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ONE HUNDRED FOURTEENTH CONGRESS

Congress of the United States

House of Representatives

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MEMORANDUM

May 17, 2016

To: Subcommittee on Health Democratic Members and Staff

Fr: Committee on Energy and Commerce Democratic Staff

Re: Hearing on "Examining H.R. 3299, Strengthening Public Health Response Act"

On **Thursday, May 19th, at 10:00 a.m., in Room 2123 of the Rayburn House Office Building**, the Subcommittee will hold a legislative hearing to review H.R. 3299, the Strengthening Public Health Emergency Response Act of 2015, introduced by Representatives Susan Brooks (R-IN) and Anna Eshoo (D-CA).

I. BACKGROUND

Efforts to protect against emerging infectious diseases and acts of terror executed with biological weapons, referred to as "biodefense," encompass a wide range of interventions, including medical research, biosurveillance, and emergency preparedness.

Following the September 11, 2001, terrorist attacks and the subsequent anthrax mailings, Congress passed legislation to address the threat of bioterrorism by increasing investments in research and preparedness to defend against biological weapons.[1] Significant legislation included the Homeland Security Act of 2002 and the Pandemic and All-Hazards Preparedness Act (PAHPA) of 2006, which established new departments and agencies to address preparedness and bioterrorism response.[2]

Currently, the federal government's biodefense initiatives span across a number of agencies, each of which varies in terms of its resources, scope, and approach. The Department of Homeland Security (DHS) was created in 2002 and tasked as the primary federal agency with

[1] Congressional Research Service (CRS), *Federal Efforts to Address the Threat of Bioterrorism: Selected Issues and Options for Congress* (R41123) (Feb. 8, 2011).

[2] *Id.*

preventing and responding to terrorist attacks within the United States.[3] DHS's mission includes preventing terrorism, enhancing security, and "ensuring resilience to disasters."[4]

The Department of Health and Human Services (HHS) plays a key role in response planning and has the primary responsibility for public health preparedness.[5] HHS operates the Biomedical Advanced Research and Development Authority (BARDA), whose goals include advancing the Department's capability to develop, manufacture, and facilitate distribution of medical countermeasures (MCMs), such as vaccines, during public health emergencies.[6] Within HHS, the Food and Drug Administration (FDA) is responsible for ensuring MCMs, which are used to counter chemical, biological, radiological, nuclear, and emerging infectious disease threats, are safe, effective, and secure.[7]

II. ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

A. Overview

PAHPA established the Assistant Secretary for Preparedness and Response (ASPR) within HHS. The purpose of ASPR is to lead the nation in preventing, preparing for, and responding to adverse health effects of public health emergencies and disasters.[8]

B. Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy And Implementation Plan

ASPR leads the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) which coordinates efforts related to MCMs aimed at enhancing chemical, biological, radiological and nuclear threats (CBRN) and emerging infectious disease preparedness.[9]

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[3] Department of Homeland Security, *Our Mission* (online at www.dhs.gov/our-mission).

[4] *Id.*

[5] U.S. Department of Health and Human Services (HHS), Biomedical Advanced Research and Development Authority, *BARDA Strategic Plan 2011-2016* (online at www.phe.gov/about/barda/Documents/barda-strategic-plan.pdf).

[6] CRS, *Federal Efforts to Address the Threat of Bioterrorism: Selected Issues and Options for Congress* (R41123) (Feb. 8, 2011).

[7] Food and Drug Administration (FDA), *About MCMi* (online at http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/AboutMCMi/default.htm).

[8] HHS, *Office of the Assistant Secretary for Preparedness and Response* (online at http://www.phe.gov/about/aspr/pages/default.aspx).

[9] HHS, *Public Health Emergency Countermeasures Enterprise* (online at http://www.phe.gov/Preparedness/mcm/phemce/Pages/default.aspx).

PHEMCE includes ASPR, the Centers for Disease Control and Prevention (CDC), FDA, the National Institutes of Health (NIH), the Department of Defense (DoD), the U.S. Department of Veterans Affairs (VA), DHS, and the U.S. Department of Agriculture (USDA). Each year, PHEMCE is required by statute to assess and update the PHEMCE Strategy and Implementation Plan for medical countermeasures to address chemical, biological, radiological, and nuclear threats. The 2015 PHEMCE Strategy and Implementation Plan can be found here.

C. Hospital Preparedness Program

ASPR administers the Hospital Preparedness Program (HPP) which is the primary source of federal funding for health system preparedness and response.[10] HPP provides funding and technical assistance to prepare the health system to respond to and recover from a disaster.[11] HPP funding is used to support program officers that oversee the program as well as to supporting program evaluation.

HPP improves health system preparedness and response by: (1) providing grants to health care coalitions that work together to prepare for public health emergencies; (2) supporting the Technical Resources Assistance Center and Information Exchange (TRACIE) which provides evidence-based applications, technology, and proven best practice to help states and communities build enhance capacity and improve their knowledge and effectiveness; (3) supporting the Emergency Care Coordination Center (ECCC) which supports strengthening systems of emergency care in order to improve the health care system's response to disasters and public health emergencies; (4) supporting the Division of Recovery which supports communities as they recover from disaster to ensure their health and social services can return to pre-disaster status as soon as possible; and (5) supporting the Critical Infrastructure Protection (CIP) effort which works through a public and private sector partnership to reduce risks to health care and public health sector critical infrastructure from all hazards.[12]

In 2014, HPP grants provided 86 percent of the total preparedness budgets for the health care coalitions and their individual health system members.[13] In 2015, the CIP program played a significant role in the Ebola response efforts by coordinating with private sector manufacturers and distributors of personal protective equipment (PPE) to ensure that our health care facilities

[10] HHS, *Fiscal Year 2017 Public Health and Social Services Emergency Fund Justification for Estimates for the Appropriations Committees* (online at http://www.hhs.gov/sites/default/files/fy2017-budget-justification-phssef.pdf).

[11] Trust for America's Health, *Fact Sheet, Hospital Preparedness Program: Saving Livings from Boston to West Texas* (online at http://healthyamericans.org/health-issues/wp-content/uploads/2013/06/HPP-Backgrounder.pdf).

[12] HHS, *Fiscal Year 2017 Public Health and Social Services Emergency Fund Justification for Estimates for the Appropriations Committees* (online at http://www.hhs.gov/sites/default/files/fy2017-budget-justification-phssef.pdf).

[13] *Id.*

with the greatest need, including facilities that functioned as domestic Ebola treatment centers, were prioritized in the distribution of scarce PPE. Additionally, according to BARDA officials, TRACIE, which launched on September 30, 2015, already has received more than 500 training and technical assistance requests as well as over 35,000 visitors to the website.

III. BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY

A. Overview

BARDA, a division within ASPR, focuses on developing and procuring needed medical countermeasures against chemical, biological, radiological, and nuclear (CBRN) terrorism agents, pandemic influenza, and emerging infectious diseases.[14]

B. Project BioShield

One way in which BARDA supports countermeasure development is through administering Project BioShield. Project BioShield was created to establish a government market guarantee for CBRN medical countermeasures.[15] Since the U.S. federal government is often the largest purchaser of CBRN medical countermeasures, this market guarantee provides a mechanism for assuring companies that the federal government is willing to purchase their product once developed as well as provide the price at which the federal government is willing to do so.[16]

Project BioShield allows BARDA to obligate funds to purchase medical countermeasures while they still need up to 10 years of development.[17] A Project BioShield contract can only be used to purchase medical countermeasures against CBRN agents for which DHS has determined pose a material threat to national security.[18] The most recent list of high-priority threats identified by the Secretary of Homeland Secretary may be found in the 2015 Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy and Implementation Plan. BARDA may also use Project BioShield contracts to stockpile countermeasures that have not yet been approved by FDA in the Strategic National Stockpile (SNS).[19] The SNS is administered by CDC and contains large quantities of medical countermeasures to protect the American public in the case of a health emergency. In addition to containing countermeasures procured by BARDA, CDC procures FDA-approved medical countermeasures for the stockpile.

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[14] CRS, *The Project BioShield Act: Issues for the 113th* Congress (R43607) (June 18, 2014).

[15] *Id.*

[16] *Id.*

[17] *Id.*

[18] *Id.*

[19] *Id.*

IV. CDC'S PUBLIC HEALTH EMERGENCY PREPAREDNESS COOPERATIVE AGREEMENTS

CDC administers the Public Health Preparedness (PHEP) cooperative agreement. This program provides funding and tools for state, local, tribal, and territorial public health departments to strengthen their ability to respond to public health incidents and build more resilient communities.[20] This program played a critical role in our Ebola response efforts. PHEP resources and guidance helped the establishment of active monitoring procedures in only 10 days for the Ebola outbreak and from October 2014 through September 20, 2015, PHEP awardees actively monitored travelers from countries in West Africa with widespread Ebola cases.[21]

V. FDA'S MEDICAL COUNTERMEASURES AUTHORITIES AND ACTIONS

FDA is responsible for evaluating the safety and effectiveness of medical products (including MCMs) before a product is approved, licensed, or cleared for marketing.

A. FDA Authority of MCMs

Section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360bbb-3) gives FDA authority to issue an emergency use authorization (EUA) to help facilitate MCM access during public health emergencies. During an emergency, FDA can issue an EUA that allows for (1) use of an unapproved medical product; or, (2) unapproved use of an approved medical product if certain statutory criteria are met. For example, FDA must find that, based on all available evidence, the known and potential benefits of the product outweigh the known and potential risks. FDA also must find there is no adequate and approved alternative available.

To help coordinate the development and availability of MCMs, FDA launched an agency-wide initiative, the Medical Countermeasures Initiative (MCMi), in August 2010. Led by the Office of Counterterrorism and Emerging Threats (OCET), in the FDA Office of the Chief Scientist, the initiative has three main missions: (1) promoting the development and availability of medical countermeasures by establishing clear regulatory pathways; (2) creating data necessary to support regulatory decision-making through a robust medical countermeasure regulatory science program; and, (3) modernizing the legal, regulatory and policy framework to

[20] Centers for Disease Control and Prevention, Office of Public Health Preparedness and Response, *Funding and Guidance for State and Local Health Departments* (online at http://www.cdc.gov/phpr/coopagreement.htm).

[21] HHS, *Fiscal Year 2017 Centers for Disease Control and Prevention Justification for Estimates for the Appropriations Committees* (online at http://www.cdc.gov/budget/documents/fy2017/fy-2017-cdc-congressional-justification.pdf).

establish effective policies and mechanisms to facilitate timely access to available medical countermeasures.[22]

B. Tropical Disease Priority Review Voucher Program

The Food and Drug Administration Amendments Act (FDAMA) of 2007 added Section 524 to the FD&C Act authorizing FDA to award a priority review voucher (PRV) to sponsors of certain tropical disease product applications that meet specified criteria. Tropical diseases disproportionately affect those living in poor and developing countries. The legislation was intended to provide sufficient economic incentives to encourage investment in research to develop new treatments.[23]

Section 524(a)(3) of the FD&C Act lists tropical diseases eligible for the tropical disease PRV program. The provision also gives FDA authority to add other infectious diseases to the list for which there is "no significant market in developed nations and that disproportionately affects poor and marginalized populations".[24] A tropical disease product application is eligible for the program if: (1) the drug is to prevent or treat a tropical disease in humans; (2) the drug does not contain a previously approved active ingredient; and, (3) FDA finds the application qualifies for a six month priority review.[25]

Upon approving an application under this program, FDA will award the sponsor a PRV. A PRV allows a sponsor to obtain a second 6-month priority review for any other human drug application. The sponsor also may transfer or sell the PRV to another sponsor of a human drug

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[22] FDA, *About MCMi* (online at http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/AboutMCMi/default.htm).

[23] Between 2000 and 2011, neglected diseases (including tropical diseases listed in § 564 of the FD&C Act) represented over 10% of the global disease burden, however only 4% of new drugs and vaccines approved worldwide were indicated to treat these diseases. Belen Pedrique, et al, *The drug and vaccine landscape for neglected diseases (2000-11): a systematic assessment*, Lancet (2013) 1(6) (online at http://www.thelancet.com/journals/langlo/article/PIIS2214-109X%2813%2970078-0/fulltext).

[24] Since enactment of FDAMA, Congress has passed legislation adding filovirus diseases (e.g., Ebola) and Zika virus to the list of tropical diseases. In 2015, FDA issued a final order adding Chagas disease and neurocysticercosis to the list.

[25] FDA generally finds an application eligible for priority review if the drug: (1) treats a serious condition; and, (2) will provide relatively significant improvements in safety and effectiveness when compared to currently marketed products.

application. The only limitation on PRV use is that a sponsor must notify FDA 90 days[26] before submitting the PRV to obtain a 6-month drug application review.

To date, FDA has awarded three tropical disease PRVs[27] and two of these PRVs have been used.[28] In 2011, Novartis used the voucher it was awarded in 2009 for its malaria drug, Coartem to expedite review of its gout drug, Ilaris. At the conclusion of the six-month review, FDA found the drug was not approvable. Gilead Sciences purchased the second PRV for $125 million and used it to expedite review of its HIV drug, Odefsey (approved in March 2016). The third PRV remains unused with the original sponsor.

V. SUMMARY AND ANALYSIS OF H.R. 3299

Section 2: Hospital Preparedness Program

This section requires ASPR to award 97 percent of HPP funds through grants to health care coalitions for emergency preparedness. As a result, the change would limit the funding available to administer the HPP program. This would make it difficult to oversee the awardees and evaluate programs for effectiveness, accountability and integrity. It would also eliminate funding for TRACIE, ECCC, Division of Recovery, and the CIP programs that have been vital in equipping our health care system with tools and information needed to prepare for, respond to, and recover following a disaster.

Section 3: GAO Report on State, Local and Hospital Preparedness Programs

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[26] FDAMA originally required a company to notify FDA one year before redeeming a PRV awarded under the program. However, in 2014 Congress reduced this to only 90 days.

[27] Alexander Gaffney and Michael Mezher, *Regulatory Explainer: Everything You Need to Know About FDA's Priority Review Vouchers*, Regulatory Affairs Professional Society (Mar. 2, 2016) (online at http://raps.org/Regulatory-Focus/News/2015/07/02/21722/Regulatory-Explainer-Everything-You-Need-to-Know-About-FDA%E2%80%99s-Priority-Review-Vouchers/).

[28] FDA also has a PRV program to incentivize development of drugs to treat rare pediatric diseases. In 2012, Congress passed the Food and Drug Administration Safety and Innovation Act which added § 529 to the FD&C Act (21 U.S.C. § 360ff) to create the rare pediatric disease PRV program and under this program FDA has awarded six PRVs. Of these vouchers, one was sold to Sanofi and Regeneron for $67 million and used to expedite review of a first-in-class cholesterol drug, Praluent (approved in July 2015). A second PRV was sold for $245 million to Sanofi who redeemed the voucher in February 2016 to expedite review of a new type 2 diabetes drug (review ongoing). A third PRV was sold to AbbVie for $350 million and has not been used. The three remaining PRVs were awarded in 2015 and have not been sold or used.

This section would require GAO to issue a report to Congress within one year of enactment on HPP and PHEP. The report could provide important information to inform Congress for upcoming reauthorization of PAHPA.

Section 4: Strategic National Stockpile

This section would require BARDA and CDC to ensure that procedures are in place to coordinate the ongoing stockpiling of medical countermeasures within the Strategic National Stockpile.

Section 5: Project BioShield Procurement Process

This section would eliminate the need for review by the Office of Management and Budget (OMB) and Presidential approval to use the special reserve fund to enter into Project BioShield contracts.

Section 6: BARDA Transaction Authorities

This section would grant BARDA's Director authority to directly negotiate and enter into any contracts, grants, or cooperative agreements without ASPR oversight.

Currently, BARDA enters into contracts by working through ASPR's Office of Acquisition Management Contracts and Grants (AMCG). Subject matter experts from BARDA work with the business officers from AMCG to negotiate and enter into contract with private entities. Working through a separate office outside of the control of the BARDA Director ensures that there is not undue influence by the BARDA Director, another program officer, or an outside source. The external contracting authority ensures that taxpayer investments will be made through open and fair competition and without any conflicts. This structure is consistent with other divisions within HHS. For example, the NIH Office of the Director administers the contracting office that is used by all NIH Institutes and Centers.

Section 7: Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy and Implementation Plan

This section requires the annual PHEMCE Strategy and Implementation Plan to include the time lapse between BARDA issuing a request for proposal or task order and awarding a contract. This section would also require the Plan to report on the efforts to develop qualified countermeasures, security countermeasures, or qualified pandemic or epidemic products for pandemic flu.

Section 8: Priority Review to Encourage Treatments for National Security Threats

H.R. 3299 proposes to expand the FDA's tropical disease PRV program by adding to the list of tropical diseases in statute any disease or other agent that is determined to be a material

threat by the Department of Homeland Security, in consultation with the HHS Secretary and heads of other appropriate agencies.

Issues to Consider

Lack of Evidence PRV Programs Work. It is unclear if existing PRV programs are having the intended effect of incentivizing investment in new research and development. Of the three PRVs awarded under the tropical disease PRV program, two were awarded to drugs that had been used for years outside the U.S. One drug was approved in over 80 countries before the sponsor filed an application with FDA – an application that included only studies conducted before 2007 to obtain approval elsewhere.[29] The second drug was registered outside the U.S. for over a decade before an application was filed with FDA and the filed application only included studies conducted by a company that previously owned the drug.[30] However, under the terms of the program, FDA was forced to award two PRV's – one to a company who conducted no new research and one to a company who conducted no research at all.

Limited Availability of Approved Drugs. The tropical disease PRV program does not ensure patients, government entities, and health care providers can access approved products. There is not even a requirement that a company market a product approved under the program.[31] Some international organizations, such as *Doctors Without Borders*, *TB Alliance*, and *Drugs for Neglected Diseases initiative*, have raised concerns that accessing drugs approved under FDA's tropical disease PRV program is challenging and sometimes impossible. For example, drugs approved under this program are expensive, in shortage, and/or only sold in bulk which can lead to waste.[32]

Broad Expansion. H.R. 3299 proposes to expand the tropical disease PRV program to award PRVs to sponsors of MCMs that address a material threat designated by DHS. This broad expansion would force FDA to award a PRV to the developer of an MCM addressing a material threat, even if the MCM does not meet U.S. government requirements for preparing and responding to public health emergencies. Such a broad expansion could incentivize development

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[29] Tatum Anderson, *Novartis Under Fire for Accepting New Reward for Old Drug*, Lancet, 2009; 373(9673):1414. (online at: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2809%2960804-7/fulltext).

[30] Aaron S. Kesselheim, *Experience With the Priority Review Voucher Program for Drug Development*, JAMA, 2015; 314(16):1687-8.

[31] This is in contrast to the pediatric rare disease PRV program which requires the HHS Secretary to revoke a PRV awarded under the program if the drug is not marketed in the U.S. within one year of approval.

[32] Letter from American Thoracic Society, Drugs for Neglected Diseases initiative, Global Alliance for TB Drug Development, IDSA Center for Global Health, Médecins Sans Frontières, Sabin Vaccine Institute, and Treatment Action Group to House Energy and Commerce Committee (Mar. 29, 2016).

of MCMs that do not align with government needs. Furthermore, the expansion is problematic as the definition of "material threat" is dynamic. DHS revises this definition based on changing risk assessments and there is potential for a large expansion of the program if additional threats are added to the list. For example, if DHS were to add pandemic influenza to the list of material threats in the future it would likely exponentially increase the number of applications submitted to FDA under the PRV program.

Existing Authorities and Incentives Sufficient. The government currently has authority to procure and support development of MCMs for material threats (including by funding MCM research and development). For example, FDA works closely with MCM developers throughout the development and regulatory review process. In 2015 alone FDA held 89 formal meetings to assist MCM developers and many more informal consultations. Since 2000, FDA has approved 89 MCMs to address CBRN threats and pandemic flu, 17 supplemental new drug applications for MCMs, and 71 modifications for MCM diagnostic devices. The large number of approved MCMs and strong regulatory support demonstrate there currently are sufficient incentives to invest in MCM development.

Reduced PRV Value. A recent article by David Ridley, the academic who conceptualized the PRV program in 2006, highlights existing issues with PRV programs, such as loopholes that award PRVs to sponsors who do not invest in new research or do not make drugs available to the intended beneficiaries. He cautions against expanding existing PRV programs without first addressing these issues and also expresses concern that expanding the program could result in a substantial decrease in the market value for PRVs. Devaluation of a PRV can reduce the programs' effectiveness by undermining incentives to develop new medicines for tropical or rare pediatric diseases.[33]

Impact on FDA. Generally, FDA will grant a six month priority review to drug applications that have potential to improve public health, such as a drug that will address an unmet medical need. However, PRVs awarded under the tropical and rare pediatric disease programs can be used to expedite review of a drug application that otherwise would not qualify. Since PRV programs essentially allow a drug sponsor to purchase a priority review at the expense of public health priorities. Increasing the burden on FDA to expedite review of more applications with limited public health value undermines FDA's ability to fulfill its mission and threatens staff morale.

FDA drug product reviewers are organized into divisions that specialize in reviewing specific drug classes, drug reviewers cannot be "reassigned" to assist another division in reviewing an application submitted for expedited review (e.g., a reviewer trained to review oncology drugs cannot be reassigned to help expedite review of a weight loss drug submitted with a PRV). When FDA receives a PRV, it must divert resources away from existing work to

[33] David B. Ridley and Stephane A. Regnier, *The Commercial Market For Priority Review Vouchers*, Health Affairs, 2016; 35(5):776-83. (online at: http://content.healthaffairs.org/content/35/5/776.full).

expedite review of a drug that may, under normal circumstances, be a lower priority. In addition, a new drug application that qualifies for the standard 10 month review generally is supported by large data sets that takes FDA reviewers significant time to evaluate. When such an application is submitted with a PRV it places a significant strain on FDA resources by reducing the time an FDA reviewer has to perform important work from 10 to six months.

VI. WITNESSES

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