millions of people throughout the world,

Congress created the Tropical Disease Priority Review Voucher (PRV) Program at FDA. Under the Tropical Disease PRV program, FDA awards PRVs to the sponsors of approved tropical disease product marketing applications for specified tropical diseases provided 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 priority review. When a marketing application receives a priority review designation, FDA's goal is to take action on that application within 6 months as compared to 10 months under standard review. Thus, a PRV enables a product developer to potentially bring a product to market sooner than it would under the standard review time, which is valuable to product developers.

The legislation that created the Tropical Disease PRV Program listed sixteen tropical diseases—including tuberculosis, malaria, and Dengue—that would qualify the developer of an approved product to prevent or treat the listed tropical disease to receive a PRV under the Tropical Disease PRV Program.

The legislation also authorized the Secretary of the Department of Health and Human Services to add an infectious disease to the list of tropical diseases that would qualify the developer of an approved product to prevent or treat an identified tropical disease to receive a PRV if: (1) there is no significant market in developed nations for that disease; and (2) the disease disproportionately affects poor and marginalized populations. This authority is delegated to FDA, and in 2015, FDA added Chagas disease and neurocysticercosis to the PRV-eligible tropical disease list.

In 2014, Congress passed S. 2917, which added filoviruses, which includes Ebola virus and Marburg virus, to the PRV-eligible tropical disease list; and in 2016, Congress passed S. 2512 which added Zika virus disease to the PRV-eligible tropical disease list.¹

Section 8 of H.R. 3299 would add any disease or other agent that is determined to be a material threat (under section 319F-2(c)(2)(A)(ii) of the Public Health Service Act) to the PRV-eligible tropical disease list. There are currently material threat determinations (MTDs) for eleven biological agents, two classes of chemical agents, radiological materials, and nuclear detonation effects.

FDA is concerned that extending the Tropical Disease PRV program to CBRN threats may not effectively incentivize medical countermeasure development and may have negative unintended consequences.

Medical Countermeasure Development

Many of the sponsors that are developing medical countermeasures for CBRN threats already receive significant incentives from the U.S. Government, such as funding for research and development and clinical trial costs, procurement contracts for government stockpiling, as well as extensive technical assistance throughout the development process. For example, in Fiscal Year 2015, FDA's medical product review centers held 84 formal meetings with medical countermeasure sponsors or applicants to provide technical assistance and clarify regulatory requirements (in addition to having significant interactions with medical countermeasure

¹ The 2014 legislation that added filoviruses to the PRV-eligible tropical disease list (S. 2917; PL: 113-233) also changed the requirement for a sponsor to notify FDA of its intent to submit a marketing application with a tropical disease PRV from 356 days to 90 days, enabled the Secretary of HHS to add diseases to the list of PCR-eligible diseases by issuing an order as opposed to by regulation, and clarified that tropical disease PRVs can be resold an unlimited number of times. The 2016 legislation that added Zika virus disease to the PRV-eligible tropical disease list (S. 2512; PL: 114-146) also changed filoviruses to filovirus disease.

sponsors and applicants outside of the formal meeting process to address issues and provide assistance).² As noted above, these incentives have been highly successful in facilitating the development of medical countermeasures. Therefore, it is uncertain whether extending the Tropical PRV Program to CBRN threats is necessary to incentivize additional medical countermeasure development.

Moreover, there has been no analysis of the Tropical Disease PRV program to assess whether the program is effective in incentivizing product development for the listed neglected tropical diseases. Only three PRVs have been issued to date under the Tropical Disease PRV Program since its inception in 2007 (for products that had been in development prior to the implementation of the Tropical Disease PRV Program) and thus it is not clear at this time how effective this program is in spurring product development.³ Given this uncertainty, FDA believes Congress should approach additional expansion of the PRV program with caution.

Potential Consequences to the Tropical Disease PRV Program

In addition to awarding PRVs under the Tropical Disease Program, FDA also awards PRVs under the Rare Pediatric Disease PRV Program that was established by Congress in 2012 to incentivize the development of products to prevent or treat rare pediatric diseases. Adding all of the CBRN threat agents with MTDs to the list of qualified tropical diseases under the Tropical Disease PRV Program has the potential to increase the number of PRVs that are issued over time, which could negatively affect the sales value of PRVs, and thus, the ability of the PRV

² *MCMi Program Update – Fiscal Year 2015*, Washington DC: Food and Drug Administration. May 2016. <http://www.fda.gov/downloads/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/AboutMCMi/UCM494658.pdf>.

³ In 2016, the Government Accountability Office (GAO) released the findings of an assessment of the effectiveness of FDA's Rare Pediatric Disease PRV Program (<http://www.gao.gov/assets/680/675544.pdf>). (The Rare Pediatric Disease PRV Program was established by Congress in 2012 to incentivize the development of products to prevent or treat rare pediatric diseases by awarding the developers of approved marketing applications for rare pediatric disease products PRVs provided certain criteria are met.) The GAO assessment found that insufficient time had passed to assess the effectiveness of the three-year-old Rare Pediatric Disease PRV Program given that the six drugs for which rare pediatric disease PRVs have been issued had been in development prior to the implementation of the Rare Pediatric Disease PRV Program.

program to incentivize product development. David Ridley, one of the architects of the PRV concept, recently published an analysis of the commercial market for PRVs that included an examination of how the PRV price is affected by the availability of additional PRVs.⁴ He found that the expected value of a PRV could be as high as \$234 million if only one PRV is available in one year, but that if four PRVs are available in one year the value could fall to as low as \$39 million. Thus, Dr. Ridley found that continuing to add more diseases and conditions to the list of qualified tropical diseases runs the risk of reducing the sales price of PRVs, which ultimately will undermine the ability of the PRV program to achieve what Congress intended it to do: incentivize the development of medical products to treat or prevent the diseases or conditions on the tropical disease PRV list.

Potential to Impact FDA's Capacity to Support Product Development

PRVs are redeemed for products that otherwise would not qualify for priority review, such as drugs to treat conditions for which safe and effective available therapies often already exist (e.g., elevated cholesterol, diabetes). The clinical trials for these applications are typically more numerous involving thousands more patients making the reviews more complex than for products that would normally qualify for priority review. Reviewing such applications within the target six month priority review timeframe is very challenging and requires many more person-hours and a larger review team. Thus, managers and reviewers must refocus time and resources away from other important public health work.

While FDA receives additional fees for the review of products that redeem a PRV, these funds are unpredictable and one-time, and thus do not translate into additional staff or resources for the

⁴ Ridley DB, Régnier SA. The Commercial Market For Priority Review Vouchers. *Health Aff (Millwood)*. 2016 May 1;35(5):776-83. <http://content.healthaffairs.org/content/35/5/776.full>

division that ultimately is called upon to review the product linked to the PRV. FDA cannot predict which review divisions will need additional staff to support PRV-related reviews, and the notification that product applicants must provide FDA of their intent to use a PRV prior to the submission of a marketing application is insufficient to enable FDA to staff up as needed.

Product reviewers are highly specialized scientists and doctors who typically cannot be hired this quickly or on an as-needed basis. Additionally, trained product reviewers are not interchangeable and cannot be moved from one review division to another. Thus, FDA must review an application linked to a PRV with existing resources within the affected review division.

Extending the Tropical Disease PRV Program to CBRN threats will significantly increase the number of PRV-eligible diseases, which will eventually result in more PRVs being issued and redeemed. This will ultimately result in FDA having fewer resources available to review other marketing applications for serious diseases, including for CBRN threats. These resource constraints also have the potential to undermine FDA's ability to conduct its entire portfolio of public health work, from providing advice and guidance in the earliest stages to help facilitate drug development (including for medical countermeasures) to monitoring safety after approval.

CONCLUSION

FDA is fully committed to sustaining our deep engagement in facilitating the development and availability of medical countermeasures to prepare for and respond to CBRN and emerging infectious disease threats. While we support the intent in H.R. 3299 to further incentivize the development of medical countermeasures for CBRN threats, we are concerned that adding the MTD threats to the PRV-eligible tropical disease list may not achieve that goal. We suggest that it would be advantageous to conduct a full assessment of U.S. Government medical countermeasure programs to determine if additional incentives are needed to improve medical

countermeasure development and, if so, bring together key experts and stakeholders to explore what are the most appropriate incentives to add.

Thank you. I am happy to answer your questions.