

# EXAMINING H.R. 3299, STRENGTHENING PUBLIC HEALTH EMERGENCY RESPONSE ACT

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## HEARING BEFORE THE SUBCOMMITTEE ON HEALTH OF THE COMMITTEE ON ENERGY AND COMMERCE HOUSE OF REPRESENTATIVES ONE HUNDRED FOURTEENTH CONGRESS SECOND SESSION

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## **EXAMINING H.R. 3299, STRENGTHENING PUBLIC HEALTH EMERGENCY RESPONSE ACT**

**THURSDAY, MAY 19, 2016**

HOUSE OF REPRESENTATIVES,  
SUBCOMMITTEE ON HEALTH,  
COMMITTEE ON ENERGY AND COMMERCE,  
*Washington, DC.*

The subcommittee met, pursuant to call, at 10:00 a.m., in room 2123, Rayburn House Office Building, Hon. Joseph R. Pitts (chairman of the subcommittee) presiding.

Members resent: Representatives Pitts, Guthrie, Shimkus, Murphy, Burgess, Lance, Bilirakis, Ellmers, Brooks, Collins, Green, Engel, Capps, Schakowsky, Butterfield, and Pallone (ex officio).

Also present: Representative Eshoo.

Staff present: Rebecca Card, Assistant Press Secretary; Carly McWilliams, Professional Staff Member, Health; Graham Pittman, Legislative Clerk; Chris Sarley, Policy Coordinator, Environment and Economy; Heidi Stirrup, Policy Coordinator, Health; John Stone, Counsel, Health; Sophie Trainor, Policy Advisor, Health; Waverly Gordon, Democratic Professional Staff Member; Tiffany Guarascio, Democratic Deputy Staff Director and Chief Health Advisor; Samantha Satchell, Democratic Policy Analyst; Andrew Souvall, Democratic Director of Communications, Outreach, and Member Services; and Kimberlee Trzeciak, Democratic Health Policy Advisor.

Mr. PITTS. Ladies and gentlemen, if our guests will take their seats, the subcommittee will come to order. The Chair will recognize himself for an opening statement.

### **OPENING STATEMENT OF HON. JOSEPH R. PITTS, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF PENNSYLVANIA**

Today's hearing will take a closer look at bipartisan legislation introduced by our Energy and Commerce Committee colleagues Representative Brooks and Eshoo, H.R. 3299.

This bipartisan bill builds upon our previous work to modernize our biodefense systems, ensuring that we are well equipped to handle current and emerging biothreats.

The biothreat is not new. Pandemics have occurred throughout history. There have been four flu pandemics in the United States since 1918, each with different characteristics such as the H1N1 flu most recently in 2010. Even more worrisome is the threat of biological weapons or infectious diseases employed as weapons of ter-

ror, such as the use of salmonella in Oregon in 1984 by the Rajneeshee cult or the anthrax scare in 2001.

Science has made significant advances in genomics and genetics and biotechnology that hold tremendous promise for those affected by illness and disease. However, that same technology could theoretically be used to biologically engineer superbugs that are more virulent, more lethal, more difficult to treat than their naturally occurring counterparts.

Imagine a weaponized and bioengineered version of the Ebola virus or polio or smallpox, and the devastating effect that would have on an American city.

Since the terror attacks on September 11, 2001, Congress took steps to build our Nation's health infrastructure and foster a development of medical countermeasures, MCM, in the event of a future chemical, biological, radioactive, or nuclear, CBRN, attack.

In 2004, Congress enacted the Project BioShield Act, and later, in 2006, enacted the Pandemic and All Hazards Preparedness Act, PAHPA, which was authorized through 2011. In addition to establishing a strategic plan to direct research, development, procurement of MCMs, PAHPA also established the Biodefense Advanced Research and Development Authority, BARDA, within the Department of Health and Human Services.

BARDA was charged with coordinating and accelerating the development of MCMs. BARDA was created from the understanding that most MCMs needed by the Nation did not yet exist, and their development is a risky, expensive, and lengthy process. There is little to no demand in the private market for vaccines and therapeutics that protect against bioterror agents.

BARDA bridges the funding gap between early stage research and the ultimate procurement of products for the National Stockpile under Project BioShield. By partnering with private industry, using money from the Biodefense Advanced Research and Development Fund, BARDA, can reduce the development risk entailed in MCM research, thereby helping to mitigate the disincentives associated with countermeasure development and ultimately improving our national readiness with regard to a CBRN attack.

The bill before us today reforms our Nation's medical countermeasure acquisition process, incentivizes research to combat the next generation of deadly diseases, and increases accountability of preparedness spending. Such improvements will go a long way toward helping our preparedness for future public health emergencies, such as Ebola, by creating new incentives for developing necessary medicines and vaccines and streamlining the contracting process for medical countermeasures.

Incentives are necessary to attract private investment in product development, and so too must the contracting processes be efficient. We must get this right. The stakes are too high, the cost of failure too dire. And I look forward to our discussion today about how to best protect our country from biological threats.

[H.R. 3299 appears at the conclusion of the hearing.]

[The prepared statement of Mr. Pitts follows:]

## PREPARED STATEMENT OF HON. JOSEPH R. PITTS

Today's hearing will take a closer look at bipartisan legislation introduced by our Energy and Commerce Committee colleagues, Reps. Brooks and Eshoo, H.R. 3299. This bipartisan bill builds upon our previous work to modernize our biodefense systems, ensuring that we are well-equipped to handle current and emerging biothreats.

The biothreat is not new. Pandemics have occurred throughout history. There have been four flu pandemics in the United States since 1918, each with different characteristics, such as the H1N1 Flu most recently in 2010. Even more worrisome is the threat of biological weapons or infectious diseases employed as weapons of terror, such as the use of salmonella in Oregon in 1984 by the Rajneeshee cult or the anthrax scare in 2001.

Science has made significant advancements in genomics, genetics, and biotechnology that hold tremendous promise for those afflicted by illness and disease. However, that same technology could theoretically be used to biologically engineer "superbugs" that are more virulent, more lethal and more difficult to treat than their naturally occurring counterparts. Imagine a weaponized and bioengineered version of the Ebola virus, or polio, or smallpox and the devastating effect that would have on an American city.

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We must get this right. The stakes are too high and the cost of failure too dire. I look forward to our discussion today about how best to protect our country from biological threats.

Mr. PITTS. Mrs. Brooks, do you seek time?

Mrs. BROOKS. Yes, Mr. Chairman.

Mr. PITTS. The Chair will recognize Mrs. Brooks for her time.

Mrs. BROOKS. Thank you, Mr. Chairman.

I want to thank you and the leadership of the Energy and Commerce Committee so much for holding this important hearing today on our bill. Congresswoman Eshoo and I and our staffs have worked very hard over the course of this Congress to craft this piece of legislation that now enjoys significant support from both sides of the aisle. And I commend the chairman for understanding the urgency of this matter.

Last Congress, I served as chairman of the Homeland Security Committee's Subcommittee on Emergency Preparedness and Response, where I was amazed to learn of truly what I thought was the dire straits our biodefense capabilities are in as a result of more than a decade of neglect. I wish I could sit here today and tell you that I think things have improved dramatically over the last couple of years. And I appreciate from your written testimony that some of you believe they have.

Mr. PITTS. If you will suspend, I will recognize you for the chairman when he comes in. You will have more time.

Mrs. BROOKS. Oh, I am sorry.

Mr. PITTS. The Chair now will recognize the ranking member of the subcommittee, 5 minutes for an opening statement.

**OPENING STATEMENT OF HON. GENE GREEN, A  
REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS**

Mr. GREEN. Thank you, Mr. Chairman, and to our witnesses for joining us this morning.

The Federal Government has undertaken many initiatives, especially since the anthrax attacks of 2001, to fortify our biodefense capabilities to address the threat of a biological outbreak or attack. With stockpiling medical countermeasures, MCMs, to build public health capacity, we are better prepared today than we were a decade ago.

But the fact is we still are dramatically underprepared to respond to biological event of disaster proportions. The current Zika virus epidemic underscores our need for a robust pipeline of vaccines and treatments effective against current and emerging threats. Over the last decade, the amount of cooperation between Government and the private sector has improved and our level of preparedness has increased, but we must do more in order to meet the new challenges we face.

Currently, the Federal Government's biodefense initiatives span across a number of agencies and vary in scope and approach. Department of Homeland Security, Department of Health and Human Services, and Department of Defense each play a role.

For example, HHS operates the Biomedical Research and Development Authority, or BARDA, which was created to advance capability to develop, manufacture, and distribute medical countermeasures, like vaccines, during public health emergencies. BARDA is housed within the Assistant Secretary for Preparedness, or ASPR, the agency responsible for leading prevention, preparations, and response to the adverse health effects of public health emergency disasters.

H.R. 3299, Strengthening the Public Health Emergency Response Act, offers a range of ideas to move our biodefense and medical countermeasures development and procurement capacities forward. I want to thank the bill's sponsors for their leadership. Medical countermeasures are essential to our Nation's health and security. There is a clear and vital role for the Federal Government to play in order to contribute to a greater public health security and ensure preparedness against biological threats.

We need meaningful countermeasures, research incentives, transparency, and predictability, and flexible contracting mecha-

nism in order to shore up our ability to respond to biological threats and infectious disease outbreaks. Without strong commitment from the Federal Government, public-private partnerships, predictable processes and incentives, this market arguably could not exist.

The Government is the only market for most of the medical countermeasures. Unlike other drugs and vaccines, these products are not sold or distributed within the healthcare system. To incentivize companies to develop and produce these critical products, Congress created the Project BioShield Special Reserve Fund in 2004. The Special Reserve Fund was a market for medical countermeasures and was originally funded through the advanced appropriations at \$5.6 billion over 10 years to procure successful product candidates.

The availability and certainty this 10-year fund offered had a positive impact on the Government's ability to attract innovative companies into this space. Twelve MCMs against several national security threats were delivered to the National Stockpile under this program. Unfortunately, in fiscal year 2014, we shifted to annual appropriations for the Special Reserve Fund, which created an uncertainty where there was once confidence that there would be a markup for urgently needed new vaccines and treatments.

The market guarantee for successful MCM candidates is much weaker, and funding has dropped significantly. While Congress has many levers and options to incentivize development, many of these simply nibble around the edges and fall short of making up with the lack of long-term sustained funding. This Congress, I cofounded the Public Health Caucus to evaluate the conversation around public health and emergency preparedness.

We need to break the cycle of lurching from crisis to crisis, outbreak to outbreak, and invest in public health infrastructure and medical product development that protects us against current future threats. H.R. 3299 puts forth a range of reforms to improve MCM development and procurement response to emerging infectious diseases and hospital preparedness.

While I have some concerns about the aspect of the legislation, I believe we can find common ground and strike the right balance to protect the health and welfare of our Nation. And I want to thank the stakeholders for their willingness to work with us and look forward to learning more about their proposals in today's hearing.

And I want to thank, again, our panel and the chairman for calling this. I think sometimes we are not topical, but with Zika and 2 years ago Ebola and not telling what is coming next, this is a very important hearing.

And, Mr. Chairman, I will yield back my time.

Mr. PITTS. The Chair thanks the gentleman.

I now recognize the gentlelady, Mrs. Brooks, for 5 minutes for opening statement.

**OPENING STATEMENT OF HON. SUSAN W. BROOKS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF INDIANA**

Mrs. BROOKS. Thank you, Mr. Chairman.

I want to thank you so very much and the leadership of Energy and Commerce for holding this hearing today.

This legislation now enjoys significant bipartisan support from both sides of the aisle, including 21 members of Energy and Commerce, and I commend the chairman for understanding the urgency of this matter.

Imagine for a second if the weapons used in San Bernardino, Paris, or Brussels were not guns and bombs, but instead aerosolized smallpox. And this isn't farfetched. In fact, I learned last week at a simulation at the McCain Institute in Washington that this easily weaponized, highly contagious disease could result in the death of upwards of 1 million people if dispersed in Madison Square Garden alone.

That number is not just for New York City. But in reality, those expose individuals would have returned home infecting every person with whom they came into contact along the way. And for a disease with a 30-percent kill rate, responsible for the deaths of 300 million people in the 20th century alone, the fallout would be global and catastrophic.

So I have been working with my good friend from California, Congresswoman Eshoo, one of the original architects of Project BioShield, to develop a set of policy changes that could make a difference in the next outbreak or, God forbid, a terrorist attack. H.R. 3299 was developed in collaboration with leading experts in bio-defense, academia, first responders, and the private sector.

Among other things, this bill would reform contracting procedures at BARDA to ensure faster development of critical medical countermeasures and create a limited priority review voucher for diseases on DHS' material threat list. Returning this negotiating authority to BARDA will alleviate the bureaucratic red tape, make an immediate impact on the development of vaccines and treatments, and the new PRV program will spur development in an effective vaccine to stockpile against threats like Ebola, anthrax, or smallpox, which often take more than a decade and cost hundreds of millions of dollars.

So when you think about how we can improve our system, we could have possibly saved lives if we had an Ebola vaccine—thousands of lives—had it been deployed to West Africa. Or the Zika vaccine could have possibly already last spring have been in process and saved pregnant women in Brazil. The impact can be immeasurable if we make improvements and acknowledge that the system can be improved.

And so these are commonsense reforms. But they are not just coming from Congress. This Blue Ribbon Study Panel, the National Blueprint for Biodefense, listed 33 recommendations to improve our biodefense. It was authored by experts, some of whom have testified before our committee. It includes leaders such as former Senators Tom Daschle and Joe Lieberman; former Governor Ridge; Donna Shalala, the former HHS Secretary under President Clinton.

Now, a similar version of our bill has been authored by Senators Burr and Casey, and it has already passed out of the Senate Health Committee by a wide bipartisan margin. Preparedness is not a partisan issue. It has never been, and it shouldn't be treated as such again. And so I assure my colleagues that any concerns we might have with this legislation can be addressed in a bipartisan

manner because it is our duty to really support and protect the American people. I think that is Federal Government's top priority and must be our first priority.

I look forward to hearing from our witnesses, working with my colleagues to pass H.R. 3299.

And at this point, I would yield the remainder of my time to Dr. Burgess.

Mr. BURGESS. I thank you for yielding.

I thank the chairman for holding this hearing.

And recognizing the topic of this hearing is strengthening public health response, I hope we will spend some time visiting the recent past and expanding upon whether or not we have learned any lessons from what has happened to us in the past few years.

Almost in a twist of cruel irony, President Obama went to the CDC in Georgia and gave a talk that Ebola has not come—this was in September of 2014. He made the statement that Ebola has not come to this country, but if it does, we will be ready. Well, less than 2 weeks later, Ebola did come to our country. It came at the back door of a hospital in the middle of the night, wasn't recognized, the patient was sent home, eventually came back, eventually died, infected two other people in the hospital. So the second part of his statement was not operative. We were not ready.

And then I saw, with this problem literally in my backyard for the section several months, just how that not being ready, how that was manifest. We didn't have the type of direction for people. And the first responders in our emergency rooms, they didn't have the type of protective equipment. What was posted on the CDC Web site was woefully inadequate, as we unfortunately learned later, when two nurses were infected at the hospital.

When people were looking for the type of protective clothing that they would need, if someone showed up in the middle of the night of their emergency room, how can they get an additional moon suit or two? Do they call a hospital across town? Are they going to be willing to give up their moon suit because they could have a patient coming in within the hour with the same set of symptoms?

I hope we have explored these situations. I hope we have learned from them. One of, I think, the biggest weaknesses from 2 years ago was the lack of a single repository, a single place that a hospital administrator or manager or doctor could call to be able to access the equipment from the National Stockpile.

So, Mr. Chairman, thank you for calling the hearing. I look forward to the testimony of our witnesses, and I think this is a timely topic. I yield back.

Mr. PITTS. The Chair thanks the gentleman.

I now recognize the ranking member of the full committee, Mr. Pallone, 5 minutes for an opening statement.

**OPENING STATEMENT OF HON. FRANK PALLONE, JR., A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY**

Mr. PALLONE. Thank you, Mr. Chairman.

Since the attacks of September 11, Congress has worked in a bipartisan manner to increase our efforts to combat and respond to

biological threats. However, experts have repeatedly warned that our ability to respond to biological threats must be improved.

Earlier this year, the Subcommittee on Oversight and Investigations heard from another member of the Blue Ribbon Panel on Biodefense and other experts about the U.S.' biodefense preparedness. According to this report, the United States, quote, "does not afford the biological threat the same level of attention as it does other threats," unquote. The report notes that we lack a centralized leader for biodefense, a comprehensive national strategic plan, and a dedicated budget for biodefense. And this review also offered 33 recommendations about how Congress and the administration can improve our preparedness.

H.R. 3299, the Strengthening Public Health Emergency Response Act, includes a number of provisions that would make progress in improving our readiness. While I support the intent of this legislation, I do have some concerns that I am interested in discussing with our panel today.

One area is related to the hospital preparedness program. This legislation would limit the amount of funding that the Assistant Secretary for Preparedness and Response can use to operate this program to 3 percent of the program's total funding. And I am concerned that this limitation, while well-intended, could limit the ability of ASPR to effectively oversee and evaluate the hospital preparedness program. And this limitation also would eliminate funding for other efforts that support our healthcare preparedness, response, and recovery ecosystem. So this is one thing we need to look at.

I am also concerned about the delegation of contract authority to the Biomedical Advanced Research and Development Authority, or BARDA. Like other HHS divisions, ASPR operates the contracting office for all divisions and programs under its authority. This structure ensures that Federal investments are made through a fair and open process that is free of any conflicts. Removing ASPR oversight could lead to some influence on the contracting process by the BARDA Director, another program officer and outside source.

Then, finally, I want to express some concern about further expanding the Tropical Disease Priority Review Voucher Program. This program, created in 2007, was intended to incentivize research and development of drugs to treat tropical diseases that disproportionately affect poor and marginalized populations. Once a qualifying drug is approved, the sponsor receives a priority review voucher that entitles the sponsor to a second 6-month review of any other human drug application, and the sponsor is also able to sell this voucher.

Recently, a priority review voucher sold for \$350 million. Since creation of the Tropical Disease PRV Program, three PRVs have been awarded, and there has been a significant interest from industry and others in expanding the program as a way to encourage development of medical countermeasures.

While I believe we should explore additional ways to incentivize medical countermeasure development, I do not believe expanding the Tropical Disease PRV Program is necessarily the answer. Not only could expansion decrease the value of a PRV and the incentive to develop drugs under such programs, but it also increases the

burden on FDA to expedite review of additional applications that may not otherwise qualify for expedited review.

I am concerned that expansion would only exacerbate known flaws in the current program. For example, current law requires FDA to award vouchers to sponsors even if a drug was previously approved in other countries. Additionally, there is no requirement that a sponsor market a product approved under the program; therefore, there is no guarantee that these drugs are actually helping.

So I look forward to hearing from our Government witnesses on these issues. And as the committee moves forward, I hope there will be an opportunity for members to hear from additional stakeholders.

I would like to yield the minute I have left to Mr. Butterfield. Oh, he left, OK.

Then I yield back.

[The prepared statement of Mr. Pallone follows:]

#### PREPARED STATEMENT OF HON. FRANK PALLONE, JR.

Thank you, Mr. Chairman. Since the attacks of September 11th, Congress has worked in a bipartisan manner to increase our efforts to combat and respond to biological threats. However, experts have repeatedly warned that our ability to respond to biological threats must be improved.

Earlier this year, the Subcommittee on Oversight and Investigations heard from members of the Blue Ribbon Panel on Biodefense and other experts about the U.S.'s biodefense preparedness. According to this report, the United States "does not afford the biological threat the same level of attention as it does other threats." The report notes that we lack a centralized leader for biodefense, a comprehensive national strategic plan, and a dedicated budget for biodefense. This comprehensive review also offered 33 recommendations about how Congress and the administration can improve our preparedness.

H.R. 3299, the Strengthening Public Health Emergency Response Act, includes a number of provisions that would make progress in improving our readiness.

While I support the intent of this legislation, I do have some concerns that I am interested in discussing with our panel of witnesses today. One such area is related to the Hospital Preparedness Program. This legislation would limit the amount of funding that the Assistant Secretary for Preparedness and Response can use to operate this program to three percent of the program's total funding. I am concerned that this limitation, while well-intended, would limit the ability of ASPR to effectively oversee and evaluate the Hospital Preparedness Program. This limitation also would eliminate funding for other efforts that support our health care preparedness, response, and recovery ecosystem. This change may harm rather than strengthen our health system preparedness.

I am also concerned about the delegation of contract authority to the Biomedical Advanced Research and Development Authority or BARDA. Like other HHS divisions, ASPR operates the contracting office for all divisions and programs under its authority. This structure ensures that Federal investments are made through a fair and open process that is free of any conflicts. Removing ASPR oversight could lead to undue influence on the contracting process by the BARDA Director, another program officer, or an outside source.

Finally, I want to express serious concerns about further expanding the tropical disease priority review voucher program. This program, created in 2007, was intended to incentivize research and development of drugs to treat tropical diseases that disproportionately affect poor and marginalized populations. Once a qualifying drug is approved, the sponsor receives a priority review voucher that entitles the sponsor to a second six-month review of any other human drug application. The sponsor is also able to sell this voucher. Recently, a priority review voucher sold for \$350 million. Since creation of the tropical disease PRV program, three PRVs have been awarded.

There has been significant interest from industry and others in expanding this program as a way to encourage development of medical countermeasures. While I believe we should explore additional ways to incentivize medical countermeasure devel-

opment, I do not believe expanding the tropical disease PRV program is the answer. Not only could expansion decrease the value of a PRV and the incentive to develop drugs under such programs, but it also increases the burden on FDA to expedite review of additional applications that may not otherwise qualify for expedited review. This undermines the agency's public health mission.

I'm concerned that expansion would only exacerbate known flaws in the current program. For example, current law requires FDA to award vouchers to sponsors even if a drug was previously approved in other countries. Additionally, there is no requirement that a sponsor market a product approved under the program. Therefore, there is no guarantee that these drugs are actually helping the people Congress intended to help.

I look forward to hearing from our Government witnesses on these issues. And, as the committee moves forward with this legislation, I hope there will be an opportunity for Members to hear from additional stakeholders about these concerns and how they can best be addressed.

Thank you.

Mr. PITTS. The Chair thanks the gentleman.

Mr. PALLONE. Mr. Chairman, could I ask, I had three letters I would like to, unanimous consent, to enter into the record, one from Kids v Cancer, regarding added medical countermeasures to the Tropical Disease PRV Program; a letter from David Ridley, the architect of the Tropical Disease PRV Program and his Health Affairs article regarding the impact of expanding the program; and a third from Trust for America's Health.

Mr. PITTS. And I would like to add to that one letter from the Blue Ribbon Study Panel on Defense.

So, without objection, these are put into the record.

[The letters appear at the conclusion of the hearing.]

Mr. PITTS. As usual, all members' opening statements will be made a part of the record. And we will now introduce the panel. We have one panel today, and I will introduce them in the order of their presentation.

First, we have Dr. Richard Hatchett, Acting Director, Biomedical Advanced Research and Development Authority, BARDA, and Acting Deputy Assistant Secretary in the Office of the Assistant Secretary for Preparedness and Response, ASPR, U.S. Department of Health and Human Services. Secondly, we have Mr. Michael Mair, Director of Strategic Operations, Office of Counterterrorism and Emerging Threats in the Food and Drug Administration; finally, Colonel Russ Coleman, Ph.D., Joint Project Manager, Medical Countermeasures Systems, Department of Defense.

Thank you for coming today. Your written testimony will be made part of the record. You will each have 5 minutes to summarize your written testimony.

So, Dr. Hatchett, you are recognized for 5 minutes for your summary.

**STATEMENTS OF RICHARD J. HATCHETT, M.D., ACTING DEPUTY ASSISTANT SECRETARY, OFFICE OF THE ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE, ACTING DIRECTOR, BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY, DEPARTMENT OF HEALTH AND HUMAN SERVICES; MICHAEL MAIR, DIRECTOR OF STRATEGIC OPERATIONS, OFFICE OF COUNTERTERRORISM AND EMERGING THREATS, FOOD AND DRUG ADMINISTRATION; AND COLONEL RUSSELL E. COLEMAN, PH.D., JOINT PROJECT MANAGER FOR MEDICAL COUNTERMEASURES SYSTEMS, JOINT PROGRAM EXECUTIVE OFFICE FOR CHEMICAL AND BIOLOGICAL DEFENSE, DEPARTMENT OF THE ARMY, DEPARTMENT OF DEFENSE**

**STATEMENT OF RICHARD J. HATCHETT**

Dr. HATCHETT. Chairman Pitts, Ranking Member Green, Mrs. Brooks, Ms. Eshoo, distinguished members of the House Energy and Commerce Committee, thank you for the opportunity to testify today regarding biosecurity issues and H.R. 3299, the Strengthening Public Health Emergency Response Act.

I am Dr. Richard Hatchett, the Acting Director of BARDA, and I will focus on steps taken by ASPR to strengthen our Nation's health security and the contributions of my own office toward that end.

We have made substantial progress in the past 10 years to advance the state of our national biodefense. Thanks to the support of this committee and others in Congress, we have established ASPR and BARDA and made critical investments in biodefense and our healthcare system. However, as highlighted by recent challenges, such as Ebola and Zika, there remain gaps in our preparedness.

Where the civilian public health and medical response to such events is concerned, the ASPR is charged by statute to play a strong leadership role. The ASPR serves as a principal adviser to the Secretary of HHS on all matters related to Federal medical preparedness and response for public health emergencies.

The ASPR is the author and custodian of the National Health Security Strategy, which focuses on protecting public health during an emergency. The ASPR chairs the Public Health Emergency Medical Countermeasures Enterprise, or PHEMCE, which coordinates medical countermeasure development efforts across the interagency. And the ASPR oversees the Hospital Preparedness Program, or HPP, which enhances medical preparedness and resiliency at the community level through its support of healthcare coalitions, which incentivize diverse and often competitive healthcare organizations to work together.

The health of communities is deeply intertwined with the abilities of its institutions to provide care to all populations. And investments in HPP are critical to limiting the cascade of negative health effects caused by disasters. The PHEMCE promotes the development and acquisition of medical countermeasures for chemical, biological, radiological, and nuclear threats, pandemic influenza, and emerging infectious diseases. And it has achieved a record of success that is now being studied as a model for global preparedness.

The strong and direct incentives we have put in place to support the development of medical countermeasures work. The PHEMCE has achieved technical success. BARDA has achieved technical success. Twenty three products that BARDA has supported have received FDA approval, licensure, or clearance. And the pace of success is accelerating. Fourteen of these approvals have occurred since 2011, and five have occurred in the last 14 months.

Seventeen products, ranging from anthrax antitoxins to an array of products for the management of thermal burns, have been procured for the Strategic National Stockpile under Project BioShield, with another seven anticipated between now and the end of fiscal year 2018. Over the last decade, we have honed a model of public-private partnership that works. It depends on combining push-and-pull incentives in the form of nondiluted funding and guaranteed market commitments with access to subject-matter expertise and product development services. We thank you for your continued support and sustained commitment to these programs.

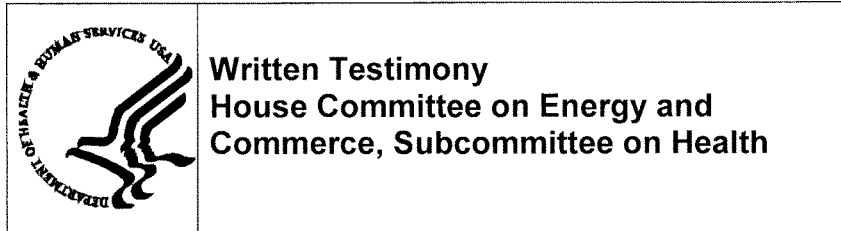
To support BARDA's activities, ASPR has established a separate Office of Acquisitions, Management, Contracts, and Grants, or AMCG. AMCG is an award-winning and innovative contracting office that has led the Department in meeting contracting timelines, and its independent line of reporting mitigates potential conflicts of interest and ensures the highest standards of program integrity.

AMCG can work fast. While the departmental benchmark for contract actions is 180 days, 70 percent of our Ebola contract actions were awarded within 60 days. And the median time for recent Project BioShield and other major acquisition awards was 90 days from the publication of the RFP. And AMCG is fair. Last year, over 95 percent of ASPR's contract actions were competed, ensuring a level playing field for businesses capable of meeting HHS requirements. Fifty-one percent of eligible contract dollars were awarded to small businesses.

These investments in preparedness have already paid dividends. Because of the workforce in capabilities ASPR has developed over the last 9 years, we and our Nation's communities are much better prepared to respond quickly to disasters and emerging threats.

Thank you again for the invitation to speak with you, and I look forward to addressing your questions.

[The prepared statement of Dr. Hatchett follows:]



**“Public Health Emergency Response”**

*Statement of*

**Richard J. Hatchett, MD**

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



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Chairman Pitts, Ranking Member Green, and distinguished Members of the House Energy and Commerce Committee, thank you for the opportunity to testify today regarding biosecurity issues and H.R.3299, the Strengthening Public Health Response Act. I am Dr. Richard Hatchett and I serve as the Acting Director of the Biomedical Advanced Research & Development Authority (BARDA) and as an Acting Deputy Assistant Secretary for Preparedness and Response. BARDA is a component of the Office of the Assistant Secretary for Preparedness and Response (ASPR). The ASPR, Dr. Nicole Lurie, serves as the principal advisor to the Secretary of Health and Human Services (HHS) on all matters related to federal medical preparedness and response for public health emergencies.

Securing our nation against biological threats is a challenging endeavor. The array of threats for which we must be prepared is vast. Such threats include bioterrorist agents such as anthrax, smallpox, and botulism; evolving and emerging threats causing substantial regional disruption such as Ebola and Zika; and highly communicable diseases with pandemic potential such as influenza. In the last fifteen years, the world has experienced the first influenza pandemic in 40 years, devastating outbreaks of foot-and-mouth disease, anthrax attacks, the re-emergence of cholera in the Western Hemisphere, the largest Ebola epidemic ever recorded, and the global dissemination of vector-borne viral diseases such as chikungunya and Zika.

Thanks to lessons learned from previous responses, biomedical breakthroughs, and sound strategic investments, we have improved our preparedness for and capability to respond to a wide-range of threats regardless of their origin and properties. We have read with interest the report and recommendations of the Blue Ribbon Study Panel on Biodefense, which I know to be

of interest to this Committee. With that in mind, I would like to update you on some of the areas in which ASPR and BARDA have progressed in recent years.

ASPR has made numerous improvements to ensure national health security and to protect the American people. One such improvement is the development and continued refinement of the National Health Security Strategy (NHSS), which unified a patchwork of public health and medical preparedness, response, and recovery strategies. The NHSS works to ensure that the nation is prepared for, protected from, and resilient in the face of public health threats. The NHSS is the first strategy specifically focused on protecting public health during an emergency. It envisions resilient and strong communities with sustainable health and emergency response systems. The NHSS, with its accompanying implementation plan, lays out actionable goals and objectives to achieve these ends.

Among her many responsibilities, the ASPR serves as the chair of the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE). The PHEMCE is a standing virtual enterprise that coordinates the entire life cycle associated with the development and procurement of medical countermeasures. It was created explicitly to improve coordination and collaboration within the Department and with our external stakeholders, including nonprofits, other federal departments, the private sector, and the international community.

The PHEMCE is comprised of ASPR, the National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), and the Food and Drug Administration (FDA), as well as the Departments of Homeland Security (DHS), Defense (DoD), Veterans Affairs, and

Agriculture. It has been uniquely successful in promoting the development and acquisition of medical countermeasures for chemical, biological, radiological and nuclear (CBRN) threats, pandemic influenza, and emerging infectious disease threats. PHEMCE activities are governed by the PHEMCE Strategy and Implementation Plan (SIP). The PHEMCE SIP is updated annually and describes the PHEMCE's governance and decision-making structure. One of the most important functions of the SIP is to provide clarity and guidance about PHEMCE objectives to our external partners and stakeholders.

PHEMCE coordination and decision-making encompass all stages of the medical countermeasure life cycle from identifying requirements and developing target product profiles through product development to distribution and dispensing. Agencies take responsibility and are held accountable for activities within their mission space and PHEMCE coordination establishes common priorities, facilitates joint decision making and information sharing, and ensures the smooth transition of products through development. The PHEMCE has an outstanding record of success and is now being studied as a model for global preparedness against emerging infectious diseases. It was established in 2007 and its processes have been iteratively refined and improved over the last 9 years.

Operationally, the PHEMCE establishes product-specific requirements for CBRN medical countermeasures based on Material Threat Assessments developed by DHS. NIH and DoD support discovery and early stage development of product candidates, often in collaboration with academic and industry partners, and prepare them for the transition to BARDA. In turn, BARDA supports and assists product candidates through advanced research and development,

including preparation for FDA review, until they are ready for acquisition under Project BioShield. After procurement, medical countermeasures are maintained at CDC's Strategic National Stockpile (SNS) locations or within virtual stockpiles maintained by commercial vendors (in so-called vendor-managed inventory). If advanced development data lead to FDA approval of a marketing application, the financial responsibility of purchasing medical countermeasures for stockpile and delivery transfers from BARDA under Project BioShield to SNS. Items that have not yet received FDA licensure can also be procured for the stockpile if they are eligible for use during an emergency under an Emergency Use Authorization.

During evolving public health emergencies, NIH, BARDA, and DoD may shift into response mode, interfacing with other federal agencies and manufacturers to develop, produce, and test products for FDA review and approval and (where necessary) distribution by CDC to state and local health departments. Our investments in preparedness have already paid dividends in this regard. Because of the workforce and capabilities we have developed over the last nine years, we are much better prepared to respond quickly to emerging threats. The PHEMCE, for example, advanced multiple vaccines and therapeutics and an innovative lateral flow diagnostic into clinical trials during the response to the Ebola epidemic and more recently has mobilized to support the development of vaccines, diagnostics, blood donor screening tests, and pathogen reduction technologies for Zika virus.

Within the overarching framework provided by the PHEMCE, BARDA supports the advanced research, development and procurement of medical countermeasures—vaccines, therapeutics,

antiviral and antimicrobial drugs, diagnostics, and medical devices. Advanced development includes critical steps needed to transform a candidate to a product that is ready to use. These steps include optimizing and validating commercial scale manufacturing processes; optimizing product formulations, storage, 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.

BARDA's considerable success with making available CBRN medical countermeasures derives from a business model that depends on a set of supporting incentives that can be likened to a three-legged stool. Each leg of the stool has proved critical to BARDA's success, and it was only after all three legs were firmly established that BARDA truly began to deliver on its promise.

The first leg is provided by Project BioShield funding, which serves as a market guarantee (or advanced market commitment) for products that otherwise might have no or very limited commercial prospects. Maintaining the integrity of this market guarantee has been critical to maintaining the confidence of our private sector partners as they undertake high-risk development programs. Project BioShield funding represents the government's bipartisan commitment to support private sector innovators who are willing to address unmet public health preparedness needs. With our private sector partners, we are building capacities to maximize a flexible, nimble response. We are also working across the government to ensure threats are identified, requirements are established, and the medical counter measures are in place to protect the nation's health. The need for medical countermeasures against threats is regularly assessed

and informed by DHS's Material Threat Determinations, to which threat information provided by the Intelligence Community contributes.

The second leg is provided by the classic push incentive of BARDA's advanced research and development contracts, grants, cooperative agreements, and other transactions. These funding vehicles provide firms with access to the substantial amounts of funding required to navigate the "valley of death" represented by late-stage clinical development. Small to mid-size biotechnology firms have found it virtually impossible to obtain funding from traditional capital markets for inherently non-commercial biodefense projects. Absent the push incentives that BARDA provides, these firms would not be able to advance their products to regulatory end points; they would simply die on the vine, victims of the market failure that underlies biodefense.

The third leg of the stool is the direct product development support that BARDA provides. Since most of BARDA's partners have been small to mid-size biotechnology firms that have gaps in their product development expertise and capabilities, BARDA has established an array of core services that it can bring to bear in support of its partners' product development efforts. These core services facilitate access to subject matter experts in a variety of disciplines germane to product development (such as clinical trial design, regulatory affairs, process engineering, etc.) as well as access to animal models and preclinical laboratories, a clinical studies network, a fill-finish manufacturing network, and BARDA's Centers for Innovation in Advanced Development and Manufacturing. These latter assets, which support BARDA's core mission of promoting biodefense product development, also enhance BARDA's response capability and collectively constitute BARDA's National Medical Countermeasures Response Infrastructure, which was

mobilized for the first time during the Ebola epidemic to accelerate the development of Ebola vaccines and therapeutics and is being engaged now to expedite the development of vaccines against Zika.

Since its creation, BARDA has built a comprehensive and formidable advanced development product pipeline that has supported close to 200 medical countermeasure development projects. To date, at least 23 medical countermeasures that BARDA has supported have been approved, licensed or cleared by FDA. Of these, 15 have been approved since 2011 and five have been approved in the last 14 months. Seventeen products, ranging from anthrax antitoxins and smallpox vaccines to anti-neutropenia cytokine therapeutics for radiation illness and an array of products for the management of thermal burns, have been procured under Project BioShield with another seven anticipated between now and the end of FY 2018. To better serve the needs of special populations, BARDA has funded the development of a smallpox vaccine (Modified Vaccinia Ankara) suitable for use in immunocompromised individuals as well as pediatric formulations of drugs like Prussian Blue (a treatment for internal radiation contamination) and solithromycin (an antibiotic candidate under investigation). BARDA has also supported the development and manufacturing of 18 influenza vaccines, antiviral drugs, and diagnostics that were either used in the 2009 H1N1 pandemic or stockpiled to enhance preparedness for H5N1 and H7N9 influenza viruses with pandemic potential.

To provide contracting support to BARDA's activities, ASPR has established a separate and specialized Office of Acquisitions Management, Contracts and Grants (AMCG) whose contracting authority is delegated from the HHS Senior Procurement Executive (SPE). This

independent line of reporting to the ASPR and the SPE mitigates potential conflicts of interest and maintains the highest standards of program integrity. AMCG is an award winning and innovative contracting office, having received the HHS Secretary's 2015 Hubert H. Humphrey Award for Service to America, the 2012 HHS Small Business Award, and the 2010 HHS Project Team Award for its contribution to the H1N1 Influenza Virus response. It introduced competitive solicitation procedures known as Broad Agency Announcements which streamline the acquisition process for basic and applied research, and initiated the use of Other Transaction Agreements to further engage industry.

AMCG has led the department in meeting contracting time lines. While the federal government and Department standard time line for awarding contracts is 180 days, AMCG awarded the majority of its Ebola contract actions within 60 days. In the same time frame (FY2014-FY2015), Project BioShield contracts were awarded within an average of 128 days from the publication of a Request for Proposals. In summary, ASPR awarded 91 grants totaling \$212,649,385.67 in FY 2015. During that fiscal year, 90 percent of ASPR's contract actions were competed, thereby ensuring that there is opportunity for businesses capable of meeting the needs of HHS to compete on a level playing field. Exceeding targets under the President's Small Business Initiative, ASPR awarded 51 percent of eligible contract dollars to small businesses. This also exceeded our own 35 percent small business goal.

The Federal Acquisition Regulation (FAR) provides flexibility in the event of an emergency to expedite contract award by the contracting officer. This emergency authority was recently put to use by AMCG in what U.S. News and World Report on March 18, 2016 called "an

unprecedented relief effort, [by] the federal government and blood banks in the United States... to provide the entire territory of Puerto Rico with safe blood to protect recipients from the Zika virus.” AMCG was notified on February 24, 2016 that FDA guidance recommended that—among other things—whole blood and blood components for transfusion be obtained from areas of the United States without active transmission and that blood collection in affected areas such as Puerto Rico would have to stop no later than March 1 until donor screening measures could be put in place to prevent transfusion transmission of Zika virus. Working closely with BARDA to define the actual requirement, conduct market research, obtain legal advice, and draft the contract document, the contracting officer awarded a \$4.6 million contract on March 3, 2016 to transport blood products from the U.S. mainland to Puerto Rico, six business days after being notified of the impending shortage. On March 5, 2016, Chris Hrouda, Executive Vice President of Biomedical Services for the American Red Cross, announced that nearly 5,000 units of blood and other products per week had commenced, enough to meet the whole territory's needs. These efforts by AMCG and BARDA prevented a public health crisis from becoming a medical crisis by demonstrating the flexibility, speed, and coordination with which the two offices can operate. As a result, a solution was eventually reached with the Roche blood screening.

ASPR strives to preserve health, mitigate suffering due to illness and injury, and expedite recovery through the development of resilient communities before, during, and after events ranging from bioterrorism attacks to natural disasters that impact public health and well-being. To achieve this goal, ASPR supports building preparedness capabilities and resiliency at the community level before disasters or public health incidents occur. ASPR's flagship program in this regard, the Hospital Preparedness Program (HPP), has provided approximately \$5.6 billion

to state, local, and territorial health departments since 2002 to better prepare the nation's health care systems and hospitals for man-made or natural disasters.

While hospitals remain at the center of a prepared health care system, events of the last decade, including the 2009 pandemic, the Joplin, Missouri tornado, and Superstorm Sandy, have highlighted how important it is for hospitals to work with one another and with other community health care entities, such as EMS and skilled nursing facilities, to prepare and execute a health care system response. Consequently, since 2012, HPP has emphasized the importance of regional health care coalitions to save lives during emergencies that exceed the day-to-day capacity of the health and emergency response systems. Health care coalitions (HCCs) incentivize diverse and often competitive health care organizations with differing priorities and objectives to work together. They ensure that each HCC member has the necessary medical equipment and supplies, real-time information, communication systems, and trained health care personnel to respond to an emergency, so that each patient impacted by a disaster receives the right care at the right place at the right time. The health of communities is deeply intertwined with the ability of its institutions to provide care to all populations and investments in HPP are critical to limiting the cascade of negative health effects that disasters can have on a community.

HCCs have already proven beneficial. For example, even as emergency crews were still onsite searching for survivors and victims of the 2015 Amtrak train derailment in Philadelphia, local health care facilities, emergency medical services, and emergency management agencies, all members of HPP-supported HCCs, were already in action, working together to facilitate a swift, coordinated response. Systems funded by HPP were able to send out notifications of emergency

room capacity to HCC members a full 30 minutes prior to the official city alerts. This enhanced communication provided responders real-time information on resources and capacity throughout the region. HCC members immediately activated another HPP-funded response platform to track and triage patients, facilitate the proper distribution of patients, and prevent any single hospital from being overburdened. The operational response of HCC members, along with their systems and training, allowed for an effective response within an organized incident command structure, thus saving lives, improving care, and increasing accountability.

ASPR has supported a number of recent initiatives to enhance the HPP program. In 2010, ASPR led an effort to ensure that HPP funding and its health care preparedness mission was better aligned with CDC's Public Health Emergency Preparedness (PHEP) cooperative agreement and its public health preparedness focus. This alignment reduced bureaucracy and administrative workload for both programs' awardees, and ensured the programs could leverage one another's work and avoid duplication. Alignment of the exercise requirements for both cooperative agreements and the integration of annual awardee meetings are just two examples of efficiencies that have been achieved through this process. Further, ASPR's and CDC's alignment efforts for HPP and PHEP also serve to ensure the programs are complementary.

Over the last several years, HPP has evolved from an individual health care facility capacity-building program to a health care system capability-development program. In 2012, ASPR identified eight national health care preparedness capabilities that awardees, health care coalitions, and health care facilities and organizations strive to achieve. These capabilities are sufficiently flexible to enable all-hazard planning for natural disasters, terrorist events, infectious

disease outbreaks, and industrial accidents. The capabilities are designed to facilitate and guide preparedness planning and to serve the needs of communities in every-day local emergencies as well as disasters eliciting state and federal disaster declarations. HPP awardees use the health care preparedness capabilities to identify gaps in their preparedness efforts and target investments to ensure that their communities are safer, more resilient, and better prepared. In a recent survey, HPP awardees indicated overwhelmingly that the Program's support—including funding, guidance, and technical assistance—is critical to developing, implementing, and maintaining health care preparedness capabilities. For example, 100 percent of awardees agreed or strongly agreed that HPP was critical to health care system preparedness, and 92 percent agreed or strongly agreed that HPP was critical to health care worker safety.

The HPP appropriation funds a health care preparedness, response, and recovery *ecosystem* that extends from day-to-day emergency department improvements to recovery from major disasters. Funding supports HPP cooperative agreements as well as a set of supporting federal efforts that help HPP awardees, coalitions, and health care facilities and providers prepare for and respond to emergencies. These include:

- The Technical Resources, Assistance Center, and Information Exchange (TRACIE), which ASPR launched in September 2015 to serve as a one-stop interchange for HPP awardees, health care coalitions, and other health system partners to gain access to best practices, guidance documents, and technical assistance as well as to share ideas and to collaborate with stakeholders on matters pertaining to healthcare emergency preparedness, response, recovery, and mitigation. TRACIE has responded to nearly 500 training and technical assistance requests in the eight months since the program launched;

the vast majority of those requests came from HPP awardees and coalition members.

TRACIE has received more than 35,000 visitors to the website, its listserv has nearly 5000 recipients, and more than 1300 individuals have registered as members of the program's Information Exchange.

- The Emergency Care Coordination Center within ASPR strengthens the day-to-day emergency care system so that the nation's emergency departments are better prepared in times of crisis.
- ASPR's Critical Infrastructure Protection for the Health Care and Public Health Sectors leads a public-private sector partnership focused on protecting the essential goods, services, and functions of health care and public health that, if destroyed or compromised, would negatively affect the nation. This program served a coordinating function during the Ebola outbreak to ensure that hospitals that served as Ebola Treatment Centers had the personal protective equipment they needed despite a national shortage. The program also leads the Department's health care cybersecurity work.
- ASPR's Division of Recovery advances the nation's ability to recover from the health and social services impacts of emergencies and disasters. ASPR's Recovery experts not only assist HPP awardees during and after emergencies, but they also promote pre-disaster health and social services recovery planning. Currently, ASPR's Recovery team is leading efforts to respond to the health and human services crisis in Flint, Michigan.

Infectious disease threats manifest in myriad forms and present unique challenges for preparedness and response. Fortunately, many of the lessons learned in responding to emerging infectious disease threats can inform our preparedness for acts of bioterrorism, while many of the

capabilities we have developed to promote preparedness for bioterrorism simultaneously enhance our preparedness for and ability to respond to natural threats.

What is required to respond effectively may differ substantially from agent to agent and over time within a given event, as recent crises demonstrate. To meet such threats, our nation requires an array of response capabilities, the ability to adapt in real time to changing circumstances, and robust mechanisms for coordination and communication. In the less than ten years that it has existed, ASPR and its component programs have made signal contributions in each of these areas and today play a critical role in preparing for public health and medical emergencies, whether natural or deliberate in origin. Through concerted effort over many years, ASPR has brought closer to realization the aspiration articulated in the NHSS of “National health security [as] a state in which the nation and its people are prepared for, protected from, and resilient in the face of incidents with health consequences.”

Mr. PITTS. The Chair thanks the gentleman.  
I will recognize Mr. Mair, 5 minutes for your summary.

**STATEMENT OF MICHAEL MAIR**

Mr. MAIR. Good morning, Chairman Pitts, Ranking Member Green, and members of the subcommittee. Thank you for the opportunity to discuss FDA's perspective on H.R. 3299, the Strengthening Public Health Emergency Response Act, which contains provisions intended to help improve preparedness for a response to chemical, biological, radiological, and nuclear, or CBRN, threats.

FDA plays a critical role in protecting the United States from deliberate CBRN threats and naturally incurring infectious diseases, such as Zika virus and pandemic influenza. FDA is responsible for ensuring that medical countermeasures, including drugs, vaccines, and diagnostic tests, to counter these threats are safe and effective.

We work closely with our interagency partners, including our partners seated here with me today, as well as with product developers to facilitate the development and availability of medical countermeasures. This collaboration has been extremely successful. 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 Countermeasures Enterprise.

As you know, H.R. 3299 contains a provision intended to help incentivize medical countermeasure development by enabling product developers to receive a priority review voucher, or PRV, under FDA's Tropical Disease PRV Program provided certain criteria are met. The PRV may be used by the product developer who receives it or sold to another product developer who may then use it to obtain priority review for a product application that otherwise would 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, the PRV enables the product developer to potentially bring a product to market sooner than it would under standard review time, which is valuable to product developers.

While FDA fully supports the intent in H.R. 3299 to further incentivize the medical countermeasure development, we do not believe that adding CBRN threats to the Tropical Disease PRV Program is likely to achieve that goal. Only three PRVs have been awarded to date under the Tropical Disease PRV Program since its inception in 2007, and these were for products that had been in development prior to the creation of the PRV program. Thus, it remains unclear at this time how effective this program is in spurring product development, particularly for new product development.

And even if PRV has ultimately proved successful in incentivizing product development, expanding the Tropical Disease PRV Program to CBRN threats 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 program to do what it is intended to do: incentivize product development.

As Dr. Hatchett noted, the U.S. Government already provides significant incentives to help facilitate medical countermeasure development, including funding for research and development, clinical trial costs, and procurement contracts, and extensive technical assistance throughout the development process. These incentives have been highly successful in facilitating the development of medical countermeasures required for emergency preparedness and response. Therefore, it is unclear that extending PRVs to CBRN threats is sufficient or even necessary to incentivize additional medical countermeasure development.

FDA is also very concerned that adding CBRN threats to the Tropical Disease PRV Program will have a negative impact on FDA's ability to support product development. PRVs are redeemed for products that would not otherwise qualify for priority review, such as drugs to treat conditions for which safe and effective therapies often already exist: for example, elevated cholesterol or diabetes.

The clinical trials for these applications are typically more numerous, involving thousands more patients, and more complex than for the types of products that would normally qualify for priority review. Reviewing such applications within the target 6-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.

If there are more PRVs being issued and redeemed as a result of the proposed expansion of the Tropical Disease PRV Program, FDA will have fewer resources available to review other marketing applications, including for serious diseases for which no available therapies exist.

These resource constraints will also undermine FDA's ability to conduct its portfolio of public health work from providing advice and guidance in the early stages to help facilitate product development, including for medical countermeasures, as well as to monitoring safety and approval. Given the uncertainty related to the utility of extending PRVs to CBRN threats and the potential negative unintended consequences associated with doing so, FDA believes Congress should approach the expansion of the PRV program to CBRN threats with caution.

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

Thank you, and I will be happy to answer any questions you may have.

[The prepared statement of Mr. Mair follows:]



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring, MD 20993

**STATEMENT OF  
MICHAEL MAIR, M.P.H.  
DIRECTOR OF STRATEGIC OPERATIONS  
OFFICE OF COUNTERTERRORISM AND EMERGING THREATS  
FOOD AND DRUG ADMINISTRATION  
DEPARTMENT OF HEALTH AND HUMAN SERVICES**

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

**STRENGTHENING PUBLIC HEALTH EMERGENCY RESPONSE ACT OF 2015**

**MAY 19, 2016**

**RELEASE ONLY UPON DELIVERY**

**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.<sup>1</sup>

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

<sup>1</sup> 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).<sup>2</sup> 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.<sup>3</sup> 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

<sup>2</sup> *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>.

<sup>3</sup> 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.<sup>4</sup> 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

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<sup>4</sup> 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.

Mr. PITTS. The Chair thanks the gentleman.  
I recognize Colonel Coleman, 5 minutes for your summary.

**STATEMENT OF RUSSELL E. COLEMAN**

Colonel COLEMAN. Good morning. Chairman Pitts, Ranking Member Green, and distinguished members of the subcommittee, thank you for the opportunity to testify on Department of Defense efforts to partner with industry on the development of medical countermeasures that threaten our deployed military forces. I am talking about chemical, biological, radiological, and nuclear agents, CBRN.

As the DOD Joint Project Manager for Medical Countermeasures Systems, my mission is the advanced development, procurement, and sustainment of FDA-approved diagnostics, vaccines, and therapeutics needed to protect the warfighters from these deadly hazards.

I am one of five Joint Project Managers within the DOD's Joint Program Executive Office for Chemical and Biological Defense, which is the material developer for the Department of Defense Chemical and Biological Defense Program, providing full-spectrum capabilities against CBRN attacks. Today, available economic and regulatory incentives have not succeeded in encouraging the industry to partner with the Department of Defense on the development of medical countermeasures against CBRN hazards.

In general, medical countermeasures against these threats for the military would be used in rare emergency situations. And the military market is small. We are talking, you know, a couple hundred thousand forces, not tens of millions or hundreds of millions. This market is small so that it is unlikely to yield an acceptable return on investment for our industry partners. And industry performers, in my talks with them, have indicated that return on investment is their top priority, and there is simply little or no benefit in targeting these low-likelihood, high-impact threats.

I personally believe that incentives are needed to inspire additional innovation in this market. There are a variety of potential incentives that could be used to encourage this investment, and the Department of Defense recognizes that the development of incentives will require a careful assessment of the risks and benefits that extend well beyond just the Department of Defense.

Please recognize that we are not idle in the face of the challenges we have. My organization is taking steps to increase the Department of Defense's ability to more rapidly develop and field medical countermeasures for the Joint Forces.

We have recently announced the award of an other transaction authority consortium specific for the development of medical countermeasures in order to make it easier for nontraditional defense contractors, such as pharmaceutical industry, to partner with the Department of Defense. The OTA is a special contracting vehicle that has flexibility that is appealing to the pharmaceutical companies.

Additionally, my office is standing up the DOD Medical Countermeasures, Advanced Development, and Manufacturing Capability, a dedicated and enduring capability to conduct advanced development and manufacturing of products for the warfighter. This facil-

ity will make it easier and more likely that small biopharmaceutical companies, with which the DOD already engages but who lack the necessary experience with the FDA and with manufacture and production, to actually succeed at filling our DOD role.

The bottom line is that the DOD is determined to field and fully fulfill those validated warfighter requirements that will provide those urgently required capabilities against CBRN threats. I applaud the conversation now ongoing as to which incentives can best meet those requirements and generate innovation in this area.

Thank you again for the opportunity to provide my perspective. I look forward to continued congressional efforts to achieve results for the warfighter and the taxpayer.

[The prepared statement of Colonel Coleman follows:]

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RECORD VERSION

STATEMENT BY

COLONEL RUSSELL E. COLEMAN, U.S. ARMY  
JOINT PROJECT MANAGER FOR MEDICAL COUNTERMEASURE  
SYSTEMS, JOINT PROGRAM EXECUTIVE OFFICE FOR CHEMICAL AND  
BIOLOGICAL DEFENSE

BEFORE THE

HOUSE ENERGY AND COMMERCE COMMITTEE  
SUBCOMMITTEE ON HEALTH

SECOND SESSION, 114<sup>TH</sup> CONGRESS

EXAMINING H.R. 3299, STRENGTHENING PUBLIC HEALTH RESPONSE  
ACT

MAY 19, 2016

NOT FOR PUBLICATION UNTIL RELEASED BY THE  
COMMITTEE ON ENERGY AND COMMERCE

Chairman Pitts, Ranking Member Green, and distinguished members of the Subcommittee, thank you for the opportunity to testify on Department of Defense (DoD) efforts to partner with industry to develop medical countermeasures to prevent or mitigate the health effects of chemical, biological, radiological, and nuclear (CBRN) threats to the Armed Forces. For the last three years, I have led the Joint Project Management Office for Medical Countermeasure Systems (JPM MCS), the organization within DoD's Chemical and Biological Defense Program that is ultimately responsible for the advanced development, procurement, and sustainment of Food and Drug Administration (FDA) approved diagnostics, vaccines, and therapeutics needed to protect warfighters against CBRN threats on the battlefield. JPM MCS is one of five joint project managers within DoD's Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD). During my tenure at JPM MCS, we have instituted a range of improvements intended to enhance our ability to deliver capabilities to the force; however, there are some fundamental challenges that require assistance which the DoD cannot provide. I therefore greatly appreciate the opportunity to discuss incentives that will improve the ability of the DoD to deliver medical countermeasures against CBRN hazards.

Available economic and regulatory incentives have not succeeded in encouraging industry to partner with DoD on the development of medical countermeasures against CBRN threats. In general, medical countermeasures against CBRN hazards will be used in rare, emergency situations. The market for these medical countermeasures is small and is unlikely to yield an acceptable return-on-investment (ROI) for our industry partners. Industry performers have indicated that ROI is their top priority and there is simply little or no benefit to targeting these low-likelihood, high-impact CBRN threats. Further narrowing the potential ROI for industry is the limited size of the military population versus the entire U.S. population. Accordingly, I believe incentives are needed to inspire additional innovation in this market. There are a variety of potential incentives that could be used to encourage this investment, and DoD recognizes that the

development of incentives will require a careful assessment of risks and benefits that extend beyond DoD.

Make no mistake, however, we are not idle in the face of this challenge. JPM MCS is taking steps to increase DoD's ability to more rapidly develop and field medical countermeasures against CBRN hazards. For instance, in order to make it easier for non-traditional defense contractors such as pharmaceutical companies to partner with DoD, we recently announced the award of an Other Transaction Authority (OTA) consortium for the development of medical countermeasures against CBRN threats. An OTA is a special contracting vehicle with flexibility regarding certain procurement regulations and statutes and is available to federal agencies for the purpose of obtaining or advancing their research and development priorities. On behalf of JPM MCS, the U.S. Army Contracting Command has entered into an OTA with the National Chemical and Biological Defense Consortium for a period of 20 years.

Additionally, JPM MCS is establishing the DoD Medical Countermeasures Advanced Development & Manufacturing Capability (MCM ADMC), a dedicated and enduring capability to conduct advanced development and manufacturing of medical countermeasures for distribution to meet warfighter needs. In coordination with the Department of Health and Human Services Centers for Innovation in Advanced Development and Manufacturing, the DoD MCM ADMC will promote competition and incentivize businesses to compete by making it more likely small innovator biopharmaceutical companies that lack the FDA regulatory and production experience can and will succeed at fulfilling DoD requirements. This broadens the community of potentially capable and potentially interested performers.

DoD depends on small contractors to address our requirements for medical countermeasures, because, as noted, large pharmaceutical companies have been unwilling to join in ventures with the Government to address the DoD requirement

given the limited market potential for the resulting end products. DoD's MCM ADMC effort will be a place where small innovators can access expertise and technology to navigate the complex processes and challenges of medical countermeasure development and production. This \$205 million project was undertaken in response to a directed requirement from the White House in 2010.<sup>1</sup>

DoD is determined to fulfill validated warfighter requirements for medical countermeasures against CBRN threats. I applaud the conversation now ongoing as to which incentives are best to generate innovation and results. DoD is an essential participant in the discussion and is well positioned to take advantage of improvements in this challenging market. The National Chemical and Biological Defense Consortium OTA and the Medical Countermeasures Advanced Development & Manufacturing Capability are just two examples of actions we are taking now to remain as ready as possible in an uncertain world. Thank you again for the opportunity to provide my perspective. I look forward to continued Congressional efforts to achieve results for the warfighter and taxpayer.

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<sup>1</sup> Brennan, John O. (2010, December 29) *Medical Countermeasures Against Biological and Other Public Health Threats* [Memorandum]. Washington, DC: The White House.

Mr. PITTS. The Chair thanks the gentleman.

We are voting on the floor. We still have time to begin questioning, so I will begin the questioning. I recognize myself 5 minutes for that purpose.

Colonel Coleman, the Department of Homeland Security has identified 13 material threats to U.S. national security. Would a PRV for threats on the material threat list help develop new MCMs for DOD? And why is it so important that we make sure these products are developed?

Colonel COLEMAN. Thank you, sir. There is a Department of Homeland Security threat list, the material threat list, and a DOD threat list. They have many commonalities. So I believe that the availability of PRVs for agents on that material threat list would be of value to the Department of Defense.

As to the second part of your question, why is this necessary for the Department of Defense? We face a myriad of threats on the battlefield. Our environment is fundamentally different from that face defending the homeland. We deploy our military forces to remote areas of the world where we have an austere environment, limited resources, difficult situations. And so the situation for the military is not the same as for the homeland.

There are a myriad of threats that we face, and we don't have capabilities against many of them. We recognize the need, and we have ongoing problems and programs. The best example I can highlight is Ebola virus in the recent outbreak that is so fresh in our minds. I deployed to Zaire in 1995 as part of a small team dealing with an Ebola outbreak. At that time, I was given a thermometer. This was the medical countermeasure available. Take your temperature, and we will throw you in the isolation ward.

Flash forward 20 years, and while the Government has been actively involved in developing countermeasures for Ebola virus, what did we have? We did not have FDA-approved products. Yes, we had experimental compounds that all of us worked to make available to help save lives, but we had not been able to get them over the finish line. From my personal perspective, again, for the military, it is the lack of industry interest just because of the lack of return on investment.

We wish that, for our military needs, we would have a large enough guarantee that we would buy enough product to make it worthwhile. That is just not the case for the military. So alternative incentives, in my mind, could replace the return on investment. Now, I have to caveat, these are my personal perspectives and not a Department of Defense position. There is no real position from the Department of Defense on the value of priority review programs, but there is great interest in better understanding the incentives that could be made available.

Thank you, sir.

Mr. PITTS. Thank you.

Mr. Mair, you said, in 2009, in an article that you authored, quote: "Priority review vouchers are an innovative, high-impact, low-cost mechanism for encouraging the development of new medicines and vaccines for infectious diseases," end quote.

In your testimony, you say that concern that extending the Tropical Disease PRV Program to CBRN threats may not effectively

incentivize medical countermeasure development. Have you changed your position? Explain, you know, the change there.

Mr. MAIR. Thank you. So back when I wrote about the value—potential value of PRVs for CBRN threats, I initially got—it was initially not even a program that was anything but an idea back in 2007 when I initially published on that. And at that time, PRVs were only an idea, and then since that time, Congress created the Tropical Disease PRV Program, and then we also have now a pediatric rare disease PRV program.

So both of those programs now exist, and they have a lot of products that you could get through under that. So my concern at this point is twofold: One is that to continue to increase the program will reduce the value of the vouchers. And so it is unclear that to keep growing the program is going to undermine the program. And so there is that problem and also the issue of the effect on FDA's ability to conduct its work. At the time, I didn't appreciate that because I was not in Government. And it sounded at the time like it was reasonable that FDA could charge an extra user fee and they would be able to bring on extra staff to do the extra work associated with those PRV reviews. But it turns out that it doesn't work that way because we can't just staff up quickly because those fees are one time and unpredictable.

And so the effect on FDA's ability to do its other work is sort of balanced against the value of the PRV. And also, at this time, it is not even clear that these PRVs are really valuable to the developers who might get them, especially if we continue to grow the program and they become less valuable.

Mr. PITTS. Thank you.

I have a question for you, Dr. Hatchett, but my time is expired for now, so I will recognize the ranking member.

Mr. Green, 5 minutes for questions.

Mr. GREEN. Thank you, Mr. Chairman.

Dr. Hatchett, thank you for joining us today. I think it is important to understand each element of H.R. 3299. I would like to focus on the provision which would give BARDA its contracting authority. When BARDA was created in 2006, Congress gave the agency sole authority to negotiate and execute medical countermeasure contracts to ensure that it would react quickly to the development of vaccines and appropriate solutions.

My understanding is that the contracting was moved from BARDA to AMCG in 2009 in order to streamline ASPR's internal process. However, I heard from stakeholders that this transition has several unintended consequences which serve to slow down the procurement process for medical countermeasures. For example, companies often respond to BARDA requests to submit proposals with a 24 to 48-hour turnaround only to have these proposals languish in the AMCG's review process for multiple weeks or months.

Countermeasure and development is critical to our national security and requires a more urgent and efficient contracting process than traditional grants at HHS. Though I am sure AMCG is well intended, they do not appear best suited to deal with the complexities of vaccine or medical countermeasures development the way BARDA does.

Dr. Hatchett, I know you have only been on a job for a couple of months, but do you believe that we could achieve more efficiencies in the contracting process? If so, what recommendations would you have for this committee?

Dr. HATCHETT. Thank you, Mr. Green. Thank you for the question.

Let me address the major part of the question first, which is whether I think that we should move the contracting activity within ASPR back into BARDA. And I actually do not think that we should do that. There were good reasons of policy, as opposed to just streamlining ASPR's contracting activity, that underlay the decision to move that contracting activity out of BARDA and to have it provide a separate line of reporting directly to the Assistant Secretary for Preparedness and Response.

Having the independent contracting authority provides checks and balances, obviously. It helps ASPR conduct its business with autonomy, without either the perception or potentially the reality of undue influence by the BARDA Director. And it allows the Assistant Secretary, which is a Senate-approved Presidential appointment, to provide direct oversight of the contracting activity within ASPR.

Mr. GREEN. I have got some other questions. And I understand the separation of powers and the checkpoints, but I also know that, if it is an emergency, you know, for the companies to submit the contract within 48 hours, why would it take months to do it if we actually had an emergency that we needed? And a good example is Zika, which we are experiencing right now.

Dr. HATCHETT. So Zika is a good example. Thank you for that question. When it is an emergency, our AMCG, our contracting office can act very, very rapidly. In fact, during the Zika crisis, there was an incident that was potentially going to turn into a medical crisis where FDA issued guidance about the collection of blood in areas where ongoing Zika transmission was occurring, and it was going to require blood collection in areas with active Zika transmission to be stopped.

We learned about the impact that this was going to have on Puerto Rico, which could potentially produce a medical crisis there, on February 24, and within 6 business days, our contracting office had issued contracts to support the emergency delivery of blood to Puerto Rico. And 1 day after the contract was issued, blood supplies began to be moved to Puerto Rico. That was in Zika.

During—

Mr. GREEN. And I appreciate that, you know, but, again, we all have to be on our toes. Two years ago, it was Ebola, and now it is Zika. And, you know, where I come from in Texas, we have a lot of other challenges that—but I appreciate it.

What other serious infectious disease threats is ASPR and BARDA monitoring and is concerned about the potential impact on public health? And what sustained approaches and questions and steps can be taken to prepare for emerging threats before they reach the level of being immediate and urgent public health concerns?

Dr. HATCHETT. So we are constantly scanning to act proactively if we detect emerging threats. We are, for example, paying very

close attention to the yellow fever outbreak in Angola at present and monitoring the manufacturing capacity in status of yellow fever vaccine stockpiles. We certainly are continuing to monitor Ebola. We are working very closely with the international community. There is an ongoing effort right now to prioritize known emerging pathogens in terms of the potential threat they face.

Mr. GREEN. OK. Mr. Chairman, thank you. I would like to ask unanimous consent to place in the record a letter from the Doctors Without Borders.

Mr. PITTS. Without objection, so ordered.

[The letter appears at the conclusion of the hearing.]

Mr. PITTS. We are voting on the floor. We still have a couple of minutes left to vote. There are 11 votes, so we are going to stand in recess until the conclusion of those votes. It should be around 11:30.

So, without objection, the committee stands in recess.

[Recess.]

Mr. PITTS. All right. Thank you for your patience. The time of recess having expired, we will reconvene the hearing.

And the Chair now recognizes the gentlelady from Indiana, Mrs. Brooks, for 5 minutes of questions.

Mrs. BROOKS. Thank you, Mr. Chairman.

And I would ask unanimous consent to provide to the record five letters of support for a bill, H.R. 3299: one from Douglas Bryce, Joint Program Executive Officer for Chemical and Biological Defense from the Department of the Army; one from the Alliance for Biosecurity; one from the California Life Sciences Association; one from the Biotechnology Innovation Organization; and one that is categorized from a number of venture capital firms.

Mr. PITTS. Without objection, so ordered.

[The letters appear at the conclusion of the hearing.]

Mrs. BROOKS. Thank you.

Dr. Hatchett, I realize that you have only taken over very recently as the BARDA Director, as recently as last month, but I am curious, and I would like to share with you some statements that your predecessor, Dr. Robin Robinson, told this committee under oath last year in November of 2015.

He was asked the question if he believed that additional incentives were needed to get the private sector involved in the medical countermeasures development, and he answered yes.

He also, when asked if he believed that creation of a priority review voucher limited to the material threats identified by DHS would be a useful incentive for the private sector, he answered yes to that as well.

And when asked if he believed Congress gave BARDA the unique contracting authority based on its unique national security mission, he answered originally yes.

When asked if it would be helpful to further expedite the medical countermeasures contracting process, he answered yes.

And, finally, he asked if it would be helpful, most directly, for BARDA to have direct control over its advance development and procurement contracts as it has in the past. And he indicated, whatever would be helpful, whatever we could do, yes.

And so could you please explain the agency's and the leader of the agency's dramatic shift in thinking? And I appreciate your praise of, you know, ASPR's contracting authority and so forth, but how is it that the leader of BARDA previously has a 180-degree different view than you do?

Dr. HATCHETT. Thank you for giving me the opportunity to address that. Would you like me to address the question about incentives in the priority review voucher first, or would you like me to tackle the contracting?

Mrs. BROOKS. Whichever you prefer.

Dr. HATCHETT. OK. Let me start with the incentives question.

We are very concerned about ensuring that we have appropriate incentives in place to support medical countermeasure development. As you and the members of the committee know, most of the medical countermeasures do not have viable commercial markets that can justify their existence. And in the absence of an appropriate set of incentives—and I do think it is important that we have a set of incentives—that development just will not take place. And it has taken us over a decade to get a set of incentives in place that have begun to show results, as I mentioned in my original testimony.

I believe, with respect to the priority review vouchers, that—I certainly also hear from our partners in industry about their interest in seeing the priority review voucher being extended into this space. My perception is that the reason they are interested in seeing a priority review voucher extended into this space—a priority review voucher is what we call a pull incentive. It is a prize for delivering, you know, the goods. It is not to help them perform research, but it is something that we give them when they succeed. We—

Mrs. BROOKS. But just, if I could clarify—

Dr. HATCHETT. Yes, ma'am.

Mrs. BROOKS [continuing]. This involves no taxpayer dollars. Is that correct?

Dr. HATCHETT. The priority review voucher does have costs. They are distributed differently. It is not a direct taxpayer-dollar-funded incentive.

But it is a pull incentive, because if a company can receive a priority review voucher, then they have this prize which they can trade on the open market, and it provides potentially a great deal of value to the company.

My perception is that the companies that have expressed support for this are expressing support for a new pull incentive because of their concern about our collective commitment to the biodefense enterprise. Without a sustained, substantial commitment to supporting medical countermeasure development, they, I believe, view the addition of a new incentive as potentially valuable.

I believe that the incentives that we have in place, if they are sustained and fully supported, are demonstrating that they can work. And that is why I differ with my predecessor about the value of a priority review voucher. I understand the interest in the priority review voucher. I am not denying that it serves as a pull incentive. But I believe there are more direct and less deleterious ways that we can achieve success.

Mrs. BROOKS. But would you agree with me, though, it is certainly not just the private-sector companies who engage in this space. It also was endorsed in a significant way by the National Blueprint for Biodefense by the blue-ribbon panel. And so a number of experts for a long period of time believed that this would be the way forward. In fact, it is a number of their recommendations.

Dr. HATCHETT. We are very interested in looking at all potential incentives that can be brought to the table.

And the one other thing that I would say is that, in the various spaces that we work in, for CBRN threats, for pan flu, for antimicrobial resistance, and now for emerging diseases, the market failures for each of those areas differ, and I believe that they will require potentially different sets of incentives to achieve success against each of those threats.

Mrs. BROOKS. Thank you.

Mr. Chairman, I failed to also ask if we could submit for the record—I know that you, I believe, in your questioning, mentioned prior articles written by Dr. Mair. And I have two articles with respect to the priority review vouchers and the value that I would like to submit for the record written, in part, by Dr. Mair.

Mr. PITTS. Without objection, so ordered.

[The articles appear at the conclusion of the hearing.]

Mrs. BROOKS. Thank you. My time has expired. I yield back.

Mr. PITTS. The Chair thanks the gentlelady.

I now recognize the vice chairman of the subcommittee, Mr. Guthrie, for 5 minutes.

Mr. GUTHRIE. Thank you.

Thank you all for being here and your patience. We appreciate it.

Mr. Mair, I know that you have claimed that when a priority review voucher is redeemed, FDA has a harder time reviewing other priority review applications on time. However, in its most recent PDUFA performance report to Congress, the FDA stated that it met review goals for 100 percent of the 29 priority review applications it received. And it appears, from FDA's own data, the use of priority review vouchers has not had any impact on review times for other priority applications.

If the FDA doesn't support the priority review voucher incentive, then what other kind of incentives could be appropriate for developing countermeasures? I know you are not going to endorse any or ask for any, but what are other incentives that we could look at?

Mr. MAIR. Thank you for the question.

So, with respect to the effect, I think—with respect to the effect of the vouchers, potential effect on our ability to do other reviews, I think our concern we are raising here is expanding the program. Well, there will be more vouchers out there that will eventually come in. And so this has the potential to affect our ability to do more of our other work down the road, especially if we continue to expand the program.

So while, you know, one or two might be doable, if we end up getting, you know, 5, 10, 15 vouchers out there, it, you know, has the potential to grow to a point where it is——

Mr. GUTHRIE. Are there other incentives that might be workable if we need priorities to move forward?

Mr. MAIR. You know, it is a difficult question and something we should look at, but there are—you know, it is a question of, you know, the incentives we currently have, can we treat them, can we hone them in some way, can we improve what is currently available, or can we add new incentives to the mix, and what is most valuable, and what can get us there in the best possible way with the most value to the taxpayer in terms of getting us there most efficiently. So it—

Mr. GUTHRIE. OK. Thanks. I am going to try to get through a couple more questions. I appreciate that. Thanks a lot. I wasn't cutting you off to be rude, just to get to a couple more questions in my 5 minutes.

Colonel Coleman, do you believe the Department of Defense has the requisite number of medical countermeasures developed, licensed, and available to protect our warfighters from biological agents? And, in your opinion, should Congress be doing more to encourage the development of medical countermeasures against these threats, like creating priority review vouchers for the medical countermeasures?

Colonel COLEMAN. Yes, sir. Thank you for that question.

So I can unequivocally say that we don't have the full array of medical countermeasures needed to combat weapons of mass destruction. Ergo, we have a robust program with funds provided by Congress for this express purpose. So, clearly, the needs continue, and we are a long way from where we ultimately need to be.

In terms of any Department of Defense position, there is no position, as I stated earlier—I mean, there is a clear belief that we need an array of incentives. Personal opinion, which I think you asked, regarding priority review vouchers, I believe they could potentially be of great value.

I will refer back to the Ebola virus outbreak. Post-outbreak, I have engaged with conversations with many of the pharmaceutical companies that chose to engage at the time of the outbreak, and their interest is waning. And some of the companies have indicated that, when they choose to stay in, it is really for the priority review voucher, which was added to that neglected tropical disease threat list. So I am getting the feedback from commercial enterprises that they see the value to this.

Mr. GUTHRIE. OK. Thank you.

And, Dr. Hatchett, some claim that it is important that BARDA does not have contracting authority because of potential conflicts of interest or undue influence of the BARDA Director. Why was your contracting authority taken away? And did the BARDA office lack program integrity?

Dr. HATCHETT. Thank you for asking about the contracting authority again because I didn't get to answer Mrs. Brooks' question—

Mr. GUTHRIE. OK.

Dr. HATCHETT [continuing]. And would like to address her question as well.

The contracting authority was removed from BARDA, I believe, in 2009, which was prior to—I joined BARDA in 2011.

Mr. GUTHRIE. Yes. There was no implication on you in there.

Dr. HATCHETT. Yes. And I believe the concern was legitimately that contracting is such an important activity, it manages the taxpayers' dollar, that it was extremely important that it be independent and that it represent the business function of Government independently in terms of negotiations with companies.

Our contracting office is right down the hall from my office. The head of our contracting authority, retired Brigadier General Jeff Scarborough, is—you know, his office is less than 100 yards from mine. We talk every single day. Our staff interact with the contracting officer staff every single day. So, you know, there are no barriers to our working together. We work together on all contracting actions.

And in point of fact, to answer Ms. Brooks' question about why I have a different opinion than my predecessor, I have looked at the data. I have looked at the data as to the timelines for individual contracting actions as well as aggregate timelines. And it is quite impressive that we are well below Federal and departmental benchmarks in terms of our performance. There are outliers, some that are large outliers that result in, you know, the average times being actually being lower than the median times. That happens.

But, overall, I think our contracting office is providing a service to the American citizen by ensuring the integrity of our procurement process. And I am very comfortable with the system as it currently exists. I just have a different opinion than my predecessor.

Mr. GUTHRIE. Thank you, Mr. Chairman. My time has expired, so I yield back.

Mr. PITTS. The Chair thanks the gentleman.

Without objection, we have a member of the Energy and Commerce Committee, not a member of the subcommittee, here, one of prime sponsors of legislation. I would like to yield to Ms. Eshoo 5 minutes for questioning.

Ms. ESHOO. Thank you very much, Mr. Chairman, for your legislative courtesy.

And I would like to thank the witnesses for their testimony today.

I am very proud of the legislation that former Congressman Mike Rogers and myself shaped and shepherded to create the law that led to BARDA. We are both members of the Energy and Commerce Committee, but, very importantly, both members of the House Intelligence Committee. And we viewed this issue in many ways as the tip of the spear, that our national security is a portfolio that contains many items that must be addressed.

And so it is a pleasure to work with Congresswoman Brooks to update BARDA, but the principles, the underlying principles still remain, and that is that we be effective, that we be limber, that we be timely, that we be able to identify, that we be able to attract those who are actually going to produce the stockpiles for our country so that we are indeed prepared.

And I hear some back and forth here, the innards and some of the weeds and the whatever. I think we have to raise our vision and keep in front of us exactly what I just said.

So, Mr. Mair, the FDA claims that allowing biodefense medical countermeasures to qualify for a priority review voucher would dra-

matically increase the number of PRVs awarded. Now, DHS has identified only 13 material threats to U.S. national security, and since the creation of BARDA in 2006, 12 years ago, there have been 3 medical countermeasures.

Now, it has been stated before, it is worth stating again, that this program is privately funded. There are no taxpayer dollars in it.

How many medical countermeasures are you aware of in the pipeline that would qualify for a PRV under this bill?

Mr. MAIR. Thank you for the question. I might defer that to Richard to speak to—

Ms. ESHOO. Yes, let's go quickly, because I only have 5 minutes.

Mr. MAIR. Sorry—to Richard, what is in the BARDA pipeline.

Ms. ESHOO. How many countermeasures are you aware of in the pipeline that would qualify?

Dr. HATCHETT. Ma'am, I don't have a specific number available to me. I would be happy to provide that information—

Ms. ESHOO. That would be great.

Dr. HATCHETT [continuing]. To you and will do so.

Ms. ESHOO. And would you please provide the committee with a list of those medical countermeasures, the candidates that you believe would qualify? All right?

Dr. HATCHETT. Uh-huh.

Ms. ESHOO. Dr. Hatchett, how long does your average vaccine procurement take from solicitation to award?

Dr. HATCHETT. The most recent numbers that I have looked at are actually aggregate numbers of major acquisition programs. And so those include Project Bioshield procurement actions, the most recent four procurement actions, as well as three additional major acquisition—

Ms. ESHOO. Yes, I just want to know how long does your average vaccine procurement take from solicitation to award.

Dr. HATCHETT. Sure.

Ms. ESHOO. Because timeliness is of the essence in all of this. If we can't be timely—identify, target, be timely, bring it up, have these measures in place, then this is just a piece of paper with good ideas on it.

Dr. HATCHETT. So the four actions that I have data for immediately available, three of them took 90 days from solicitation to award.

Ms. ESHOO. I am asking about vaccine procurement.

Dr. HATCHETT. OK. I will have to get back to you with definitive data.

Ms. ESHOO. OK. I would appreciate that.

Dr. HATCHETT. OK.

Ms. ESHOO. I really don't get your reason, your thinking, and what you have testified today, Dr. Hatchett, about contracting authority under BARDA. It is the way the legislation was written originally. The Commission—I mean, if there was ever a bipartisan commission of some of the most highly regarded individuals in public service—they don't agree with you.

How did you arrive at your thinking? I mean, does it make it faster? More effective? What is it that you don't like about it?

Dr. HATCHETT. First, in terms of how the Department of Health and Human Services handles contracting throughout the operating divisions——

Ms. ESHOO. No, I am asking you. I am asking you.

Dr. HATCHETT. So I am trying to address your question, ma'am.

The contracting activity at NIH, at FDA, at CDC report directly to the director of those agencies and provide services to the components of those agencies. The contracting activity within ASPR reports directly to the ASPR and provides——

Ms. ESHOO. I think you are talking about an organization chart. I want to know, in terms of our national security and the import of what this law is about, why do you take the position that you do?

Dr. HATCHETT. I take the position that I do because I understand the complaints that have been articulated by our private-sector partners, and they have gone on to propose a solution, which is to move the contracting authority back into BARDA.

Their complaints relate to concerns about the length of time it takes, about their interactions with the contracting authority. I believe there are other ways to address the complaints that they have articulated that preserve the integrity of our procurement process in a way that would be more effective than moving the contracting authority back into BARDA.

Ms. ESHOO. Thank you.

Thank you, Mr. Chairman.

Mr. PITTS. The Chair thanks the gentlelady.

Dr. Hatchett, I didn't get to ask my question of you, so I would like to do that and let the ranking member or anyone else ask a followup if they would like.

I would like to read from a letter sent to Congress by a group of venture capital investors who have experience with MCMs. And they say, quote, "We have watched the biodefense enterprise struggle to attract and sustain investment and participation from companies and financial partners. The lack of sustainable and predictable incentives for companies who have promising technologies for biodefense applications is the primary driver of this struggle. Quite simply, the decision to invest in the biodefense sector is infinitely more risky than any other portion of the biotech sector," end quote.

So, Dr. Hatchett, I would like—and I will enter into the record this letter, without objection.

Mr. GREEN. No objection.

Mr. PITTS. With no objection, so ordered.

[The letter appears at the conclusion of the hearing.]

Mr. PITTS. Multiple developers have indicated that investors actually devalue the biodefense work they do with the U.S. Government because it is so risky and unpredictable. So my question is, if this is the case, why would anyone oppose this limited incentive for MCMs? What are your thoughts on this issue?

Dr. HATCHETT. Well, thank you, Mr. Chairman, for the question.

I think you are actually making the same point that I was making earlier, which is that, in the absence of predictable and sustained incentives, it does become an extremely risky business to be in because of the absence of the commercial markets for the products at the end of the day.

I believe if the administration, whatever that flavor is, and Congress agree to provide the sustained incentives and strong support, that we have demonstrated that the system can work technically. We can bring countermeasures forward; we can address the technical challenges.

In terms of it being a risky and unpredictable business to be in, in 2010 we undertook an interagency review of the entire medical countermeasures enterprise specifically to address areas of risk that the Government had some control over that could reduce that risk and make the Government better partners with our private-sector partners.

And I think the results of the last 6 years since that review was performed have demonstrated an acceleration in the delivery of countermeasures. And so many of the steps that we have undertaken have addressed the different risks—the financial risk, the technical risk, the regulatory risk, the risk of working with Government as a partner because of the way the political winds blow.

We are extremely mindful of the risks that our partners face. We are working to address those risks, reduce those risks. And we certainly thank you for the support that you have provided so far. We ask for continued strong support for this effort because, without that support, the enterprise is jeopardized.

Mr. PITTS. Thank you.

The Ebola and Zika outbreaks have been lessons in the seriousness of the challenges we face in this space, and H.R. 3299 was written to increase the efficiency of this program administratively and incentivize the product development. And I think you agree every minute is critical. It is important that we continue to work in a bipartisan manner to improve our emergency preparedness, incentivize medical countermeasures development.

I will yield to the ranking member for any closing questions or thoughts.

Mr. GREEN. Thank you, Mr. Chairman.

I would like to ask unanimous consent to place an article from Health Affairs—

Mr. PITTS. Without objection—

Mr. GREEN [continuing]. Into the record.

Mr. PITTS [continuing]. So ordered.

Mr. GREEN. Thank you.

[The article appears at the conclusion of the hearing.]

Mr. PITTS. All right. We will have followup questions. We have been interrupted. We apologize for that. Thank you for your patience. But members do have followup questions, and other members have written questions. We will submit those to you in writing and ask that you would please respond.

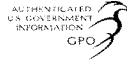
And I would remind members that they have 10 business days to submit questions for the record. Members should submit their questions by the close of business on Thursday, June the 2nd.

Very, very important issue, very important hearing. Thank you. We look forward to continuing to work with you on this issue.

Without objection, the hearing is adjourned.

[Whereupon, at 12:31 p.m., the subcommittee was adjourned.]

[Material submitted for inclusion in the record follows:]



114TH CONGRESS  
1ST SESSION

# H. R. 3299

To amend the Public Health Service Act to ensure preparedness for chemical, radiological, biological, and nuclear threats, and for other purposes.

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## IN THE HOUSE OF REPRESENTATIVES

JULY 29, 2015

Mrs. BROOKS of Indiana (for herself and Ms. ESTERO) introduced the following bill; which was referred to the Committee on Energy and Commerce

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## A BILL

To amend the Public Health Service Act to ensure preparedness for chemical, radiological, biological, and nuclear threats, and for other purposes.

1 *Be it enacted by the Senate and House of Representa-*  
2 *tives of the United States of America in Congress assembled,*

3 **SECTION 1. SHORT TITLE.**

4 This Act may be cited as the “Strengthening Public  
5 Health Emergency Response Act of 2015”.

6 **SEC. 2. HOSPITAL PREPAREDNESS PROGRAM.**

7 Subsection (j) of section 319C–2 of the Public Health  
8 Service Act (42 U.S.C. 247d–3b) is amended by adding  
9 at the end the following:

1           “(5) MINIMUM FUNDING LEVEL FOR  
2       AWARDS.—Of the amounts appropriated to carry out  
3       this section for a fiscal year, not less than 97 per-  
4       cent shall be awarded to eligible entities as described  
5       in subsection (a).”.

6 **SEC. 3. GAO REPORT ON STATE, LOCAL, AND HOSPITAL**  
7 **PREPAREDNESS PROGRAMS.**

8       (a) IN GENERAL.—Not later than 1 year after the  
9       date of enactment of this Act, the Comptroller General  
10      of the United States shall submit a report to the Congress  
11      on the programs for awarding cooperative agreements and  
12      grants under section 319C–1 of the Public Health Service  
13      Act (42 U.S.C. 247d–3a; improving State and local public  
14      health security) and section 319C–2 of such Act (42  
15      U.S.C. 247d–3b; partnerships for State and regional hos-  
16      pital preparedness to improve surge capacity).

17      (b) CONTENTS.—The report under subsection (a)  
18      shall address each of the following:

19           (1) The goals of the programs specified in sub-  
20           section (a).

21           (2) The extent to which such goals are being  
22           met, including performance metrics that could help  
23           assess whether such programs are succeeding.

24           (3) How such programs could be improved.

1 (4) How such programs complement other pre-  
2 paredness programs of the Department of Health  
3 and Human Services.

4 (5) How funds awarded through such programs  
5 should be allocated and whether that allocation  
6 should be based on risk.

7 (6) Progress made toward State and local pre-  
8 paredness entities being self-sustaining.

9 (7) Whether the level of funding for such pro-  
10 grams is sufficient.

11 **SEC. 4. STRATEGIC NATIONAL STOCKPILE.**

12 Section 319F–2(a)(2) of the Public Health Service  
13 Act (42 U.S.C. 247d–6b(a)(2)) is amended—

14 (1) in subparagraph (G), by striking “and” at  
15 the end;

16 (2) in subparagraph (H), by striking the period  
17 at the end and inserting “; and”; and

18 (3) by adding at the end the following:

19 “(I) ensure procedures are in place to co-  
20 ordinate the ongoing stockpiling by the Bio-  
21 medical Advanced Research and Development  
22 Authority and Centers for Disease Control and  
23 Prevention of qualified countermeasures (as de-  
24 fined in section 319F–1), security counter-  
25 measures (as defined in this section), and quali-

1           fied pandemic or epidemic products (as defined  
 2           in section 319F–3) for which funds have been  
 3           made available under section 319L in order to  
 4           avoid any gaps in preparedness.”.

5 **SEC. 5. PROJECT BIOSHIELD PROCUREMENT PROCESS.**

6           Section 319F–2(c) of the Public Health Service Act  
 7 (42 U.S.C. 247d–6b(c)) is amended—

8           (1) in paragraph (4)(A)(ii), by striking “make  
 9           a recommendation under paragraph (6) that the spe-  
 10          cial reserve fund as defined in subsection (h) be  
 11          made available for the procurement of such counter-  
 12          measure” and inserting “make available the special  
 13          reserve fund as defined in subsection (h) for pro-  
 14          curement of such countermeasure”;

15          (2) in paragraph (6)—

16                (A) by striking subparagraphs (A), (B),  
 17                (C), and (E); and

18                (B) by striking “(6) RECOMMENDATIONS  
 19                FOR PRESIDENT’S APPROVAL” and all that fol-  
 20                lows through “(D) SUBSEQUENT SPECIFIC  
 21                COUNTERMEASURES.—” and inserting “(6)  
 22                SUBSEQUENT SPECIFIC COUNTERMEASURES.—  
 23                Procurement under”; and

24          (3) in paragraph (7)—

25                (A) by striking subparagraph (A);

1 (B) by redesignating subparagraph (B) as  
2 subparagraph (A) and amending such subpara-  
3 graph (A), as redesignated, to read as follows:

4 “(A) PAYMENTS FROM SPECIAL RESERVE  
5 FUND.—The special reserve fund as defined in  
6 subsection (h) shall be available for payments  
7 made by the Secretary to a vendor for procure-  
8 ment of a security countermeasure in accord-  
9 ance with the provisions of this paragraph.”;  
10 and

11 (C) by redesignating subparagraph (C) as  
12 subparagraph (B).

13 **SEC. 6. BARDA TRANSACTION AUTHORITIES.**

14 Section 319L(e)(5) of the Public Health Service Act  
15 (42 U.S.C. 247d–7e(c)(5)) is amended by adding at the  
16 end the following:

17 “(II) CONTRACTING AUTHORITY.—The  
18 Secretary shall delegate authority for negoti-  
19 ating and entering into any contracts, grants,  
20 or cooperative agreements under this section to  
21 the Director.”.

1 **SEC. 7. PUBLIC HEALTH EMERGENCY MEDICAL COUNTER-**  
2 **MEASURES ENTERPRISE STRATEGY AND IM-**  
3 **PLEMENTATION PLAN.**

4 Section 2811(d)(2) of the Public Health Service Act  
5 (42 U.S.C. 300hh–10(d)(2)) is amended—

6 (1) in subparagraph (A), by inserting after “de-  
7 scribe the chemical, biological, radiological, and nu-  
8 clear agent or agents that may present a threat to  
9 the Nation” the following: “(which shall include pan-  
10 demic influenza)”;

11 (2) by striking “and” at the end of subpara-  
12 graph (J);

13 (3) by redesignating subparagraph (K) as sub-  
14 paragraph (L); and

15 (4) by inserting after subparagraph (J) the fol-  
16 lowing:

17 “(K) report on the amount of time between  
18 the issuance of each request for proposal or  
19 task order from the Biomedical Advanced Re-  
20 search and Development Authority and the  
21 award of a contract pursuant to such request  
22 for proposal or task order; and”.

23 **SEC. 8. PRIORITY REVIEW TO ENCOURAGE TREATMENTS**  
24 **FOR NATIONAL SECURITY THREATS.**

25 Section 524(a)(3) of the Federal Food, Drug, and  
26 Cosmetic Act (21 U.S.C. 360n(a)(3)) is amended—

1           (1) by redesignating subparagraph (R) as sub-  
2     paragraph (S); and

3           (2) by inserting after subparagraph (Q) the fol-  
4     lowing:

5           “(R) Any disease or other agent that is de-  
6     termined to be a material threat under section  
7     319F–2(c)(2)(A)(ii) of the Public Health Serv-  
8     ice Act.”.

○

# KIDS CANCER

Changing the landscape of pediatric research

May 17, 2016

The Honorable Fred Upton  
Chairman  
Energy and Commerce Committee  
U.S. House of Representatives Washington,  
DC 20515

The Honorable Frank Pallone  
Ranking Member  
Energy and Commerce Committee  
U.S. House of Representatives Washington,  
DC 20515

Dear Chairman Upton and Ranking Member Pallone:

I am writing to express my concern about Strengthening Public Health Emergency Response Act of 2015, H.R.3299. I request that you not support Section 8 of this bill, to establish a new priority review voucher program.

Section 8 of this bill would directly harm American children with cancer and life threatening illnesses. It would break what is now a very effective drug development incentives program for seriously ill children: the Rare Pediatric Disease Priority Review Voucher Program, also known as the Creating Hope Act, 21 U.S.C. 360ff (Pediatric PRV). Protecting Americans from a possible risk of bioterrorism is also an important goal, but please do not pursue it at the expense of ill children.

Although the United States has a robust pharmaceutical industry, very few drugs have been developed for children with cancer. In the 20 years leading up to the passage of the Pediatric PRV, there had been only one initial FDA approval for a drug expressly for pediatric cancer, the leading cause of death by disease for children. Children's cancers are different from adult cancers and children are treated with drugs that are decades old, even as cancer research has undergone transformative leaps forward.

In 2012, Congress responded to this crisis in pediatric cancer by including in the U.S. Food and Drug Administration Safety and Innovation Act the Pediatric PRV, which was based on the Neglected Tropic Disease Priority Review Voucher program. With the passage of the Pediatric PRV, companies are now, for the first time, actively developing drugs expressly for children with cancer and in the next 10 years we will finally see newly approved life saving cancer drugs for our kids.

Of course the sweeping success of the PRV program has attracted attention and as a result you are considering a new bioterrorism PRV. However, as Dr. David Ridley of Duke University explains, expansion of PRV program will break the Pediatric PRV because the value of the voucher will plummet quickly.<sup>1</sup> Current pricing for vouchers can only be supported if the number of vouchers is not increased by the creation of new PRV programs. Even a small increase in the number of

<sup>1</sup> David B. Ridley and Stephane A. Régnier, The Commercial Market For Priority Review Vouchers,



vouchers will dramatically depress the value of the Pediatric PRV -- and of every other PRV -- and undermine the incentive to which companies are now responding.

A new PRV program would be directly at the expense of children's health. It also would not be an effective incentive because the value of *all* PRVs would be depressed. The Strengthening Public Health Emergency Response Act includes other important provisions to increase development of new bioterrorism drugs. These provisions are uniquely suited for bioterrorism because they take into consideration the importance of military leadership in identifying and directing the prioritization of bioterrorism drug development. If these provisions are insufficient, they should be fixed or new incentives should be developed.

The problem is simple: if everything is a priority, then nothing is a priority.

Thank you again for protecting the Pediatric PRV and protecting American children by not supporting a new bioterrorism PRV.

Sincerely,

A black rectangular box redacting the signature of Nancy Goodman.

Nancy Goodman  
Executive Director  
Kids v Cancer



David Ridley, PhD  
Faculty Director  
Health Sector Management

Duke University  
The Fuqua School of Business  
Durham, NC 27708-0120

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May 17, 2016

The Honorable Frank Pallone, Jr.  
House Committee on Energy & Commerce  
United States House of Representatives  
Washington, D.C. 20515

The Honorable Gene Green  
House Committee on Energy & Commerce  
United States House of Representatives  
Washington, D.C. 20515

Dear Mr. Pallone and Mr. Green,

I am writing regarding the Strengthening Public Health Emergency Response Act of 2015 (H.R. 3299) which would extend the priority review voucher program to medical countermeasures.

I was one of the authors of the 2006 *Health Affairs* paper that proposed the priority review voucher program (Ridley, Grabowski, and Moe 2006). Our aim was to encourage development of new drugs for neglected diseases. In 2012, Congress extended the voucher program to rare pediatric diseases. I am writing to highlight the trade-offs associated with extending the voucher program to more diseases.

Like neglected diseases, there is little private financial incentive to develop medical countermeasures. Furthermore, there is potentially enormous need. Hence, it is important to create incentives to develop new treatments as medical countermeasures.

Viewed in isolation, it makes perfect sense to add medical countermeasures to the diseases eligible for priority review vouchers. However, members of Congress should be aware that adding voucher-eligible diseases will drive down the price of vouchers and thus drive down the incentive to develop treatments for diseases already on the list. In the current issue of *Health Affairs*, my coauthor and I estimated that if one voucher is available in a year, it will be worth more than \$200 million, but if four vouchers are available, then the price could fall below \$100 million (Ridley and Régnier 2006). If voucher prices fall below \$100 million, then the expected net present value of the voucher would fall below the typical cost of a Phase III clinical trial and FDA submission. Hence, the voucher would not provide sufficient incentive for drug development and additional incentives would be needed, such as a profitable commercial market or the promise of government purchase.

To limit the supply of vouchers and thus maintain high voucher prices, members of Congress have two levers: limiting the eligible diseases and limiting the characteristics of the drugs. For example, Congress could restrict voucher eligibility to only truly novel drugs or only drugs for which the drug developer conducted new trials. Furthermore, Congress could require the voucher recipients have filed a report describing their access plan prior to drug submission. In the case of medical countermeasures, the access plan would be providing the drug to the government.

If Congress does not make medical countermeasures eligible for vouchers, then a prize should be considered. The US government could create a prize of \$350 million per approved new drug for medical countermeasures. A prize of this size would replicate the highest sales price of a

voucher. Perhaps the funds could be found in the existing budgets of the Department of Defense or Health and Human Services. A \$350 million prize will likely be too small to excite large pharmaceutical manufacturers, because of their high cost structure (unless they choose to participate as a source of pride for their employees). However, even if large manufacturers are not interested, many small drug developers would likely be interested. There are many small developers, and surely some developers have drugs for infectious diseases that would be easy to test at relatively low cost. An advantage of a prize (pull) mechanism is that government officials need not know about these small companies in advance, they need only know about the companies if they succeed. My experience with the priority review voucher has been that there are many small companies that few have heard of, but are willing and able to develop drugs for infectious diseases at relatively low cost.

One way in which Congress could strengthen the voucher program and drug review more broadly would be to loosen the limits on pay for scientific reviewers at the Food and Drug Administration. The priority review voucher puts an extra strain on the FDA because it requires faster review. However, every priority review voucher redeemed comes with \$5 million in user fees (\$2.4 million for the standard fee and \$2.7 million for the voucher) from the developer. So FDA has extra money to hire staff, but if FDA cannot attract new staff given pay restrictions, then the extra fees are not particularly helpful, and the voucher program creates a heavy burden for the FDA.

I am grateful to the members of Congress for their enthusiasm for the voucher program and for looking for ways to strengthen it. As I've worked with Congressional staff on the voucher program, I have been thoroughly impressed with those I have met on both sides of the aisle. They seem genuinely interested in getting things right.

Sincerely,



David Ridley, PhD  
Duke University

C: Chairman Fred Upton



**House Energy & Commerce Subcommittee on Health Hearing on  
“Examining H.R. 3299, Strengthening Public Health Emergency & Response  
Act”**

**May 19, 2016**

**Testimony for the Record of Richard Hamburg, Interim President & CEO  
Trust for America’s Health**

Chairman Pitts, Ranking Member Green and members of the Committee: thank you for the opportunity to submit testimony for the record on today’s important topic, the Strengthening Public Health Emergency Preparedness and Response Act (HR 3299). Trust for America’s Health (TFAH) is a nonprofit, nonpartisan organization dedicated to saving lives by making disease prevention a national priority. We are an independent organization and accept no federal or private sector funds. At TFAH, we have long advocated for strengthening the ability of our public health and healthcare systems to prevent and respond to disasters. Our organization is grateful to Representative Brooks and Representative Eshoo for shining a light on the need for continuous improvement in the nation’s health security.

The ongoing Zika virus outbreak, the impact of natural disasters on our healthcare system, and the threat of bioterrorism are constant reminders that the nation must remain vigilant in protecting the health of all Americans. TFAH publishes an annual report, *Outbreaks: Protecting Americans from Infectious Diseases*, which looks at steps the nation should take to prevent and mitigate the impacts of infectious disease threats ranging from measles to Zika. This year, the report included several recommendations related to issues before the committee today:

- We must support the entire medical countermeasure enterprise, from initial research through stockpiling and community-level distribution and dispensing;
- We must create new incentives to encourage private sector partners to continue investing in medical countermeasures development; and
- We must continue to rebuild and modernize the Hospital Preparedness Program.

This testimony will focus on this last issue, modernizing the Hospital Preparedness Program (HPP), which is addressed in sections 2 and 3 of the legislation. We are pleased that the bill includes a focus on this program, and the sponsors share our goal of making HPP as strong as possible. HPP, administered by the Assistant Secretary for Preparedness and Response (ASPR), is the main federal program that provides leadership and grants to improve medical surge capacity and enhance coordinated health system preparedness for public health emergencies. HPP supports regional coalitions of healthcare facilities and public and private partners to better coordinate planning and response efforts. There are nearly 24,000 healthcare coalition (HCC) members nationwide organized in about 500 HCCs, including hospitals, outpatient facilities, long-term care, emergency medical services (EMS) and public health departments. The program

has transitioned from its initial focus on individual hospitals purchasing equipment and supplies to developing HCCs and healthcare capabilities such as health system preparedness and recovery, emergency operations coordination, and information sharing.

Funding for the program has been cut from a high point of \$515 million in FY2004 to currently about \$255 million annually to support the entire nation's health system preparedness, including a 30 percent drop from FY2013. As a result, we are asking our nation's healthcare system to prepare for pandemics and disasters with insufficient funding to incentivize meaningful participation, although we do want to ensure HPP is as effective as possible with available resources. We believe there needs to be better oversight and evaluation of HCCs. ASPR should be able to define and evaluate the minimum capabilities that a coalition must meet in order to be considered a successful coalition, better delineate the funding level that can be retained at the state level and for what purposes, and require better evaluation of coalition performance. We hope the upcoming funding opportunity announcement (FOA), which begins in FY2017, will address those concerns.

While we support the goal of section 2 of HR 3299 – ensuring more money is reaching healthcare coalitions and their members – we are concerned that the language as written would have a counterproductive impact on the effectiveness of those coalitions. As written, only three percent of the HPP funding line would remain for intramural use at the federal level for all healthcare preparedness activities, including grant administration and evaluation. Under current allotments, there are only 11 regional Health and Human Services (HHS) staff members to oversee approximately 50 coalitions in each region and ensure an appropriate level of funding is being disbursed from states to coalitions. Further, this level of staffing makes it challenging to provide adequate technical assistance regarding preparedness and response operations to achieve the cooperative agreement's requirements and goals. We believe the language proposed in the bill would greatly reduce the staff that are needed to provide technical assistance, evaluation, and management of the program.

In addition, the HPP appropriations line supports more than just the grant program. HPP is the only funding line within the HHS budget focused upon health system emergency preparedness. Therefore, the Critical Infrastructure Program, the Emergency System for Advance Registration of Volunteer Health Professionals (ESAR-VHP), the Science Healthcare Preparedness Evaluation and Research branch, the Emergency Care Coordination Center, Division of Recovery, and the Technical Resources Assistance Center and Information Exchange (TRACIE) are all funded out of HPP. As the legislation is written, these programs would likely all be eliminated. The funds that remain at the federal level are not simply overhead and administration of the cooperative agreement, but support substantive work that contributes to health system preparedness.

As an alternative, we suggest adjusting the language to state that eligible entities should ensure a greater proportion of their grant goes directly to coalition activities and substantively supports coalition capabilities. This would allow more money to reach the end user but ensure effective grant management and evaluation. To that end, we also support the language in Section 3 to

request a Government Accountability Office (GAO) study addressing key questions about HPP operations and outcomes.

Many healthcare coalitions are achieving impressive results. In recent years, we saw healthcare coalitions react to a massive train derailment in Pennsylvania, tornados in Mississippi and Missouri, and the West, Texas explosion.<sup>1</sup> The coordination and systems put in place under HPP likely saved lives. We want to see these results replicated in coalitions across the country. To do so, we need to build effective coalitions and ensure we are measuring their capabilities. We are grateful that this committee is committed to ensuring we are achieving the best possible outcomes from the Hospital Preparedness Program. We look forward to working with you to ensure HPP is as effective as it could be in protecting the health security of our nation.

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<sup>1</sup> U.S. Department of Health and Human Services, *HPP In Action: Stories from the Field*.  
<http://www.phe.gov/Preparedness/planning/hpp/events/Pages/default.aspx> (accessed May 11, 2016).

## Blue Ribbon Study Panel on Biodefense

Representative Susan Brooks  
1505 Longworth House Office Building  
Washington, DC 20515

Representative Anna Eshoo  
241 Cannon House Office Building  
Washington, DC 20515

February 11, 2016

Dear Representatives Brooks and Eshoo,

As co-chairs of the bipartisan Blue Ribbon Study Panel on Biodefense, we write to offer our support for H.R. 3299, the *Strengthening Public Health Emergency Response Act of 2015*.

Last October, our Panel released its comprehensive report, *A National Blueprint for Biodefense: Leadership and Major Reform Needed to Optimize Efforts*. For a year, we worked to examine the state of U.S. biodefense. We found significant effort and progress hampered by insufficient high-level leadership and strategic focus. We believe that this deficit has led to challenges in three areas of our domestic biodefense policy: interagency coordination, stakeholder collaboration, and technological innovation. Shortfalls have resulted in challenges at the department and agency level that compromise America's public health security.

The House Committee on Energy and Commerce has been responsible for the passage of critically important legislation, including the *Pandemic and All-Hazards Preparedness Act* and its reauthorization. Your bill, H.R. 3299, would further strengthen the statutory underpinnings of biological preparedness by addressing certain unresolved issues. For example, the Ebola events of 2015 revealed specific weaknesses in hospital readiness and medical countermeasure (MCM) availability. H.R. 3299 would: ensure that the Hospital Preparedness Program operates optimally; assure that the funding Congress allocates to this program reaches its intended recipients; eliminate bureaucratic delays in contracting and providing incentives for MCM development; and emplace a plan for the stockpiling of needed MCM.

As Ebola, Zika, and avian influenza prominently emphasize, the fight against infectious disease has been and will continue to be long and sustained. In *A National Blueprint for Biodefense*, we identify specific opportunities for Congress and the Administration to improve our preparedness for such biological events. Many of these actions, like those in your bill, can be implemented in the near term. Passage of H.R. 3299 would meet at least four of our recommendations – 19a, 19b, 29a, and 29c – while adding value in additional areas. We strongly believe that Congress can facilitate measureable progress in our nation's readiness by pursuing the provisions of H.R. 3299. We, therefore, encourage your committee to deliberate on this legislation as soon as possible.

We look forward to working with you in the coming year to implement these and other recommendations of the Study Panel. Please do not hesitate to contact us with any questions. You may reach us through the Panel's co-directors, Ellen Carlin ([ellen.carlin@biodefensестudy.org](mailto:ellen.carlin@biodefensестudy.org), 202-669-7830) and Asha George ([asha.george@biodefensестudy.org](mailto:asha.george@biodefensестudy.org), 301-351-5723).

Sincerely,



Joseph I. Lieberman  
Chair



Thomas J. Ridge  
Chair



**Submission Regarding Bill H.R. 3299:**  
**Suggestions to Fix the FDA PRV for Neglected Diseases**

The Honorable Joseph Pitts, Chairman  
 The Honorable Gene Green, Ranking Member  
 Committee on Energy and Commerce, Subcommittee on Health  
 United States House of Representatives

CC:

The Honorable Fred Upton, Chairman, Committee on Energy and Commerce  
 The Honorable Frank Pallone, Ranking Member, Committee on Energy and Commerce

May 19, 2016

Dear Chairman Pitts and Ranking Member Green:

We are writing to request that you support proposed changes to the Food and Drug Administration (FDA) Priority Review Voucher (PRV) program to ensure that it effectively accomplishes its goal of incentivizing new research and development (R&D) for neglected diseases, and that new neglected diseases products brought to market through the PRV program are made accessible and affordable to those who need them.

As several of the most recent and ongoing global health emergencies have reminded the world, the need for well-functioning incentives for R&D for neglected diseases is today more urgent than ever. Yet, despite representing more than 10% of the global disease burden, only 4% of new drugs and vaccines approved across the world were indicated for neglected diseases between 2000 and 2011.<sup>1</sup>

In March 2016, the American Thoracic Society, Doctors Without Borders/Médecins Sans Frontières, the Drugs for Neglected Diseases *initiative*, the IDSA Center for Global Health Policy, the Sabin Vaccine Institute, the TB Alliance and the Treatment Action Group sent a letter to the Committee on Energy and Commerce leadership raising several concerns with the design of the FDA PRV program for neglected diseases and proposed legislative amendments.<sup>2</sup>

The monetary value of PRVs has been established through sales, with the most recent voucher being sold for \$350 million in August 2015.<sup>3</sup> However, the value of these vouchers as an incentive to promote innovation for new therapeutic options for populations affected by neglected diseases depends on the PRVs being awarded only to truly new products that are accessible to those who need them.

<sup>1</sup> Pedrique B, et al. The drug and vaccine landscape for neglected diseases (2000-11): a systematic assessment. *Lancet* 2013, 1(6): [http://www.thelancet.com/journals/lanjlo/article/PIIS2214-109X\(13\)70078-0/fulltext](http://www.thelancet.com/journals/lanjlo/article/PIIS2214-109X(13)70078-0/fulltext).

<sup>2</sup> Letter sent March 29, 2016. Copies available upon request.

<sup>3</sup> See: <http://www.wsj.com/articles/united-therapeutics-sells-priority-review-voucher-to-abbvie-for-350-million-1439981104?alg=y>.

Nevertheless, the lack of requirements for a product to be novel or to be made available to and affordable for those whom the product is designed to treat or protect are two critical flaws in the design of the neglected disease PRV program that remain unaddressed. Now, as Congress is examining the PRV program, we hope that the Committee will use this opportunity to fix the neglected disease FDA PRV program to ensure that novel neglected disease medical products, including treatments and vaccines, are appropriately incentivized and are accessible to the patients and health care providers who urgently need them.

There are two key amendments to the PRV program for neglected diseases that we strongly recommend:

1. **The PRV program should have a novelty requirement.** Under current law, a PRV for neglected diseases can be awarded even when new R&D investments have not been made by the entity receiving the award or if the medical product awarded a PRV for neglected diseases is not new.

The PRV rewards successful FDA registration of drugs for select neglected diseases that have not been registered in the U.S., even if that drug has already been in use in other countries for years. Two of the three FDA PRVs for neglected diseases, awarded to Knight Therapeutics and Novartis for products for treatment of leishmaniasis (miltefosine)<sup>4</sup> and malaria (artemether-lumefantrine) respectively, were for drugs already in use for a long time in other countries. This has resulted in the granting of PRVs, but not in new investment in R&D. A PRV should only be awarded to products that are truly new, or that are registered with the FDA in a timely manner after initial registration in disease-endemic countries.

2. **The PRV program should require an access strategy.** The PRV program for neglected diseases does not include any mechanism to ensure patients, governments and health care providers will have affordable and appropriate access to products for which a PRV has been awarded.

Critically, the PRV program for neglected diseases does not ensure that the qualifying products will be accessible and affordable to patients in need.<sup>5</sup> PRV recipients are not even required to market a product that earns a PRV. Additionally, products that are marketed do not need to be priced affordably. For example, in the case of miltefosine, health care providers like MSF, R&D organizations like DNDi, governments and others are still struggling to access this product at an affordable price – or in some cases to access it at all. A PRV should only be awarded to companies who commit to serious efforts to make the PRV-earning neglected disease product available and accessible to patients in disease-endemic countries, whom the PRV program is intended to benefit.

Straightforward statutory changes, based on existing law for the rare pediatric disease PRV program and proposed legislation for PRV programs, could help to remedy the functioning of the PRV for neglected diseases. We have discussed these proposals with many Committee member offices, and we hope you will advance these solutions.

In addition to introducing these two critical fixes, we hope the Committee will also request a US Government Accountability Office (GAO) study and report to evaluate the effectiveness of the PRV programs as an incentive for promoting innovation, and whether and to what extent global unmet needs for biomedical innovation have been met by the PRV program. As organizations working to develop and provide access to neglected disease treatments and vaccines, we see every day the need for more effective strategies to incentivize needs-driven R&D for neglected diseases, including appropriate rewards for investments.<sup>6</sup> Improvements to the PRV program will be one important step toward broader changes that are urgently needed to ensure the R&D system delivers appropriate and affordable health technologies for those who need them. We therefore hope that you will consider not only leading the Committee in amending the PRV program for neglected diseases, but also in considering the potential creation of additional mechanisms to ensure that R&D for neglected diseases is successfully and appropriately incentivized, and that all patients in need can benefit from the fruits of biomedical innovation.

<sup>4</sup> Doshi P. US incentive scheme for neglected diseases: a good idea gone wrong? BMJ 2014; 349:g4665 <http://www.bmj.com/content/349/bmj.g4665>

<sup>5</sup> See, for example: <http://www.msfaccess.org/about-us/media-room/press-releases/patient-access-miltefosine-developing-countries-not-secure>, <http://blogs.plos.org/speakingofmedicine/2015/01/20/fda-voucher-leishmaniasis-treatment-can-patients-companies-win/> and <https://www.msfaccess.org/content/ready-set-slow-down>

<sup>6</sup> 2008 WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (WHA61.21) and 2012 Report of the WHO Consultative Expert Working Group on Research and Development: Financing and Coordination (CEWG report), see: <http://www.who.int/phi/en/>

Sincerely,



American Thoracic Society



Drugs for Neglected Diseases *initiative*



HIV Medicine Association



Infectious Diseases Society of America



Médecins Sans Frontières/Doctors Without Borders USA



Sabin Vaccine Institute



TB Alliance

The American Thoracic Society (ATS), a 15,000 member international multi-disciplinary society, improves global health by advancing research, patient care, and public health in pulmonary disease, critical illness and sleep disorders. Founded in 1905 to combat TB, the ATS has grown to tackle asthma, COPD, lung cancer, sepsis, acute respiratory distress, and sleep apnea, among other diseases. For more information please visit [www.thoracic.org](http://www.thoracic.org).

The Drugs for Neglected Diseases *initiative* (DNDi) is an international not-for-profit research and development (R&D) organization that discovers and develops new, improved, and affordable medicines for neglected diseases afflicting millions of the world's poorest and most vulnerable people. DNDi accomplishes its work through innovative, collaborative partnerships with public sector research institutions, particularly in disease-endemic countries, pharmaceutical and biotechnology companies, academia, non-governmental organizations, and governments worldwide. For more information please visit [www.dndi.org](http://www.dndi.org).

TB Alliance is a non-profit organization dedicated to the discovery and development of new, faster-acting and affordable tuberculosis medicines. For more information please visit [www.tballiance.org](http://www.tballiance.org).

The HIV Medicine Association (HIVMA) is an organization of medical professionals who practice HIV medicine. We represent the interest of our patients by promoting quality in HIV care and by advocating for policies that ensure a comprehensive and humane response to the AIDS pandemic informed by science and social justice. For more information please visit [www.hivma.org](http://www.hivma.org).

The Infectious Diseases Society of America (IDSA) represents physicians, scientists and other health care professionals who specialize in infectious diseases. IDSA's purpose is to improve the health of individuals, communities, and society by promoting excellence in patient care, education, research, public health, and prevention relating to infectious diseases. For more information please visit [www.idsociety.org](http://www.idsociety.org).

Médecins Sans Frontières/Doctors Without Borders (MSF) is an independent international medical humanitarian organization that delivers medical care to people affected by armed conflicts, epidemics, natural disasters and exclusion from healthcare in nearly 70 countries. In order to fulfill its mission, MSF needs access to affordable medicines to treat a range of medical conditions, including neglected diseases, for which new treatments are urgently needed. For more information please visit [www.doctorswithoutborders.org](http://www.doctorswithoutborders.org).

Sabin Vaccine Institute (Sabin) is a non-profit, 501(c)(3) organization of scientists, researchers, and advocates dedicated to reducing needless human suffering caused by vaccine preventable and neglected tropical diseases. Sabin works with governments, leading public and private organizations, and academic institutions to provide solutions for some of the world's most pervasive health challenges. Since its founding in 1993 in honor of the oral polio vaccine developer, Dr. Albert B. Sabin, the Institute has been at the forefront of efforts to control, treat and eliminate these diseases by developing new vaccines, advocating use of existing vaccines and promoting increased access to affordable medical treatments. For more information please visit [www.sabin.org](http://www.sabin.org).

Treatment Action Group (TAG) is an independent AIDS research and policy think tank fighting for better treatment, a vaccine, and a cure for AIDS. TAG works to ensure that all people with HIV receive lifesaving treatment, care, and information. We are science-based treatment activists working to expand and accelerate vital research and effective community engagement with research and policy institutions. TAG catalyzes open collective action by all affected communities, scientists, and policy makers to end AIDS. For more information please visit [www.treatmentactiongroup.org](http://www.treatmentactiongroup.org).

Please contact Judit Rius Sanjuan, U.S. Manager and Legal Policy Adviser of the MSF Access Campaign of Médecins Sans Frontières/Doctors Without Borders USA, if you are interested in scheduling a meeting or learning more about the content of this letter. Email: [judit.rius@newyork.msf.org](mailto:judit.rius@newyork.msf.org) / Phone: +1 212 655 3762



DEPARTMENT OF THE ARMY  
JOINT PROGRAM EXECUTIVE OFFICE  
FOR CHEMICAL AND BIOLOGICAL DEFENSE  
5101 HOADLEY ROAD  
ABERDEEN PROVING GROUND, MD 21010-5424

APR 01 2016



The Honorable Susan W. Brooks  
U.S. House of Representatives  
Washington, D.C. 20515

Dear Congresswoman Brooks,

Thank you for your letter requesting my perspective as the Joint Program Executive Officer for Chemical and Biological Defense regarding Food and Drug Administration (FDA) priority review vouchers. I appreciate hearing from you on this important aspect of facilitating and expediting development of medical countermeasures.

I support establishing a new priority review voucher (PRV) program for medical countermeasures for items on the Department of Homeland Security (DHS) Material Threat List. I believe such a program will incentivize investment and partnership, thereby benefiting the Department of Defense (DoD) in the advanced development of products that are essential to the Warfighter. Today there are few economic or regulatory incentives to encourage industry to innovate in the chemical and biological defense medical countermeasure market space. In general, chemical and biological defense medical countermeasures will be utilized in rare, emergency situations and, accordingly, the market for product sales is unlikely to yield a high return-on-investment. A new PRV program can inspire additional innovation in this market and greatly enhance the DoD's ability to rapidly deliver certain medical treatments and prophylaxis to the warfighter.

Because this issue is so important to my mission space, I have been in discussions, along with my DoD leadership, with House Armed Services Committee staff to determine the best approach to getting a PRV program specifically for DoD's validated chemical and biological threat list. Although the DHS' materiel threat list overlaps to a large degree with DoD's validated chemical and biological threat list, there are some differences based on the distinct missions of DoD. Lastly, the only additional recommendation I would make is to consider adding 'prophylaxis' or 'vaccines' to 'treatments' in the title of Section 8 ("Priority Review to Encourage Treatments for National Security Threats") to affirm the point that both pre-exposure and post-exposure capabilities are required to address this tremendous threat to the Nation.

Thank you again for your letter and for your efforts to incentivize innovation.

Sincerely,

DOUGLAS W. BRYCE  
Joint Program Executive Officer  
for Chemical and Biological Defense

# Alliance for Biosecurity

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1500 K Street, NW, Suite 1100  
Washington, DC 20005  
Telephone 1.202.230.5133 • Facsimile: 1.202.842.8465  
[www.allianceforbiosecurity.org](http://www.allianceforbiosecurity.org)

The Honorable Susan Brooks  
U.S. House of Representatives  
1505 Longworth House Office Building  
Washington, DC 20515

The Honorable Anna Eshoo  
U.S. House of Representatives  
241 Cannon House Office Building  
Washington, DC 20515

July 29, 2015

Dear Congresswomen Brooks and Eshoo:

On behalf of the Alliance for Biosecurity, we write today in strong support of your bill, the *Strengthening Public Health Emergency Response Act of 2015*. This bill would support preparedness for potential public health emergencies by increasing accountability and streamlining the contracting process for medical countermeasures (MCMs). Ensuring that these essential programs are sufficiently funded and effectively managed is critical to sustaining our national security.

Biosecurity companies tackle some very complex scientific puzzles, which are no less challenging than those faced by the biopharmaceutical sector as a whole but face a much more limited market. The medical countermeasures enterprise represents the government's commitment to develop and procure the products necessary to protect our national interests and encourage further innovation by the private sector. A combined and concerted effort among government agencies has greatly improved our preparedness capabilities over the last decade, but as these programs must evolve to ensure that they continue to function efficiently.

Given that MCMs are essential to our national security and that private sector partners play a critical role in their development, the contracting process must be expeditious. Government funded projects progress at a slower pace than privately funded ones due to unpredictable funding and a lengthy contracting process. This bill addresses this concern by taking steps to make the contracting process more transparent, predictable, and flexible and by removing the requirement that OMB review all contracts already approved and funded by HHS. These reforms will speed up the procurement process and facilitate the public private partnerships necessary for countermeasure development.

This bill also encourages private sector development of MCMs by including the 13 material threats identified by the Department of Homeland Security in the tropical disease Priority Review Voucher program. This model has proved successful in encouraging the development of vaccines and therapeutics for neglected tropical diseases and rare pediatric diseases and its application to MCMs for material threats is an important step toward ensuring necessary products are developed, approved, and stockpiled for use in a potential disease outbreak or chemical, biological, radiological and nuclear (CBRN) attack.

Bavarian-Nordic • CUBRC, Inc. • Elusys Therapeutics • Emergent BioSolutions • GlaxoSmithKline • Meridian  
Medical Technologies, Inc., a Pfizer Company • Nanotherapeutics, Inc. • Neumedicines, Inc. • Novartis  
Vaccines • Romark Laboratories, Inc. • Siga Technologies • Soligenix, Inc. | Lovelace Respiratory Research  
Institute • Texas A&M University System • University of Texas Medical Branch

The Honorable Susan Brooks  
July 29, 2015  
Page 2

Again, we thank you for your support of the programs that contribute to greater public health security and ensure preparedness against biological threats and appreciate your efforts to improve the effectiveness of these critical programs. The Alliance for Biosecurity stands ready to help you and your staff in any way possible. If you should have any questions please contact Maureen Hardwick (202-230-5133, [Maureen.Hardwick@dbi.com](mailto:Maureen.Hardwick@dbi.com)) or Rebecca McGrath (202-230-5679, [Rebecca.McGrath@dbi.com](mailto:Rebecca.McGrath@dbi.com)).

Respectfully,



Elisabeth Posillico, President & CEO, Elusys Therapeutics, Inc.



Paul Chaplin, President & CEO, Bavarian Nordic, A/S

*Co-Chairs, Alliance for Biosecurity*



September 16, 2015

The Honorable Susan Brooks  
1505 Longworth House Office Building  
Washington, DC 20515

The Honorable Anna G. Eshoo  
241 Cannon House Office Building  
Washington, DC 20515

Dear Representatives Brooks and Eshoo:

On behalf of California Life Sciences Association (CLSA) – the statewide public policy organization representing California's leading life science innovators, including over 750 medical device, diagnostic, biotechnology and pharmaceutical companies, research universities and private, non-profit institutes, and venture capital firms – I am writing to express our support for your legislation, H.R. 3299, the *Strengthening Public Health Emergency Response Act of 2015*. CLSA is pleased to endorse this legislation that will improve our nation's biodefense preparedness.

As you know, the recent Ebola outbreak exposed our nation's continued vulnerability to bioterror and pandemic threats, demonstrating the need for robust biodefense preparedness. Strengthening existing public-private partnerships, such as the Biomedical Advanced Research and Development Authority (BARDA), as well as creating new incentives for the research and development of medical countermeasures are critical for the United States to appropriately prepare against chemical, biological, radiological and nuclear threats as well as dangers like pandemic influenza.

The *Strengthening Public Health Emergency Response Act* is an important step forward in ensuring our nation's biodefense infrastructure is adequately prepared in the event of a bioterrorism event or pandemic outbreak. The bill creates a priority review voucher program to incentivize the research, development and licensure of medical countermeasures in a space where there is no commercial application for the product, bridging a serious gap in the nation's readiness against national security threats. In addition, the legislation will streamline the BARDA procurement process, improving this essential public-private partnership by creating a more efficient, predictable and seamless approval process for these vital products.

CLSA applauds your leadership on this important legislation and we are pleased to join a broad group of stakeholders in offering our strong support for H.R. 3299, the *Strengthening Public Health Emergency Response Act of 2015*. Please let me know if CLSA can be of assistance to you – I can be reached at [tgillenwater@califesciences.org](mailto:tgillenwater@califesciences.org) or (202) 743-7562.

Sincerely,

Todd Gillenwater  
Executive Vice President – Advocacy & External Relations

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September 14, 2015

The Honorable Susan Brooks  
1505 House Office Building  
United States House of Representatives  
Washington, D.C. 20515

The Honorable Anna Eshoo  
241 Cannon House Office Building  
United States House of Representatives  
Washington, D.C. 20515

Dear Representatives Brooks and Eshoo:

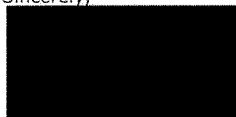
On behalf of the Biotechnology Industry Organization (BIO), I am writing with our support for H.R. 3299, the Strengthening Public Health Emergency Response Act of 2015. I wish to commend you for introducing this legislation, and look forward to continuing to work with you this year on this important measure.

BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States. BIO members are involved in the research and development of healthcare, agricultural, industrial and environmental biotechnology products. Our member companies play a central role in ensuring the development and manufacture of medical countermeasures (MCMs) to protect our nation's citizens against chemical, biological, radiological, and nuclear (CBRN) attacks as well as naturally-occurring infectious disease threats, such as pandemic influenza.

Your legislation recognizes that more must be done to incentivize MCM research and development, improve the public-private partnership by streamlining the contracting process, and increase transparency around future MCM funding needs across all types of threats. This is particularly important since most products do not have a commercial market to help spur investment. Significant barriers to countermeasure development still exist and your legislation takes critical steps towards addressing these so that we as a nation are more fully prepared to effectively respond to health security threats.

Again, BIO supports H.R. 3299, and looks forward to working with you both, as well as Chairman Fred Upton (R-MI) and Ranking Member Frank Pallone (D-NJ) and all the Members of the Energy and Commerce Committee to further this important bill.

Sincerely,



James C. Greenwood  
President & CEO

October 14, 2015

The Honorable Susan Brooks  
1505 Longworth House Office Building  
Washington, D.C. 20515

The Honorable Anna Eshoo  
241 Cannon House Office Building  
Washington, D.C. 20515

Dear Representative Brooks and Representative Eshoo:

We write to thank you for your leadership in the area of biodefense. We strongly support your efforts in the House (H.R. 3299, the Strengthening Public Health Emergency Response Act) to provide certainty and new incentives for the development of medical countermeasures (MCMs).

As members of the investment community who have invested in the life sciences space for years, we have watched the biodefense enterprise struggle to attract and sustain investment and participation from companies and financial partners. The lack of sustainable and predictable incentives for companies who have promising technologies for biodefense applications is the primary driver of this struggle.

As you know, the decision for investors to fund MCM candidates is incredibly risky relative to other areas where investment firms can invest. Given there is no private market for MCMs, the government's commitment to a robust biodefense enterprise is the key factor we look for when deciding whether or not to invest in MCMs. Quite simply, the decision to invest in the biodefense sector is infinitely more risky than any other portion of the biotech sector.

This lack of a dependable market for biodefense also makes it difficult for investors to gauge the value of MCM products upon their successful development. The federal biodefense enterprise is immature relative to other government partners, such as the Department of Defense. And the recent conversion of Project BioShield's advanced appropriations has subjected MCM funding to the unpredictable whims of the annual appropriations process.

While there is no substitute for sustained federal funding for MCMs, the incentive you have proposed in H.R. 3299 to create a biodefense Priority Review Voucher (PRV) at the Food and Drug Administration (FDA) would be a game-changer for investment in this space. The PRV is a proven and valuable incentive that has worked to spur investment in other neglected areas of research and development, such as rare pediatric diseases and neglected tropical diseases. The creation of a biodefense PRV would revitalize interest in MCM development and provide much needed certainty that MCM products can have value in the marketplace.

In addition, H.R. 3299 would create transparency in the long-term plans for development and procurement of MCMs by the U.S. government. Establishing predictability and accountability in MCM contracting would be incredibly valuable to us as investors in this space.

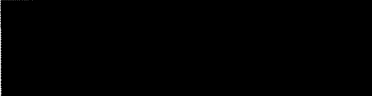
Existing contracting procedures at the Department of Health and Human Services (HHS) are cumbersome at best and obfuscate the path to approval and procurement for most MCM products.

We look forward to supporting your efforts to move these critical policies through Congress.  
Thank you again for your continued leadership in this critical space.

Sincerely,



Bertrand C. Liang  
Pfenex Inc.  
Forward Medical Science Partners



Standish M. Fleming  
Forward Ventures  
Managing Member



Steven Kornfeld, CFA  
Franklin Templeton Investments Inc.



Evan McCulloch  
Franklin Templeton Investments Inc.

## POINT/COUNTERPOINT

## Drug and Vaccine Development for Infectious Diseases: The Value of Priority Review Vouchers

J Matheny,<sup>1</sup> B Smith,<sup>2</sup> B Courtney<sup>2</sup> and M Mair<sup>2</sup>

Priority review vouchers (PRVs) are an innovative, high-impact, low-cost mechanism for encouraging the development of new medicines and vaccines for infectious diseases. Infectious diseases kill more than 14 million people per year—around a quarter of deaths worldwide.<sup>1</sup> For many of these diseases, cost-effective drugs and vaccines do not currently exist, and less than 15% of molecules reported to be under development are anti-infectives (i.e., vaccines or therapeutics targeting infectious diseases).<sup>2</sup> This neglect is due in large part to the unfavorable economics surrounding anti-infectives.

Pharmaceutical firms have a fiduciary responsibility to shareholders to maximize profits. Absent other incentives, firms will invest in research and development (R&D) for products that possess a profitable market and a high likelihood of technical success. In contrast, the global burden of infectious diseases is concentrated in developing countries with small budgets and weak patent protection, among poor patients who can pay only low prices for drugs—or cannot pay at all. Anti-infectives are thus typically not profitable products. In addition, the probabilities of technical success at each R&D stage are lower for anti-infectives than for most other pharmaceuticals, making R&D investments in anti-infectives high-risk.<sup>3</sup> Market failures surround anti-infectives because of their positive externalities:

for instance, your receipt of a vaccine reduces not only your risk of disease but also mine, yet I do not compensate you or the vaccine producer for the benefit I gain. Thus, private investment in R&D for anti-infectives is below the level that would be socially optimal.

Several approaches to increasing R&D for anti-infectives have been implemented, including government and foundation funding for R&D, the Orphan Drug Act provisions, and purchase agreements such as advance market commitments. The PRV, a cost-effective addition to these incentives, was originally proposed by Ridley *et al.*<sup>4</sup> and later established in law under the Food and Drug Administration (FDA) Amendments Act of 2007 (Public Law 110-85).

Under the law, a PRV is awarded to a successful developer of a New Molecular Entity that receives FDA approval and targets any one of 16 tropical diseases listed in the law or "any other infectious disease for which there is no significant market in developed nations and that disproportionately affects poor and marginalized populations, designated by regulation by the [Department of Health and Human Services (HHS)] Secretary." (Of importance, what qualifies as a "significant market" is not defined in the law.) The developer can then hold the PRV or sell it to another firm. The PRV entitles its holder to FDA priority review of any drug in its portfolio that otherwise would receive standard review. Priority review shortens an FDA review period by several months, by concentrating more FDA resources on an application. With a shorter review, a product is marketed earlier than it otherwise would be. In most cases, the product does not produce more revenue as a result, but because the revenues are received sooner—and firms, like individuals, prefer to receive money sooner rather than later—the "net present value" of the revenues is higher.

By one estimate, the net present value of a PRV to a firm is around \$300 million when applied to a blockbuster product that has annual global revenues of US\$1 billion or more (in the 1990s, 29 blockbusters were launched).<sup>4</sup> Because a PRV is transferable, an innovative biotechnology company could develop a tropical disease product, earn a PRV, and sell it to a pharmaceutical firm that has a blockbuster in its pipeline. The exact value of a PRV will depend on the number awarded, the number and expected value of potential blockbusters, and the difference between standard and priority review times. (In 2007, the difference between median standard and priority review times for New Molecular Entities and Biologic License Applications was 7 months.<sup>5</sup>) In our own conversations with pharmaceutical and biotechnology companies, estimates of a PRV's value ranged from less than \$100 million

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doi:10.1038/clpt.2009.53

## PERSPECTIVES

to more than \$500 million. No PRVs have yet been awarded, so their value remains an open question.

To prevent delayed reviews of other medically important products, the FDA would, ideally, need to hire additional staff to review PRV holders' products. The cost of this additional labor has been estimated at \$1 million per product and is billed to the firm that exercises the voucher.<sup>4</sup> The FDA PRV program allows the agency to set the fee each year, ensuring that the government is adequately compensated for the added labor. Because a PRV increases the value of a tropical disease product by hundreds of millions of dollars, at a net cost to the public of approximately zero, the PRV is highly cost-effective.

We are aware of only a few published negative critiques of the PRV program. Goozner<sup>6</sup> argued that PRVs will cause first-world consumers to pay substantially more for drugs than they otherwise would because, in his view, the PRV extends a drug's effective patent life. In fact, PRVs are not expected to have this effect. Under the Hatch–Waxman Act, the duration of FDA review is added back to a drug's effective patent life—the patent life remaining after a product is marketed—with conditions on the maximum restoration allowed. As a result, priority review usually has no effect on effective patent life: whatever time is lost under standard review is added back, and whatever time is gained under priority review does not alter the patent's expiration date.

Around 10% of drugs have long clinical trial and review periods that “max out” the Hatch–Waxman provision,<sup>7</sup> and for these drugs priority review can increase effective patent life up to several months. But even in these cases, priority review does not delay the introduction of generics. Effective patent life is lengthened by beginning earlier, rather than by ending later, so generics are introduced no later than they otherwise would be. In most cases, consumers will have access to both a branded product and a generic product sooner than they otherwise would.

Kesselheim<sup>8,9</sup> expressed concern that products receiving priority review

under a voucher may not be adequately evaluated because of time pressures on FDA staff. However, as Moe *et al.*<sup>10</sup> note, priority review “does not omit safety or efficacy studies or require approval within a given time frame.” There is a 6-month target for priority review, but actual review times are as long as needed. Moreover, there is no consistent evidence that shorter review times at the FDA are associated with safety problems.<sup>11</sup> A challenge in implementing the new PRV program will be expanding the pool of qualified FDA personnel for additional priority reviews. This challenge can be met but will need to be part of the broader effort at the FDA to increase review capacity.

The FDA is reviewing public input regarding diseases that could qualify for PRVs in addition to the 16 tropical diseases named in the law. As noted previously, section 524 of the law allows the FDA to designate by regulation any other infectious disease for which there is no significant market in developed nations and that disproportionately affects poor and marginalized countries. Products for emerging infectious diseases are natural candidates, as are products for neglected diseases such as Chagas disease and *Shigella*. Biodefense products could also be eligible for PRVs, because Ebola, typhus, and other potentially weaponizable diseases have no significant market in developed nations and disproportionately affect poor countries. These products suffer the same market failures that affect tropical diseases, and although some government funding exists, it is insufficient to cover the costs of drug and vaccine development. By one estimate, the current US government funding for advanced development of biodefense products is less than 10% of what is needed to meet the HHS Public Health Emergency Medical Countermeasures Enterprise requirements.<sup>12</sup>

Expanding eligibility for PRVs beyond the current 16 tropical diseases would help accelerate the development of many other pharmaceuticals needed to reduce death and disease worldwide. In reviewing existing and proposed incentives for anti-infective R&D, we concluded that the PRV is among the

most efficient.<sup>13</sup> PRVs alone will not be sufficient to generate all the pharmaceuticals the world needs. There is still an urgent need to invest in basic research on infectious diseases and in product-development partnerships for drug and vaccine development. Although PRVs may play a modest role compared with these other efforts, they are a valuable and highly cost-effective addition.

## ACKNOWLEDGMENTS

The authors are grateful to Luciana Borio and two anonymous reviewers for comments on an earlier draft.

## CONFLICT OF INTEREST

The authors declared no conflict of interest.

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## INCENTIVES FOR BIODEFENSE COUNTERMEASURE DEVELOPMENT

Jason Matheny, Michael Mair, Andrew Mulcahy, and Bradley T. Smith

Therapeutics and vaccines are available for only a fraction of biological threats, leaving populations vulnerable to attacks involving biological weapons. Existing U.S. policies to accelerate commercial development of biodefense products have thus far induced insufficient investment by the biopharmaceutical industry. In this article, we examine the technical, regulatory, and market risks associated with countermeasure development and review existing and proposed federal incentives to increase industrial investment. We conclude with several recommendations. To increase industry's engagement in biodefense countermeasure development, Congress should expand BioShield funding, giving HHS the flexibility to fund a portfolio of biodefense countermeasures whose revenues are comparable to those of commercial drugs. Congress should establish tradable priority review vouchers for developers of new countermeasures. A National Academy of Sciences or National Biodefense Science Board should formally evaluate incentive programs and a government-managed "Virtual Pharma," in which HHS contracts separate stages of research, development, and production to individual firms.

**B**IODEFENSE PLANNING BY THE U.S. government emphasizes the use of medical countermeasures, including drugs and vaccines, to prepare for and respond to attacks involving biological weapons.<sup>1-4</sup> Currently, medical countermeasures are available for only a fraction of biological threats, including those representing the highest risk, as determined by the Department of Homeland Security's (DHS) threat assessments.<sup>2</sup> It is generally acknowledged that incentives of the scale and structure needed to motivate the biopharmaceutical industry sufficiently to invest in countermeasure research and development (R&D) have been lacking.<sup>5-7</sup> Although federal investment in countermeasure R&D has increased since 2001,<sup>8</sup> few private pharmaceutical and biotechnology companies are engaged in countermeasure development, fewer have advanced candidates through clinical trials, and fewer still are likely to market products.<sup>9</sup> Out of 11 requests for proposals issued by the Department of Health and Human Services (HHS)

for biodefense countermeasures, only six products have been procured—none from a large pharmaceutical firm.<sup>10</sup>

In this article, we discuss the challenges to industrial investment in countermeasure development, review existing and proposed federal incentives for countermeasure R&D, and recommend measures to increase industry's engagement in the medical countermeasure enterprise.

### COMMERCIAL PHARMACEUTICAL R&D: LENGTHY, COSTLY, RISKY

Pharmaceutical R&D is a lengthy, costly, and risky process (Table 1). The transformation of a promising drug candidate into a marketable product typically takes 10 to 15 years from basic research to Food and Drug Administration (FDA) approval.<sup>13</sup> The cost of R&D for a single product, including the cost of capital and the cost of failures, is in the

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hundreds of millions of dollars. One commonly cited estimate of the mean R&D cost per new drug (including the cost of failures and the cost of capital) was \$800 million in 1997; current costs are likely to exceed \$1 billion per drug.<sup>11,13</sup> Between five<sup>12</sup> and nine<sup>14</sup> drug candidates enter clinical trials for every one approved by the FDA. Even drugs that reach market may not generate enough revenues to cover costs.<sup>15</sup> Thus, the profitability of a pharmaceutical company depends on a small number of blockbuster drugs.

In markets for traditional drugs (e.g., those that address cholesterol, diabetes, or cancer), drug developers can estimate demand, price, and expected return on R&D investments from data on disease prevalence, willingness-to-pay, and market competition. A developer decides to move forward with a project when its expected profits are higher than those of any other possible project.<sup>16</sup> Absent other incentives, developers will invest in R&D for mainstream products with which they have prior experience and that possess a broad, well-defined market, clear clinical research goals, and an established path to regulatory approval. These characteristics are scarce in the anti-infectives market and virtually absent in the biodefense countermeasures market.

#### WHY ANTI-INFECTIVES ARE UNATTRACTIVE TO THE PHARMACEUTICAL INDUSTRY

Anti-infectives include all therapeutics and vaccines that treat or prevent infectious diseases. In 2004, among the world's 15 largest pharmaceutical companies, only 10% of

publicly disclosed New Molecular Entities were classified as anti-infectives.<sup>17</sup> Anti-infectives are generally a low priority in pharmaceutical R&D because of technical, regulatory, and market risks. Developers see high financial returns in targeting chronic diseases that offer repeated sales, while infectious diseases are typically acute in developed countries (HIV being a notable exception).

From 1998 to 2002, FDA approval of new antibacterial agents decreased by 56%, compared with the period 1983 to 1987.<sup>17</sup> Between 1998 and 2004, only two antibacterials were approved that had novel mechanisms.<sup>17</sup> Most major pharmaceutical companies have left the antibacterial market because of increased regulatory risk, shrinking margins, and a short drug life cycle due to bacterial resistance.<sup>18–20</sup> By one estimate, a fourfold increase in antibacterial R&D effort would be needed to generate just one novel-mechanism antibacterial by 2012.<sup>21</sup>

The number of pharmaceutical companies producing vaccines has decreased from 26 in 1967 to 17 in 1980, to 5 in 2004.<sup>22</sup> Among these five companies, vaccines generate less than 10% of their total revenue.<sup>22</sup> Investments in vaccine R&D are generally unattractive to industry for several reasons:

- Vaccines are generally used only a few times in a lifetime and thus generate low expected revenues;
- By reducing disease transmission in a population, vaccines provide broad benefits for which vaccine producers are not fully compensated;<sup>23</sup>
- Large government purchases lead to low margins;

Table 1. R&D Process for a Typical New Drug

| Stage                                | Discovery/<br>preclinical<br>testing                          | Clinical trials                   |                                                        |                                                                                  | FDA                            | Phase IV                                                          |
|--------------------------------------|---------------------------------------------------------------|-----------------------------------|--------------------------------------------------------|----------------------------------------------------------------------------------|--------------------------------|-------------------------------------------------------------------|
|                                      |                                                               | Phase I                           | Phase II                                               | Phase III                                                                        |                                |                                                                   |
| Years                                | 6.5                                                           | 1.5                               | 2                                                      | 3.5                                                                              | 1.5                            | Additional<br>post-<br>marketing<br>testing<br>required<br>by FDA |
| Test population                      | Laboratory and<br>animal studies                              | 20–100 healthy<br>volunteers      | 100–500 patient<br>volunteers                          | 1,000–5,000 patient<br>volunteers                                                | Review<br>process/<br>approval |                                                                   |
| Purpose                              | Assess safety,<br>biological<br>activity, and<br>formulations | Determine<br>safety and<br>dosage | Evaluate<br>effectiveness,<br>look for side<br>effects | Evaluate<br>effectiveness,<br>monitor adverse<br>reactions from<br>long-term use |                                |                                                                   |
| Capitalized<br>costs<br>(\$M, range) | 335–381                                                       | 467–487                           |                                                        |                                                                                  |                                |                                                                   |
| Success Rate                         | 5,000<br>compounds<br>evaluated                               | 5 enter trials                    |                                                        |                                                                                  |                                |                                                                   |

Source: Adapted from Adams<sup>21</sup> and Pharmaceutical Research and Manufacturers of America (PhRMA).<sup>22</sup>

## INCENTIVES FOR BIODEFENSE COUNTERMEASURE DEVELOPMENT

- Since vaccines are given to healthy people, they face higher regulatory requirements and litigation risks;<sup>22,24,25</sup>
- For vaccines and other biologics, the FDA requires that companies begin building physical manufacturing capacity prior to product approval;<sup>26</sup>
- The probabilities of success at each R&D stage are lower for vaccines than for many other pharmaceuticals;<sup>27,28</sup> and
- The basic research pipeline for vaccines is small: between 2000 and 2005, only 3% of NIH grants included “vaccine” as a keyword.<sup>29</sup>

## WHY BIODEFENSE COUNTERMEASURE DEVELOPMENT IS UNATTRACTIVE TO THE PHARMACEUTICAL INDUSTRY

Virtually all biodefense countermeasures are anti-infectives and, as such, face the general challenges described above, as well as risks peculiar to biodefense.

Clinical trials cannot be used to assess the efficacy of most biodefense countermeasures against rare and lethal pathogens. There are few, if any, naturally occurring cases of most of these diseases in humans, and it is unethical to infect a person with a potentially lethal pathogen.

While safety must be shown in humans, the FDA’s Animal Efficacy Rule establishes a pathway for countermeasures to be proven effective using validated animal models.<sup>30</sup> However, for many biodefense diseases of concern, animal models have yet to be developed and validated. Moreover, animal models represent, at best, a rough approximation of efficacy in humans, and, as such, countermeasures developed using animal models will be untested until their use in humans during an emergency.<sup>31</sup>

The FDA has yet to release comprehensive guidance on the Animal Efficacy Rule, and no novel products have been approved using the Rule; the Rule has thus far been used to extend the indicated use of previously licensed products.\* Emergency use of a countermeasure that is in late-stage development but has not yet been approved by the FDA is possible through the Emergency Use Authorization (EUA) provision under the BioShield legislation.<sup>32</sup> Currently, the FDA is expected to require extensive safety and efficacy

data prior to granting a product EUA status. However, it is unclear what standards for safety and efficacy will qualify some products and disqualify others—and the determination is made during, not before, an emergency.

The scope, magnitude, and type of a future biological attack is uncertain, as is the demand for countermeasures.<sup>33</sup> Because the response to a major biological incident will be coordinated by governments, government purchases will be the major (if not the only) sale for most countermeasures. (At present, the U.S. government is by far the largest purchaser of biodefense countermeasures.) Countermeasure developers must thus rely on governments to determine and communicate the market for biodefense countermeasures. But government purchasing is subject to evolving threat assessments and shifting political priorities, which create market uncertainties.

Developers’ dependence on government purchases presents additional problems. A government has every incentive to negotiate prices for countermeasures just above their marginal cost of production, thus severely limiting profits. If companies resist low prices, governments can, in extreme cases, threaten compulsory licensing or purchase patent-breaching generics. In 2001, following the first anthrax attacks, the U.S. government threatened such actions during negotiations with Bayer over its antibiotic, Cipro. The threat was credible, and Bayer lowered its (already wholesale) price for the drug.<sup>34</sup> When a developer’s R&D costs are already spent, the best a developer can do in such cases is accept the government price. The prospect of a hard bargain causes drug developers to be wary of developing products whose prices are not guaranteed to cover R&D costs.

The technical, regulatory, and market risks associated with biodefense countermeasures lead to weak commercial investment and thus few products. Given companies’ fiduciary responsibility to investors, even countermeasures that are profitable at the margin will be ignored as long as companies can focus their investments on more profitable products.

## EXISTING INCENTIVES FOR BIODEFENSE COUNTERMEASURE R&amp;D

Given the importance of biodefense to national security, the U.S. government has employed a broad menu of financial incentives to spur commercial investment in countermeasure R&D (Table 2). This menu can be separated into “push” incentives, which reduce industry’s cost of R&D and are typically used to motivate early-stage research, and “pull” incentives, which increase industry’s revenues from R&D and are typically used to motivate late-stage development and production. To date there has been little analysis of the effectiveness of these incentives in accelerating coun-

\*Two products have been approved using the Animal Efficacy Rule; both were products previously approved for use in the U.S. or Europe and used the Animal Efficacy Rule only to obtain approval for additional indications. Pyridostigmine bromide for prophylaxis against nerve agents has been approved using the Animal Rule, but this drug had already been approved in 1955 for the treatment of myasthenia gravis. Hydroxocobalamin received an indication for cyanide poisoning as well as smoke inhalation, but it had been approved in France since 1996. It remains to be seen how a genuinely new product will fare under the Animal Efficacy Rule.

Table 2. Incentives for Biodefense Countermeasure R&amp;D

| <i>Incentive Mechanism</i>               | <i>Examples</i>                                                                        | <i>Strengths</i>                                                              | <i>Weaknesses</i>                                                                         |
|------------------------------------------|----------------------------------------------------------------------------------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| <b>Push Incentives</b>                   |                                                                                        |                                                                               |                                                                                           |
| Government R&D and technology transfer   | NIH/DoD intramural research                                                            | Control over research path<br>Open results                                    | Weak financial incentives for performance                                                 |
| Government research grants and contracts | NIH/DoD extramural grants                                                              | Self-selection of quality researchers<br>Open results                         | Difficult to judge value of applications                                                  |
| Government-industry R&D collaborations   | CRADA                                                                                  | Avoids duplication of infrastructure                                          | Complicated IP environment                                                                |
| Liability protection                     | Safety Act<br>PREP Act                                                                 | Reduces developers' risks                                                     | Potential to reduce safety                                                                |
| Tax credits                              | Standard R&D tax credit<br>Orphan drug tax credit                                      | R&D may be more efficient than average tax spending                           | Less attractive to companies with low profits                                             |
| <b>Pull Incentives</b>                   |                                                                                        |                                                                               |                                                                                           |
| Regulatory rewards                       | Priority Review designation                                                            | Reduces time to market                                                        | Increased FDA costs                                                                       |
| Exclusivity reward                       | Patent protection<br>Orphan drug market exclusivity<br>Pediatric exclusivity provision | Valuable industry                                                             | Limited value for products with small markets<br>Reduces competition on price and quality |
| Procurement contracts                    | DoD procurement<br>HHS procurement (e.g., BioShield)                                   | Bidding promotes cost control<br>Familiar to government<br>No duplicate costs | Difficult to predict success of winning bidder<br>Contract must be adequately specified   |

termesure development. A range of existing and possible incentives are discussed below.

### *Push Incentives Used for Biodefense Countermeasure R&D*

#### **Government R&D and technology transfer**

HHS and the Department of Defense (DoD) conduct in-house (intramural) basic R&D focused on biodefense countermeasure development. Discoveries produced by federal scientists conducting basic R&D are often made available to the private sector through publication in scientific literature, or they may be patented by the federal government and made available to the private sector through technology transfers. Examples of biodefense-related technology transfers include the AVA and rPA vaccines for anthrax, which were initially developed by DoD and licensed to BioPort (now Emergent) and VaxGen, respectively. Government R&D allows government managers to retain control over the direction of research, but it does not provide them with the financial incentives common in private firms to motivate performance. It is not clear, however, that the lack of financial incentives leads to a lower rate of success or to reduced efficiency; the cost-effectiveness of government-managed drug development projects, such as that at the United States

Army Medical Research Institute for Infectious Diseases (USAMRIID), appears not to have been evaluated.

#### **Government research grants and contracts**

HHS, DoD, and, to a lesser extent, DHS award research grants to institutions for countermeasure development. Most grants for research in biodefense are awarded by HHS through the National Institute of Allergy and Infectious Diseases (NIAID).<sup>35</sup> In FY2006, NIAID awarded \$1.7 billion in funding for biodefense-related research.<sup>8</sup>

On December 19, 2006, President Bush signed the Pandemic and All-Hazards Preparedness Act into law (P.L. 109-417), which created the Biomedical Advanced Research and Development Authority (BARDA) within HHS. One of the purposes of BARDA is to fund the development of products across the so-called "valley of death" between NIAID-funded basic research and end-stage procurement by the BioShield program (described below). Recipients of government grants and contracts are motivated to use funds judiciously, as evaluations of their results are typically used in future grant and contract reviews. But it can be difficult for reviewers to accurately judge the value of a project based solely on an application or bid, and the application process is slow: The NIH R01 grant review process, for instance, takes 9 months, on average, from application to award.<sup>36</sup>

## INCENTIVES FOR BIODEFENSE COUNTERMEASURE DEVELOPMENT

**Government R&D collaborations**

Collaborations allow government, academia, and industry to share scientists, materials, facilities, and other resources. Over the past 3 years, NIH has entered into about 250 Cooperative Research and Development Agreements (CRADAs).<sup>37</sup> A 2005 CRADA teamed MedImmune researchers with government scientists in NIH laboratories to develop vaccines against pandemic influenza strains. USAMRIID has entered into CRADAs to develop anthrax therapeutics. NIAID makes several of its resources available to industry, including a program to screen drug candidates against biological agents.<sup>38</sup> By sharing resources, CRADAs reduce the duplication of equipment and space, thus reducing R&D costs. The chief disadvantage of CRADAs is that technologies resulting from joint public-private research face complicated disputes over intellectual property.

**Liability protection**

Liability protection reduces the financial risks to developers by lowering the costs of possible litigation. The first use of a medical countermeasure may be during an emergency, when the product is given to a large number of people. The potential for unforeseen side effects is significant. Liability protection can be made available to countermeasure developers under the SAFETY Act (part of the 2002 Homeland Security Act, P.L. 107-296) and under the Public Readiness and Emergency Preparedness (PREP) Act (part of the 2006 DoD Appropriations Act, P.L. 109-148).

**R&D tax credits**

R&D tax credits allow developers to write off R&D expenditures against their taxable profits in the year the expenditures were made. Government pays the costs of tax credits through reduced tax revenues. From studies in other industries, a dollar in tax credit stimulates a dollar of additional R&D.<sup>39,40</sup> This is efficient when a dollar in tax revenues would not be used as cost-effectively, on average, as a dollar in R&D. Arguably, countermeasure R&D represents such a case. Most companies receive an R&D tax credit equal to around 20% of qualified research expenses. Companies with drugs in development that prevent or treat diseases with a natural prevalence less than 0.05% can be given Orphan Drug Designation (ODD) by the FDA and receive a 50% tax credit on clinical trial expenses. Most if not all biodefense countermeasures should be eligible for ODD.

***Pull Incentives Used for Biodefense Countermeasure R&D*****Regulatory rewards**

Regulatory rewards increase revenues by shortening a product's time-to-market. The average FDA review process for a standard new drug takes 18 months.<sup>41</sup> New drugs thought to offer a significant improvement over existing products

qualify for "priority review" status, which shortens the average review period to 6 months.<sup>41</sup> This review, however, comes at some cost to the FDA. The additional FDA labor needed to provide priority review has been estimated at \$1 million per product.<sup>41,42</sup>

**Exclusivity rewards**

Exclusivity rewards allow developers to increase their revenues by reducing competition. The most common exclusivity reward is patent protection. Patents allow developers to hold a time-limited monopoly on, and thus charge a high price for, a novel technology. Patents generally last 20 years, but much of this time is consumed by R&D. Companies with drugs that have been given ODD receive a 7-year market exclusivity period for the orphan indication, which prevents competition from even chemically distinct products for the same indication, as long as the latter are not therapeutically superior. The value of patent and market exclusivity rewards is limited for products that have small markets: Extending a monopoly on an unprofitable product is still unprofitable.<sup>43</sup> These rewards are thus unlikely to be a strong incentive for most biodefense countermeasures, which will be sold only to government(s). However, exclusivity rewards could be valuable for some broad-spectrum anti-infectives that are effective against both biological weapons and more common infectious diseases.

**Procurement contracts**

Procurement contracts allow developers to earn revenues from developing and manufacturing countermeasures. HHS purchases countermeasures using the Special Reserve Fund created under the 2004 Project BioShield Act, which authorized \$5.6 billion over 10 years for procurement, thereby avoiding the uncertainty of the annual appropriations process. Under BioShield, the federal government can sign purchase agreements with companies whose products are expected to be eligible for approval or licensing within 8 years. The federal government pays only upon delivery of the product. The 2006 Pandemic and All-Hazards Preparedness Act allows HHS to make multiple milestone-based advanced payments (up to 50% of the total contract) under BioShield awards, thus allowing manufacturers to earn revenues from developing and manufacturing countermeasures prior to delivery of the product. The Act also gives HHS the authority to contract with a developer to establish "warm base" manufacturing capacity for a countermeasure. To date, six products have been procured under BioShield at a total cost of \$1.45 billion.

Procurement contracts are commonly used in government purchases. Competitively bid contracts increase efficiency when the government can accurately assess a firm's prospects for successfully delivering a high-quality product. These assessments are likely to be more accurate in tradi-

tional defense contracting, where developers have a long history of government contracts, than in biodefense contracting, where developers are often new companies developing pharmaceutical products with a low probability of success.

#### POTENTIAL INCENTIVES FOR BIODEFENSE COUNTERMEASURE R&D

Given the threat of bioterrorism and natural epidemics, and the relatively limited commercial investment in countermeasure development, HHS should explore additional R&D incentives that have been used in, or proposed for, other technology initiatives (Table 3).

##### *New Grant Incentives*

The immediate threat posed by biological weapons and the long development times required to produce a useable product warrant a faster NIH grant review process. The BioShield Act of 2004 granted NIAID expedited review authority for grants that are clearly biodefense-related.<sup>10</sup> But because biodefense depends on advances made in many biomedical disciplines, the entire NIH grant review process should be accelerated. Alternatives to traditional reviews exist and others have been proposed, including allocating a portion of the NIH funding to be managed by entrepreneurial program managers who seek out opportunities, rapidly fund promising research, then work closely with the scientists to monitor progress.<sup>44</sup> This process has been used with great success by the Defense Advanced Research Projects Agency (DARPA). Others have suggested creating NIH "prediction markets," in which a large community of

reviewers can quickly place bets on which research projects will be most productive.<sup>45-48</sup>

##### *Reward Vouchers*

Developers have expressed interest in making regulatory or exclusivity rewards transferable across products, in the form of vouchers (also called "wild cards").<sup>6</sup> A developer that successfully produced a countermeasure could be rewarded by being granted a patent extension, market exclusivity, or priority review for any other product in its portfolio, increasing that product's revenues. Vouchers could also be made tradable, allowing one developer to sell its voucher to another developer.

Patent extension and market exclusivity vouchers would increase developers' revenues by delaying the introduction of competition.<sup>15</sup> These would be highly valuable to developers with blockbuster drugs but could be costly to society by delaying the introduction of generics, thus boosting drug prices. Concerns over the costs of these incentives made them unpopular during Congressional debates on BioShield and BARDA.<sup>49</sup>

In contrast, priority review vouchers could be highly valuable to developers without imposing social costs. As explained above, priority review reduces a product's time to market by a year. At the same time, priority review does not delay the introduction of generics, and consumers have access to new medicines a year sooner. A priority review voucher that is *tradable* between developers would allow a biotech firm that successfully develops a countermeasure to sell its voucher to a pharmaceutical firm that has a potential blockbuster entering FDA review. There is risk to a firm in buying a priority review voucher: There is no guarantee that the product to which a voucher is applied will be ap-

Table 3. Proposed Incentives for Biodefense Countermeasure R&D

| <i>Incentive Mechanism</i> | <i>Examples</i>                                                               | <i>Strengths</i>                                                                                           | <i>Weaknesses</i>                                                                                                                                  |
|----------------------------|-------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|
| Exclusivity reward         | Roaming patent extensions                                                     | Valuable to industry                                                                                       | Patent extensions and market exclusivity have high social costs                                                                                    |
| Regulatory reward          | Priority review vouchers                                                      | Valuable to industry<br>Priority review vouchers could be highly cost-effective                            | Voucher could be applied to product that does not become commercially successful                                                                   |
| Prizes                     | DARPA Grand Challenge<br>NASA Centennial Challenges<br>InnoCentive Challenges | No direct payment for failure<br>Defers costs to future                                                    | Optimal prize amount hard to determine<br>Need to specify rules and product characteristics in detail<br>Sponsor may default<br>Duplicate research |
| Advance market commitment  | Pilot AMC for pneumococcal vaccine                                            | No direct payment for failure<br>Defers costs to future<br>Market induces competition on quality and price | Optimal AMC size unknown<br>Need to specify rules and product characteristics in detail<br>Sponsor may default<br>Duplicate research               |

proved by the FDA or become a commercial success. But most products that successfully navigate the clinical trials process and are submitted to FDA for final review are approved, and the risk of failure is likely to be outweighed by the voucher's value: One study estimated a value greater than \$300 million when transferred to a blockbuster drug (most of which do not already receive priority review).<sup>41,42</sup> To prevent delayed reviews of medically important products, FDA would need to hire additional staff to review voucher recipients' products. The cost of this additional labor has been estimated at \$1 million per product and could be billed to the voucher recipient.<sup>41,42</sup>

Tax credits also could be made tradable. Tax credits are little incentive for the many biopharma firms that are not profitable. However, credits could be made tradable across developers: Unprofitable firms could sell their credits to profitable companies. Alternatively, tax credits could be made deferrable to a future time when a firm is profitable.

### Prizes

"First-past-the-post" prizes offer rewards to the first researcher to complete a given research task. "Best entry" prizes reward whichever entry produces the most promising result within a fixed period. Historically, prizes have motivated inventions such as the Harrison Clock, steam locomotion, and photography.<sup>50</sup> They became less common in the 20<sup>th</sup> century but have enjoyed a resurgence in the past few years. (Patents are, in effect, a "first-past-the-post" prize, where the award is a time-limited monopoly.)

Modern prizes include the DARPA Challenge, the National Academy of Engineering's Grainger Challenge, NASA's Centennial Challenges, the Ansari X-Prize, and InnoCentive's prizes for inventions in chemistry and the life sciences. These prizes offer cash rewards to inventors who develop technologies meeting pre-established specifications. The FY2006 Science, State, Justice, Commerce and Related Agencies Appropriations Act (P.L. 109-108) directed the National Science Foundation to establish a prize program. And in 2007, a National Academy of Sciences committee proposed a program of experimental prizes and evaluations that would offer cash rewards for inventions of public value, under an Office of Innovation Prizes within the National Science Foundation.<sup>50</sup>

One study concluded that a prize is theoretically the best mechanism for eliciting innovation, "if the size of the prize can be linked to the social value" of the innovation.<sup>51</sup> Setting the prize's size is critical, as one can underpay and not motivate any R&D effort, or overpay and waste funds that could have been spent on other priorities. Other weaknesses of prizes are: competing developers will duplicate costs, and sponsors must pay developers a premium to compensate for the risks of default, failure, and competition. The strengths of prizes are: the sponsor pays nothing until a product is successfully developed, the sponsor need not audit or otherwise manage research, and developers will be motivated by competition.

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### Advance Market Commitments

An advance market commitment (AMC) is a guarantee by a government or other sponsor to pay developers a minimum price per dose of a medical product purchased in the market up to a specified volume.<sup>52</sup> The government issues a detailed set of technical specifications. Products meeting those specifications and purchased in the commercial market are guaranteed a co-payment from the sponsor up to a specified volume of sales. AMCs are distinguished from conventional purchase contracts, as there is a minimum price open to multiple competing developers and no guarantee on the number of doses purchased.

AMCs are untested but have been proposed for tropical diseases, such as malaria, tuberculosis, and HIV; one \$1.5 billion AMC has been secured for a (late-development) pneumococcal vaccine.<sup>53</sup> The necessary size of an AMC for a malaria vaccine with one entrant has been estimated at \$3 billion—the expected revenues from developing one commercial drug.<sup>52</sup> If a developer expected to split the market with a competitor, the AMC would have to be almost twice as large to spur R&D.

A theoretical model found that combining both an advanced market commitment and a payment of a fixed fraction of the developer's R&D costs is more cost-effective than either incentive independently.<sup>43</sup> Others have similarly recommended that AMCs be combined with milestone payments that provide financial support to companies while they are developing a product.<sup>54</sup>

The strengths and weaknesses of AMCs are like those of prizes.<sup>55</sup> One advantage of AMCs over prizes is that in markets with multiple purchasers, several products can be introduced that compete for market share. However, it is unlikely that the market for biodefense countermeasures will have many purchasers.

### RECOMMENDATIONS

Given the urgency of biological threats and the need to engage both large and small biopharmaceutical companies in developing countermeasures, we recommend the following:

1. Congress should expand BioShield funding, giving HHS the flexibility to fund a portfolio of biodefense countermeasures whose revenues are comparable to those of commercial drugs.

To date, the incentives used to promote countermeasure development have succeeded in motivating significant biodefense R&D effort by only a modest number of biotech companies and no large pharmaceutical companies. Project BioShield has been successful in awarding a small

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number of contracts for relatively mature products.<sup>10</sup> The first and largest BioShield contract—\$877 million for anthrax vaccine—was cancelled in December 2006 because of technical problems with the product and subsequent delays in the development of the vaccine candidate.

BioShield contracts do not resemble the scale and structure of the private drug market. BioShield's effectiveness will always be limited by its funding, which has been insufficient to attract large, profitable pharmaceutical companies. With \$5.6 billion to be allocated over 10 years available to purchase countermeasures for at least 14 top priority CBRN threat agents,<sup>2</sup> the expected revenues from developing a countermeasure are significantly lower than the \$3 billion or more expected, on average, from developing a single commercial drug.<sup>32</sup> It is not surprising that pharmaceutical companies prefer to chase blockbusters over BioShield contracts. BioShield has so far attracted only small biotechnology companies with lower revenue expectations than large pharmaceutical companies—and limited resources to carry drugs through clinical trials. Perhaps most important, the modest scale of the BioShield fund has prevented HHS from developing a broad portfolio and taking risks with individual contracts. Most products fail in clinical trials; HHS thus needs a budget sufficiently large to fund, in parallel, multiple countermeasure candidates targeting the same threat.

Regardless of how its costs are distributed across society and across time, biopharmaceutical research is expensive, with the average cost of developing one drug around \$1 billion.<sup>13</sup> Debate about which incentives are more or less cost-effective than others may be academic when total public investment has to significantly increase—perhaps tenfold—to address existing and foreseeable biological threats. No “funny mirror” incentive exists that can make a \$900 million BioShield contract appear as attractive to industry as a \$3 billion commercial drug.

Congress has not yet indicated whether additional monies will be added to the BioShield purchase fund once the initial funds are exhausted. This uncertainty complicates management of the fund by HHS and may reduce pharmaceutical companies' investments in R&D for products that will reach maturity after BioShield's expiration.

## **2. HHS should replicate features of the pharmaceutical market that have succeeded in generating drugs and vaccines of commercial value.**

More money is necessary but not sufficient to create a strong biodefense. Success also depends on HHS's ability to create a predictable and well-managed market for countermeasures. The private market has offered sufficient incentives to generate many drugs for chronic diseases such as

high cholesterol or acid reflux. For commercial products, developers estimate potential market volume from epidemiologic data and competitive intelligence, and market price from marketing surveys; they anticipate a predictable regulatory process; and they receive push funding from private capital markets and pull funding from repeated sales in consumer markets. HHS can replicate these features of the private market by:

- increasing the detail of price, volume, and product specifications in requests for proposals;
- improving its Tech Watch to identify and fund promising new technologies at early stages;
- clarifying the path for licensure under the Animal Rule and Emergency Use Authorization;
- increasing transparency in procurement decisions;
- providing a mix of push and pull funding, with push funding directed toward early-stage research, and pull funding directed toward late-stage development and production;
- making large volume purchases; and
- shortening the period from when a pathogen is deemed a threat to when a BioShield contract is signed (currently more than 2 years on average).<sup>10,56</sup>

Perhaps most important, HHS can hire managers to lead the government's countermeasure effort who have a history of success in the biopharma industry.<sup>56</sup>

## **3. Congress should establish tradable priority review vouchers for developers of new countermeasures.**

Of the proposed incentives reviewed here, only tradable priority review vouchers have theoretical merits clear enough to warrant immediate implementation. With a potential benefit to industry of \$300 million and a public cost of \$1 million or less, tradable priority review vouchers would be highly cost-effective.

## **4. An NAS or NBSB committee should evaluate existing and potential incentives for commercial development of biodefense countermeasures—particularly “flexible” technologies effective against a range of threats.**

Despite the billions of federal dollars invested annually in incentives for industrial R&D, few data exist on their cost-effectiveness. HHS should commission a panel of experts from the economic and pharmaceutical development sectors to evaluate incentives for countermeasure R&D. Incentives for other important pharmaceuticals, such as drugs for orphan and neglected diseases, could also be evaluated. This task could be charged to a National Academy of Sci-

## INCENTIVES FOR BIODEFENSE COUNTERMEASURE DEVELOPMENT

ences (NAS) committee or to a working group of the National Biodefense Science Board (NBSB, established by the Pandemic and All-Hazards Preparedness Act in 2006, but not yet constituted).

As biotechnologies become more powerful and more accessible, the range and severity of biological threats will increase.<sup>57</sup> Eventually it will be too slow and costly to stockpile countermeasures for every threat. Two recent U.S. government documents—the White House's Homeland Security Presidential Directive 18 and HHS's Public Health Emergency Medical Countermeasure Enterprise (PHEMCE) Strategy—recommend addressing this problem by developing broad-spectrum countermeasures and platform technologies effective against a range of threats. Given this new strategic shift by the government, incentives should be evaluated that can engage academia and industry in the development of these new "flexible biodefense" technologies.<sup>58</sup> As many of these technologies are early-stage, improvements to existing push incentives should be explored.

**5. An NAS or NBSB committee should evaluate Virtual Pharma models of government-managed countermeasure development, in which separate stages of research, development, and production are contracted to individual firms.**

In principle, government could adopt the "Virtual Pharma" model used by some pharmaceutical companies, in which discrete stages of the R&D process are contracted to separate developers.<sup>59</sup> Under this model, BARDA or a BARDA-like organization could manage a portfolio of products from basic research to production, inviting developers to bid for each step in the R&D process, and tailor the size and structure of incentives accordingly. This model could decrease the costs and risks for both government and developers.

The success of Virtual Pharma depends on the ability of a management team to efficiently contract projects and cancel dead-ends. The experience of Virtual Pharma Public-Private Partnerships (PPPs) in developing drugs for tropical diseases such as malaria, HIV, and tuberculosis suggests that effective management is possible. The R&D costs of PPP projects are significantly lower than pharma's, although their clinical success rates remain to be established.<sup>60,61</sup> It is possible that PPPs gain efficiency by outsourcing R&D to the lowest-cost developers, without regard for potential intellectual property violations or trade secret piracy. Secrecy reduces commercial developers' tolerance for outsourcing, but government-managed programs would not be so constrained.

There is a historical precedent for government successfully managing countermeasure R&D. The greatest period

of vaccine discovery was during World War II, when industrial vaccine developers partnered with the lead users of vaccines—the military. Industry scientists reported directly to military managers, who set clear objectives and ambitious schedules for every vaccine and used a combination of push and pull funding.<sup>62</sup> The experience of government-managed countermeasure development should be evaluated and, where appropriate, replicated.

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## The Commercial Market For Priority Review Vouchers

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**ABSTRACT** In 2007 the US Congress created the priority review voucher program to encourage the development of drugs for neglected diseases. Under the program, the developer of a drug that treats a neglected disease receives both a faster review of the drug by the Food and Drug Administration and a voucher for a faster review of a different drug. The developer can sell the voucher. We estimated the commercial value of the voucher using US sales of new treatments approved in the period 2007–09. A third of the commercial value of a voucher comes from capturing market share from competitors, nearly half from the value of earlier sales because of the expedited review, and less than a quarter from lengthening the time between approval and the launch of a generic competitor. We estimate that if only one priority review voucher is available in a year, it will be worth more than \$200 million, but if four vouchers are available, the value could fall below \$100 million. Congress should be cautious about expanding the voucher program, because increasing the number of vouchers sharply decreases the expected price. Lower voucher prices could undermine the incentive to develop new medicines for neglected diseases.

**T**he standard review of a new drug by the US Food and Drug Administration (FDA) takes about ten months. However, the FDA offers priority review—which takes about six months—to drugs that provide significant improvements in safety or effectiveness over existing drugs. The difference of four months in review times could be highly valuable to a drug developer with a potential blockbuster drug.<sup>1</sup>

In 2007 Congress leveraged the value of an earlier FDA approval by creating the priority review voucher program to encourage the development of new drugs for neglected diseases. And in 2012 Congress expanded eligibility for priority review vouchers to include rare pediatric diseases. Under the voucher program, the developer of a drug for a neglected or rare pediatric disease receives priority review for that drug, as well as a bonus priority review voucher for

another drug treating any disease. Thus, the following two drugs are involved: the drug that earns its manufacturer a bonus priority review, and the drug that uses that bonus priority review. The drugs need not be from the same company, because the voucher may be sold. The ability to sell a voucher increases its value, especially for smaller firms with fewer drugs.<sup>2</sup>

The objectives of this article are to estimate the commercial value to the potential buyer of a priority review voucher, based on current regulatory and market conditions, and to show how the voucher price falls as the quantity of available vouchers increases. The price of a priority review voucher is critical to the success of the program in encouraging new drug development.<sup>3</sup>

As of the end of 2015 nine vouchers had been awarded, and four of them had been sold. Vouchers were awarded for drugs for neglected diseases, including malaria and leishmaniasis, as

cally net of rebates. In instances where net sales were not available in annual reports, we used analysts' reports or sales reported by IMS Health.

We converted net sales to 2014 dollars using the prescription drug index of the Consumer Price Index—All Urban Consumers. As Ernst Berndt and colleagues did,<sup>17</sup> we projected future sales for recently launched drugs. We predicted future sales using the prescription uptake curve of twenty-six standard-review products, fifth-year sales, and an annual price increase of 3.2 percent (the compounded average growth rate for the period 2009–14 of the prescription drug index of the Consumer Price Index—All Urban Consumers). We estimated sales for twenty years after submission to the FDA.

**ESTIMATING THE COMPETITIVE EFFECT** First, we estimated the competitive effect, in which value comes from earlier market entry relative to the entry of competitors within the same therapeutic area. A drug with earlier market entry is adopted by more providers and patients than a drug with a later entry, and if the first drug is effective for those patients, they are reluctant to switch to a later market entrant. Hence, earlier market entry yields higher sales.

To estimate the competitive effect, we used the same approach that we did previously,<sup>12</sup> when we estimated peak share (that is, the highest monthly market share within the first four years after launch) as a function of speed to market, promotional spending, order of market entry (for example, whether the drug entered second or third in its therapeutic class), and number of competitors. We then used the increase in peak share from launching four months earlier to estimate the increase in annual sales that would result from having a priority voucher. More information about our estimation of the competitive effect is available elsewhere<sup>12</sup> and in the online Appendix.<sup>18</sup>

**ESTIMATING THE TIME VALUE AND EXCLUSIVITY EFFECTS** Second, we estimated the time value effect, meaning the value of generating earlier sales. Earlier sales are more valuable than later sales in part because, as noted above, the money from sales can be invested. We assumed a cost of capital of 10.5 percent.<sup>19</sup> As discussed above, we estimated sales for the twenty years following submission to the FDA, including zero sales during review. In a sensitivity analysis, we used a different cost of capital and a time horizon beyond twenty years.

Third, we estimated the exclusivity effect. Compared to a drug that receives a standard review, a drug with a priority review voucher is approved earlier, but its patent does not necessarily expire earlier. This means that it can have a longer period of time between drug launch and

## The changing regulatory and commercial environment necessitates a new analysis of the value of a voucher.

patent expiration, which we refer to as the effective patent life. Under the Drug Price Competition and Patent Term Restoration Act of 1984 (commonly known as the Hatch-Waxman Act), the patent expiration date depends on the length of clinical testing and review (for more on the patent term and how it affects voucher value, see the Appendix).<sup>18</sup>

In addition to the assumptions described above, to calculate the time value and exclusivity effects, we made the following assumptions, which are summarized in Exhibit 1: that the probability of approval of a drug for which a voucher would be used was 90 percent;<sup>19</sup> that the marginal corporate tax rate was 28 percent;<sup>20</sup> that the marginal cost of making a drug was 20 percent, based on the ratio of the price of generic drugs to brand-name drugs when there are many generic competitors;<sup>21</sup> that the time between the purchase of a voucher and submission for FDA approval was six months (which means that approval would come twelve months after the purchase of a voucher, as was the case when Regeneron/Sanofi purchased a voucher for alirocumab, its cholesterol drug);<sup>22</sup> that the drug would have market exclusivity of 12.9 years, with a standard deviation of 3.2 years;<sup>23</sup> and that after patent expiration, brand-name sales would erode, falling to 11 percent of the molecule market share as of one year after the entry of a generic competitor (with 9 percent as the standard deviation).<sup>23</sup> In a sensitivity analysis, we modified the erosion rate to examine how the value of a voucher would increase with limited generic competition, as could happen with biologics.

**VOUCHER PRICE** To estimate the voucher price, we estimated the value of a voucher for each drug approved in a given year after a standard review. We ordered the values of these vouchers from highest to lowest in a given year and then estimated the range of possible voucher prices: For

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**VOUCHER PRICE** To estimate the voucher price, we estimated the value of a voucher for each drug approved in a given year after a standard review. We ordered the values of these vouchers from highest to lowest in a given year and then estimated the range of possible voucher prices: For

**EXHIBIT 1****Assumptions used to estimate the value of a priority review voucher**

| Description                                           | Value         | Source                                                                                                              |
|-------------------------------------------------------|---------------|---------------------------------------------------------------------------------------------------------------------|
| Voucher acceleration of regulatory review             | 4 months      | FDA goals are 6 months for priority review and 10 months for standard review (see Note 14 in text)                  |
| Fifth-year sales for a top-selling drug               | \$914 million | Authors' analysis of data on average sales of lisdexafetamine, regadenoson, ustekinumab from company annual reports |
| Discount rate                                         | 10.5%         | DiMasi et al., 2016 (see Note 19 in text)                                                                           |
| Market exclusivity with voucher                       | 12.9 years    | Grabowski et al., 2014 (see Note 23 in text)                                                                        |
| Probability of approval after submission              | 90%           | DiMasi et al., 2016 (see Note 19 in text)                                                                           |
| Marginal cost                                         | 20%           | Grabowski et al., 2007 (see Note 21 in text)                                                                        |
| Tax rate                                              | 28%           | Mintz and Chen, 2014 (see Note 20 in text)                                                                          |
| Brand share of molecule 12 months after generic entry | 11%           | Grabowski et al., 2014 (see Note 23 in text)                                                                        |
| Time between voucher purchase and FDA decision        | 12 months     | Sanofi/Regeneron purchased a voucher in 2014; the FDA decision was in 2015 (see Note 4 in text)                     |
| Time horizon                                          | 20 years      | Authors' assumption                                                                                                 |
| Annual price increase                                 | 3.2%          | Authors' analysis of data from the prescription drug index of the Consumer Price Index—All Urban Consumers          |

**SOURCE** Authors' analysis of data from the sources in the exhibit. **NOTE** FDA is Food and Drug Administration.

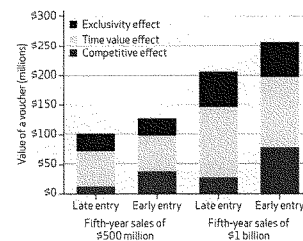
each voucher, the price could be as high as the voucher value and as low as the value to the alternative buyer (alternative buyers are discussed below). We assumed that the relevant time period was one year (that is, we estimated the potential voucher value and prices per calendar year).

For example, consider three drugs for which the value of priority review would be \$300 million, \$200 million, and \$100 million, respectively. If there were just one voucher for sale, the bidder that values the voucher at \$300 million would buy the voucher, and the bidder that values the voucher at \$200 million would be the alternative buyer. We expect the price to be between \$200 million and \$300 million, because at prices below \$200 million, two bidders (the manufacturers of the drugs for which the voucher would have a value of \$200 million or \$300 million) would bid up the price to \$200 million, and at prices above \$300 million no one would be willing to purchase the voucher. Likewise, if there were two vouchers for sale, then we would expect the price to be at least \$100 million.

Additional details about the theoretical model, estimation methods, and sensitivity analyses are available in the Appendix.<sup>14</sup>

### Study Results

**COMPETITIVE EFFECT** For the first or second drug in the same therapeutic area to enter the market, accelerating drug launch by four months is associated with an increase in peak share of 1.2 percentage points (for example, from 50 percent to 51.2 percent).<sup>15</sup> If two drugs launch at the same time, each drug is expected to achieve 50 percent peak share in the first four years, so 1.2 percentage points would be a 2.5 percent increase in sales. Similarly, for the third drug to enter the

**EXHIBIT 2****Estimated value of a priority review voucher by its three effects**

**SOURCE** Authors' analysis using the assumptions in Exhibit 1. **NOTES** The value of the priority review voucher is divided into three effects—competitive effect, time value effect, and exclusivity effect (explained in the text)—according to whether the fifth-year sales are \$500 million or \$1 billion and whether the drug in question is first or second to enter the market (early entry) or third (late entry).

## PRESCRIPTION DRUG POLICY

## EXHIBIT 3

## Priority review voucher value based on fifth-year sales and approval acceleration

| Fifth-year sales<br>Millions of dollars | Approval acceleration (months) |       |       |       |       |       |       |
|-----------------------------------------|--------------------------------|-------|-------|-------|-------|-------|-------|
|                                         | 1                              | 2     | 3     | 4     | 5     | 6     | 7     |
| \$ 250                                  | \$ 28                          | \$ 40 | \$ 52 | \$ 64 | \$ 76 | \$ 87 | \$ 99 |
| 500                                     | 56                             | 81    | 105   | 128   | 151   | 175   | 197   |
| 750                                     | 85                             | 121   | 157   | 192   | 227   | 262   | 296   |
| 914                                     | 103                            | 147   | 191   | 234   | 277   | 319   | 361   |
| 1,000                                   | 113                            | 161   | 209   | 256   | 303   | 349   | 395   |
| 1,250                                   | 141                            | 202   | 261   | 320   | 379   | 436   | 493   |
| 1,500                                   | 169                            | 242   | 314   | 384   | 454   | 524   | 592   |
| 1,750                                   | 197                            | 282   | 366   | 448   | 530   | 611   | 691   |

**SOURCE** Authors' analysis using the assumptions in Exhibit 1. **NOTE** The exhibit shows the voucher values only for drugs that were first or second entrants into the market and whose effective patent life would be extended by the duration of the accelerated review time.

market, accelerating drug launch by four months is associated with an increase in sales of less than 1 percent (or 0.30 percentage point).

**EXPECTED VOUCHER VALUE FOR TOP-SELLING DRUGS** The value of the voucher depends on many factors, including entry order and effective patent life, denoted in Exhibit 2 as the exclusivity effect, and approval acceleration (Exhibit 3). For a drug that has fifth-year sales of \$1 billion and is an early mover to the market (which means no competing drug has locked in many providers and patients), the voucher value is \$256 million if the drug extends effective patent life and \$196 million if it does not (Exhibit 2).

For a drug that has fifth-year sales of \$914 million (the average for the top-selling drugs of

2007, 2008, and 2009), the voucher value is \$234 million if the voucher extends the effective patent life by four months (Exhibit 3). Of that value, almost half (\$106 million) is attributable to the time value effect, roughly a third to the competitive effect (\$73 million), and less than a quarter to the exclusivity effect (\$55 million). The voucher value decreases to \$179 million if the voucher does not extend the drug's effective patent life (data not shown).

If the drug that benefits from priority review is the third to enter the market instead of the first or second, the voucher value decreases from \$234 million to \$189 million (assuming that potential fifth-year sales remain at \$914 million). This is because of the reduced competitive effect of an earlier approval of a drug on third entrants into the market, compared to second entrants (\$27 million versus \$73 million).

If a drug has potential fifth-year sales of \$250 million and the voucher extends the effective patent life by the four months provided by the priority review, the voucher value for a first or second entrant into the market decreases to \$64 million (Exhibit 3). If a product reaches blockbuster status at that time instead (sales of \$1 billion), the voucher value is \$256 million.

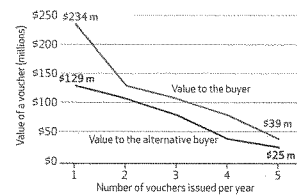
We assumed that generic competition eroded fourteenth-year and later sales. However, the assumption has little effect on the present value of a voucher, because sales in the distant future are heavily discounted. Without generic competition, the voucher value increases from \$234 million to \$263 million (data not shown). Likewise, the voucher value increases from \$234 million to \$267 million if the discount rate is 8 percent instead of 10.5 percent. Extending the analysis from twenty years to twenty-five years after FDA submission increases the voucher value by less than \$2 million.

**VOUCHER VALUE AND PRICE** If there were only one voucher to be sold per year, the value of the voucher would be between \$234 million (the value to the buyer willing to pay the highest price) and \$129 million (the value to the buyer, known as the alternative buyer, willing to pay the second-highest price) (Exhibit 4). The steep decline in value as the number of vouchers increases is a result of a skewed sales distribution. The highest-grossing drug has sales that are nearly double those of the second-highest-grossing drug (\$900 million compared to \$500 million, as shown in the Appendix).<sup>18</sup>

In Exhibit 4 we assumed that the patent expiration date was unchanged, so that a voucher gave a drug an extra four months of effective patent life. However, if the voucher moved the expiration date forward, the voucher value and price would both fall by about 25 percent.

## EXHIBIT 4

## Value of priority review vouchers, by number of vouchers issued per year



**SOURCE** Authors' analysis of products approved in the period 2007-09 with a standard review by the Food and Drug Administration. **NOTES** The expected price is between the value to the buyer and the value to the alternative buyer. If there are two vouchers available, there will be two buyers (those willing to pay the first- and second-highest prices; the alternative buyer will be the one not willing to pay either of those prices).

## The estimates presented here apply to the economic value of earlier drug launch in general.

### BUSINESS IMPLICATIONS OF THE VOUCHER

**VALUE** We showed that the expected value of a voucher for a drug with \$914 million in fifth-year sales is \$234 million (assuming an exclusivity effect). If four vouchers are available in one year, our estimates predict prices as low as \$39 million (the value to the would-be fifth buyer). If there is one price for all four vouchers, the price will be between \$39 million and \$79 million. If there is not a single price for all four vouchers, perhaps because the voucher sellers and buyers are not all in the market at the same time, the price could be as high as \$234 million.

How do the estimates compare to actual selling prices? Recall that vouchers have been sold for prices ranging from \$67.5 million in 2014 to \$350 million in 2015.<sup>7</sup> Regeneron paid \$67.5 million for a voucher to speed the review of alirocumab, which suggests that Regeneron expected sales of the drug to exceed \$250 million. Indeed, before alirocumab's launch, analysts projected fifth-year sales of more than \$1 billion in the United States.<sup>24</sup> Thus, the value of the voucher would be more than \$256 million (Exhibit 3)—well in excess of the price of \$67.5 million paid by Regeneron.

AbbVie paid \$350 million for a voucher to be used in the future on an unspecified drug. A \$320 million voucher price is associated with fifth-year US drug sales of \$1.25 billion (Exhibit 3), so clearly AbbVie expected the voucher to be used for a blockbuster drug. Moreover, because only one voucher was available at the time, the price suggests that the voucher had a high value to both AbbVie and another bidder.

Whether the voucher will provide a positive return for the developer depends on whether the expected net present value of a voucher exceeds the cost of conducting a Phase III clinical trial. The expected net present value of a voucher sold for \$234 million is approximately \$99 million at the beginning of such a trial. This estimate assumes that only a Phase III trial is required, the probability of submission is 70 percent, the probability of approval is 90 percent, the discount

rate is 10.5 percent, and four years elapse between the beginning of the trial and FDA approval.<sup>10,25</sup>

A net present value of \$99 million will typically cover the cost of a Phase III trial plus FDA submission for a drug for a parasitic or infectious disease. While the average out-of-pocket cost for such a trial and submission is \$190 million,<sup>25</sup> the cost of a trial for an anti-parasitic or anti-infective drug tends to be about half of the average,<sup>26</sup> and orphan drug tax credits cut those costs in half again. Therefore, a voucher price of \$234 million should cover the cost of a Phase III trial plus FDA submission.

If voucher prices fall below \$100 million, as we would expect with four or more vouchers per year (Exhibit 4), then the expected net present value of the voucher would fall below the cost of a Phase III clinical trial. Hence, the voucher (even with orphan drug tax credits) would not provide sufficient incentive for drug development, and additional incentives would be needed—such as an advance market commitment<sup>5</sup> or a profitable commercial market.

Finally, while the focus of this article is on the priority review voucher program, the estimates presented here apply to the economic value of earlier drug launch in general. Thus, they are relevant for estimating the economic gains from faster completion of clinical trials and faster FDA review.

### LIMITATIONS

► **LIMITATIONS OF THE MODEL:** There are several reasons why the potential voucher value could be higher than the value in our model. First, the competitive effect value would double if two companies were racing to have the first drug approved in a class and only one voucher were available. In such a race, the competitive effect of a voucher would include not only the impact on its buyer's drug, but also the impact of preventing the competitor from increasing its drug's market share through earlier market entry. The competitive effect would double from \$80 million to \$160 million and the voucher value would rise from \$256 million to \$336 million for an early entrant with fifth-year sales of \$1 billion (Exhibit 2).

Second, the voucher value would be higher than our estimates if drug sales were higher than the sales of the drugs in our data sample. Our three-year sample period (2007–09) did not include mega blockbuster drugs such as atorvastatin and esomeprazole magnesium that achieved multiple billions of dollars in annual sales while under patent protection.

Third, if one company controlled the market for vouchers, either through its own drug development or through buying vouchers from

others, then it could charge higher prices than we estimated. Similarly, while many vouchers might be sold in a given year, if a company had only a small window of time during which to purchase a voucher (that is, between receipt of the results from a Phase III clinical trial and submission to the FDA), and only one voucher were available during that window of time, then the seller would have market power and the price might be close to the buyer's value.

Conversely, recall that the voucher value would be lower if there were no exclusivity effect (Exhibit 2). Also, the voucher value would be lower if earlier market entry did not translate to earlier sales because of delays by payers waiting to grant reimbursement until a competitor drug entered the market.

► **LIMITATIONS OF THE VOUCHER PROGRAM:**

This article has focused on the commercial value of the priority review voucher program. However, there are several concerns about the social value of the program. First, vouchers have been awarded for drugs that would have been developed without the incentive.<sup>27</sup> This is analogous to giving tax breaks for charitable donations that would have been made even without the tax incentive. However, unlike tax breaks, the costs of the voucher program are not necessarily borne by the government. In some cases, the costs of the program are borne by competing drug companies that lose market share to the company that uses the voucher for its drug. Regardless of who bears the costs, it appears that some voucher recipients received a windfall. One possible regulatory mechanism for reducing such windfalls would be to require a minimum investment in research and development by voucher recipients. However, such cost-based rewards might encourage inefficient investment.

Second, while the voucher program encourages innovation, it does not ensure access to drugs developed as a result of the program.<sup>1,27-29</sup> Drug developers should be required to submit to FDA their plans for how to make their drugs accessible. Also, funding from governments or foundations might be needed to purchase treatments for people with neglected diseases who live in low-income countries. Other mechanisms for encouraging drug development for neglected diseases include direct government or foundation subsidies of clinical trials and advance commitments to purchase the drugs.<sup>5,30</sup>

### Policy Implications

As more diseases are included in the priority review voucher program, the number of vouch-

## Congress and the FDA should carefully consider the conditions for eligible diseases and drugs.

ers will increase. However, we have demonstrated how eligibility expansion could decrease the expected vouchers' price and reduce the incentives to invest in neglected or rare pediatric diseases.

If four vouchers were granted per year for products that would otherwise receive standard review, the price of a voucher could fall as low as \$39 million (Exhibit 4). The net present value would be even lower and might not cover the cost of a Phase III clinical trial. Because a lower price for vouchers would reduce the incentive for developing drugs for these diseases, policy makers should think carefully about making additional diseases eligible for vouchers.

To avoid the substantial decline in the price and value of priority review vouchers that would be caused by having a large number of vouchers in the marketplace, Congress and the FDA should carefully consider the conditions for eligible diseases and drugs. Additional diseases should be evaluated for inclusion in the program based on need—which might include factors such as the burden of the disease, current drugs in use or in late-stage development, and alternative incentive mechanisms. Furthermore, Congress could reduce the supply of vouchers by excluding from eligibility those drugs that were already widely available outside the United States (for example, drugs that had been available for a given indication for more than five years before FDA submission). Finally, Congress should require that manufacturers have a plan for ensuring drug access.

### Conclusion

Congress and the FDA might find it easier to say "no" to expansions of the priority review voucher program if they used the evidence in this study about the impact of additional vouchers on the price of all vouchers. ■

The authors thank Dana Randall for editing assistance. David Ridley was an author of the original priority review voucher proposal. Stéphane Régner is

an employee of Novartis Pharma AG but has not been involved in any work related to the priority review voucher at Novartis Pharma AG. The views

presented in the article are those of the authors.

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June 17, 2016

Dr. Richard Hatchett MD  
Acting Director  
Biomedical Advanced Research and  
Development Authority  
U.S. Department of Health and Human Services  
200 Independence Avenue, S.W.  
Washington, DC 20201

Dear Dr. Hatchett:

Thank you for appearing before the Subcommittee on Health on May 19, 2016 to testify at the hearing entitled "Examining H.R. 3299, Strengthening Public Health Emergency Response Act."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on July 1, 2016. Your responses should be mailed to Graham Pittman, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, DC 20515 and e-mailed in Word format to [graham.pittman@mail.house.gov](mailto:graham.pittman@mail.house.gov).

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

  
Joseph R. Pitts  
Chairman  
Subcommittee on Health

cc: The Honorable Gene Green, Ranking Member, Subcommittee on Health

Attachment

**Attachment — Additional Questions for the Record**

**The Honorable Marsha Blackburn**

One of the mechanisms proposed by the Federal Government to offset development costs for essential medical countermeasures is the support of so-called “Dual Use Compounds.” These medical interventions are designed to address a specific bioterror threat, but are simultaneously being developed for the treatment of specific patient populations. In the setting of these parallel development programs, safety concerns may emerge which are specific to a limited patient population or are related to an extended duration of treatment.

1. Are there mechanisms in place to prevent a safety concern which is relevant to a specific patient population from negatively impacting the development or procurement of a medical countermeasure, particularly when the safety concern is not applicable to the general population in the event of a bioweapon attack?

**The Honorable Michael C. Burgess**

1. The Ebola crisis exposed weaknesses in our healthcare system’s ability to identify and respond to biological public health threats. In what specific ways does H.R. 3299 address gaps in our national biological preparedness? Additionally, how will the bill improve HHS’s ability to both proactively identify biological pathogens, such as Ebola or Zika, and make available medical countermeasures in a timely and effective manner?
2. When BARDA was created in 2006, Congress provided the agency with authority to negotiate its own contracts. In 2009, ASPR moved all of BARDA’s authority to negotiate contracts to ASPR’s Office of Acquisitions Management, Contracts, and Grants. While this move was intended to simplify the contracting process it created confusion and unnecessary delays. There is a consensus among industry that sole contracting authority should return to BARDA. H.R. 3299 would direct the Secretary of HHS to delegate contracting authority for negotiating and entering into any contracts, grants, or cooperative agreements back to BARDA. Please describe the specific ways this authority would improve BARDA’s ability to execute its mission.

**The Honorable Billy Long**

On January 20, 2004, the Secretary of Homeland Security determined that anthrax is a material threat to the U.S. population sufficient to affect national security. Since that time, the U.S. Department of Health and Human Services (HHS) has been pursuing a comprehensive strategy to address this threat. This approach has included acquisition of vaccines, antibiotics, and therapeutics to meet immediate public health needs in the event of an anthrax attack. While progress has been made in preparing against anthrax, I would like to learn more about BARDA’s plans for the future of its anthrax vaccine program.

1. Can you please provide an update on the next-generation anthrax vaccine candidates currently being supported by BARDA?

I also understand that BARDA continues to pursue multiple next-generation Recombinant Protective Antigen (rPA) anthrax vaccines. The president's FY17 budget reinforced the support and need for an rPA anthrax vaccine, and indicated that in the next three years BARDA anticipates new procurements of an rPA anthrax vaccine for the U.S. Strategic National Stockpile. Additionally, in the PHEMCE Multi-Year Budget submitted to Congress, BARDA says it intends to procure \$300 million of an rPA anthrax vaccine in FY18. The budget includes timelines indicating BARDA's plans to transition from development to procurement of an rPA anthrax vaccine in FY2017–FY2018.

2. Can you please describe the potential benefits associated with an rPA anthrax vaccine, as compared to traditional anthrax vaccines?
3. Can you please provide a detailed summary of the developmental status and projected timelines for each of the rPA anthrax vaccine programs?

