Answers to Post-Hearing Questions for the Record
and Member Requests for the Record
Submitted to the Honorable James C. Greenwood
from Representative Tim Murphy, Chairman, Representative Michael C. Burgess, MD, and Representative Susan Brooks
Subcommittee on Oversight and Investigations
House Committee on Energy and Commerce

"Outbreaks, Attacks, and Accidents: Combating Biological Threats"

February 12, 2016

The Honorable Tim Murphy

1. **During the hearing, we discussed a recent GAO report on the failings of the BioWatch programs. In your view, should the Federal government continue to fund such programs in the absence of valid performance data? (*Question for the Record and Member Request for the Record*)**

   As our Study Panel states on page 59 of our bipartisan report, *A National Blueprint for Biodefense: Leadership and Major Reform Needed to Optimize Efforts*, "The biodetectors designed to inform biosurveillance of the air (commonly referred to as environmental detection) have not progressed significantly since their initial deployments… The BioWatch program was launched in 2003 with great urgency, but its potential remains unrealized. As of 2015, BioWatch uses the same technology – manual filter collection and laboratory polymerase chain reaction testing – as it did twelve years ago… The entire BioWatch system is dying for lack of innovation... To date, no fully automated, tested, and evaluated autonomous detection system has been deployed that adequately addresses the airborne biological threat or sufficiently provides operational response information."

   Recommendation 31 of our report calls for the development of an environmental detection system that takes advantage of 21st Century technology. We believe that Congress should consider funding the development of advanced environmental detection systems to replace BioWatch. Ideally, we would recommend that the Secretary of Homeland Security replace BioWatch Generation 1 and 2 detectors within five years with the systems developed per action item 31a of our report. If they cannot be replaced within that timeframe, we recommend the Secretary of Homeland Security evaluate whether or not they should still be in service. Congress should require that the Department of Homeland Security and any other federal agencies that deploy biodetection systems: 1) measure and evaluate performance on a periodic basis; 2) make good faith efforts to obtain evaluative feedback from state, local, and other hosts for their systems; 3) use resulting data to improve upon current and inform future systems; and 4) provide these data and analysis to Congress for its use in oversight. If the responsible departments do not obtain these data, conduct analyses, use those analyses to optimize biodetection and

biosurveillance performance and inform procurements, and report data and analyses to Congress, Congress should no longer provide funding for, and responsible federal departments and agencies should no longer maintain, these programs.

The Honorable Michael C. Burgess, M.D.

1. **Are there any strategies the Blue Ribbon panel considered regarding the availability of diagnostic testing to achieve rapid local response as well as surveillance? Has the Panel explored the role of diagnostics in outbreaks?**

   The Blue Ribbon Study Panel dedicated an entire meeting to discussing surveillance and detection issues in some depth. The meeting, on March 12, 2015, consisted of five panels with 19 speakers that included a former CDC Director, former Chief Medical Officer from the U.S. Department of Homeland Security, state laboratory directors, public health professionals, industry representatives, and many others.

   The Blue Ribbon Study Panel recognizes that diagnostic tests play a critical role in the detection of and response to an outbreak. Our report notes that availability of point-of-care diagnostic testing would have significantly improved management of the Ebola outbreak last year. Without point-of-care testing, screening of suspected patients was often based on little more than thermometer readings and a series of questions. Diagnostics would have significantly improved quarantine and isolation decisions at home and abroad, and offered information that would have spared treatments when they are not needed. Diagnostic testing is a valuable tool to help responders establish situational awareness, screen and triage patients who have been exposed, and determine appropriate intervention strategies.

   The Panel assessed that the technologies needed for the quick patient-side diagnostics of the kind used in doctors' offices to screen for influenza exist or are in development in the private sector. However, the U.S. government has not been prioritizing or adequately incentivizing the development of these technologies to maturity. Without rapid point-of-care diagnostics, the Nation remains vulnerable to biological threats. In Recommendation 30 of our report, the Panel recommends that the government develop requirements for rapid point-of-care diagnostics for all material biological threats and emerging infectious diseases. The Director of the Biomedical Advanced Research and Development Authority should determine the suite of rapid diagnostics that are needed, prioritize their development and acquisition, and implement a plan to work with industry and academia to achieve success in meeting its requirements.

2. **In 2009 during the H1N1 flu epidemic, as soon as the genetic sequence of the virus was identified, hospital and public health labs were able to rapidly develop laboratory procedures to test patients suspected of having the flu. While the FDA does have the ability to issue an emergency use authorization for commercially manufactured test kits, it is laboratory developed testing procedures that provide necessary and timely local testing. You may be aware**

that the FDA intends to finalize guidance requiring premarket review for all laboratory developed testing procedures. I'm concerned that these proposed changes to FDA policy could hinder the development of these diagnostics and create regulatory challenges in these situations when time is of the essence. What recommendations do you have for the FDA on how to ensure that hospital labs are able to mobilize quickly to provide diagnostics for outbreaks such as the Zika virus and other even more pathogenic infectious diseases?

Hospital and other laboratories (e.g., public health laboratories) develop and use assays to test clinical samples for pathogens of serious public health concern; as a result, they play a critical role in our ability to quickly assess and respond to emergent epidemics like that caused by Zika. In my role as President and CEO of the Biotechnology Innovation Organization (BIO), I have worked with companies developing a range of diagnostic products. Any FDA regulatory pathway designed to expedite the emergency development of diagnostic tests should be clear, apply a uniform standard, and be flexible enough so that In Vitro Diagnostic (IVD) test kit manufacturers, independent laboratories, and academic medical centers alike are able to leverage the mechanism in response to disease outbreaks. BIO welcomes the opportunity to work with the FDA to assist the Agency in developing a streamlined and efficient approach to regulating these types of emergency use tests. The FDA should continue to incorporate stakeholder feedback when developing regulatory policies for these tests and consider practical approaches that maximize the ability for diagnostic test developers to comply to ensure availability of these important products during times of emergency.

3. **In the opening statement you mentioned that the medical countermeasures market is small, and lacks market incentives for investment. You also mentioned that the current regulatory pathways that exist for emerging infectious diseases can be unclear, which results in low innovation in the space. Aside from necessary appropriations from the BioShield Special Reserve Fund, what are some additional recommendations you or the panel could make to spur innovation in medical countermeasures?**

As we state on page 55 of our report, the best way to incentivize industry to a level that allows it to participate in biodefense programs and pursue truly innovative ideas is to: 1) fund MCM development to legislatively authorized levels; 2) re-establish multiyear advanced appropriations through the [BioShield Special Reserve Fund]; and 3) eliminate unnecessary red tape within the partnership. To further enhance the environment for innovation, especially as the partnership model between government and industry evolves, many have urged Congress and BARDA to adopt other incentives that would invigorate MCM developers.

The Panel calls upon the ASPR and DASD for Chemical and Biological Defense to convene non-governmental stakeholders to identify meaningful incentives that are independent of Congressional appropriations for MCM developers and manufacturers. Among the incentives that should be explored are success-based milestone payments and monetary prizes; minimum

procurements/advanced market commitments; guaranteed pricing; patent extensions; orphan drug status expansions; wild-card exclusivity; transferable data exclusivity extensions; and priority review vouchers (PRVs).

Several of these recommendations are addressed in existing legislation. H.R. 3299, the Strengthening Public Health Emergency Response Act *(Senate companion is S. 2055, the Medical Countermeasure Innovation Act)*, introduced by Representatives Susan Brooks and Anna Eshoo, includes provisions to streamline contracting processes, coordinate stockpiling plans, and increase transparency around future MCM funding needs. The bill also provides a meaningful incentive for medical countermeasure development by extending the neglected tropical disease PRV program to the 13 deadly pathogens identified by the Department of Homeland Security as material threats to U.S. national security.

The PRV is a proven and valuable incentive that has helped to spur investment in other complex and neglected areas of R&D. Congress has recognized this and recently acted to pass a bipartisan bill adding Zika to the PRV program in an effort to encourage the private sector to prioritize and expedite the development of drugs and vaccines to treat and prevent Zika. An extension of the PRV program to include material treats is viewed by many as a way to offset the dramatic decline in federal procurement funding for MCMs. Adding MCM targets to the PRV program may help convince investors that the government is committed to this endeavor and provide increased certainty that MCMs can have value in the marketplace.

Our report calls for a revolution in the U.S. approach to the development of medical countermeasures for emerging infectious diseases with pandemic potential. BARDA, NIAID, and DOD should establish a joint program to rapidly develop MCMs as the need arises. The recent experience with Ebola showed us that rapid mobilization of government resources and private sector ingenuity could significantly shorten the amount of time needed to develop viable countermeasure candidates. We must glean lessons learned from this experience that could be applied to a new development and manufacturing paradigm. Establishment of an antigen bank as described on Page 54 of our report could help operationalize a plug-and-play strategy using proven platform technologies for use in an emergency for both human and animal pathogens.

The Panel's broader recommendations for improving the biodefense enterprise, such as institutionalizing leadership for biodefense in the Office of the Vice President, development of a comprehensive national biodefense strategy, and a unified budget, would also provide more stability, transparency, and certainty to companies looking to invest in MCMs. When companies know that the government is a committed partner in this endeavor, investment and innovation will likely increase.

As we state on pages 52 of our report, "The Nation remains unprepared for known, unknown, and unexpected threats." To address these threats, the federal government should work closely with industry to develop new strategies

that strike the right balance between stockpiling MCMs against known high consequence/low probability threats, and surge manufacturing for emerging and unknown threats. Due to the limited market for these products, federal funding for the Special Reserve Fund, BARDA, and pandemic influenza programs is extremely critical to maintaining an environment conducive to MCM innovation, and it remains the most important incentive the federal government can provide. The current shortfall we are facing for the Special Reserve Fund risks leaving critical products unfinished, and puts the nation in danger of losing the important progress we have made to date.

4. **As a physician, I understand that the development and validation of precise diagnostics for emerging outbreaks is crucial to combating biological threats such as Zika virus. We need to quickly develop diagnostics for these purposes and work to ensure that public health laboratories and hospital laboratories throughout the country are able to screen people for the disease and that patients have access to these tests. I'm concerned that the CDC is creating barriers for laboratories to quickly disseminate the test and by not enabling competing tests, there's no way to assess whether or not the CDC test is adequate. Please describe the process CDC engages in for sharing necessary information, test reagents, and reference materials to laboratories to develop tests for emerging infectious diseases. I've also heard that despite the lack of cooperation from the CDC, some physicians have already developed tests for Zika virus at Texas Children's Hospital and Stanford University. Have you considered collaborating with these academic medical centers on developing diagnostics?**

While our Study Panel is aware of the CDC process for sharing information, test reagents, and reference materials with laboratories for the purposes of developing tests for emerging infectious diseases, we do not possess sufficient information with which to describe this process in detail for you. We recommend that you obtain this information directly from the CDC.

I can offer some additional insight from my role as the President and CEO of the Biotechnology Innovation Organization (BIO). BIO itself, an industry trade organization, has not entered into any collaborations with academic medical centers to develop diagnostics. However, many of our member companies have entered into various collaborations with academic medical centers, state and federal governments, non-governmental organizations (NGO), and other organizations and agencies to develop medical countermeasures to respond to emerging infectious diseases, pandemic influenza, and material threats and they will continue to do so in the future.

In a 2015 BIO report titled, "Advancing Translational Research for Biomedical Innovation," we highlighted that industry direct funding for university biomedical-related research stands at 49% of all industry-funded university research in 2013, reaching $1.73 billion or just over 5% of total university biomedical-related research. Industry is relying more and more on academic research for technological development and the launch of new products. This is evident by a sharp rise in the share of patents associated with new therapies

citing academic research over the past decade. Industry-university research collaborations continue to evolve and BIO will play in critical role in bridging the worlds of biotechnology industry and academic research.

The Honorable Susan Brooks

1. **Your testimony notes the past effectiveness of priority review vouchers (PRVs) in incentivizing research. Please identify existing PRV programs for rare pediatric diseases and neglected tropical diseases, and share your assessment of any related increases in biotech investments in these areas. (*Question for the Record and Member Request for the Record*)**

Priority review vouchers provide a powerful incentive to stimulate drug development in complex and underserved diseases or conditions. The current programs focus on neglected tropical diseases (NTDs) and rare pediatric diseases which, like medical countermeasures, often lack the market opportunity to attract significant investment. The priority review voucher is awarded to a company when a new product for a qualifying disease is approved. The company may use the voucher to expedite the review of another product by 4 months or they may sell the voucher to another company. Recent sale prices for priority review vouchers demonstrate the significant value of this incentive to manufacturers.

To date, nine priority review vouchers have been awarded – three through the neglected tropical disease program and six through the rare pediatric disease program. A chart summarizing these awards is included below.

Year	Disease	Drug	Company	Program
2009	Malaria	Coartem (artemether/lumefantrine)	Novartis	NTD
2012	Tuberculosis	Sirturo (bedaquiline)	Janssen (J&J)	NTD
2014	Morquio A syndrome	Vimizim (elosulfase alfa)	BioMarin	Rare pediatric
2014	Leishmaniasis	Impavido (miltefosine)	Knight	NTD
2015	High-risk neuroblastoma	Unituxin (dinutuximab)	United Therapeutics	Rare pediatric
2015	Rare bile acid synthesis disorders	Cholbam	Asklepion	Rare pediatric
2015	Hereditary orotic aciduria	Xuriden	Wellstat	Rare pediatric
2015	Hypophosphatasia	Strensiq (asfotase alfa)	Alexion	Rare pediatric
2015	Lysosomal acid lipase (LAL) deficiency	Kanuma (sebelipase alfa)	Alexion	Rare pediatric

BIO believes that these programs, and the neglected tropical disease priority review program in particular, have been successful in stimulating new drug

development in these critical areas of unmet medical need. In evaluating the impact of these programs on investment in the areas of neglected tropical disease and rare pediatric disease, however, the available data are not sufficiently granular to identify investment in rare pediatric disease and neglected tropical disease from broader categories of biopharmaceutical investment.

Using the number of clinical development programs as a proxy for overall investment in neglected tropical diseases, we have seen an increase in research and development pipeline activity and, therefore, investment in the area of neglected tropical diseases. At present, there are at least 43 clinical development programs focused on the eligible neglected tropical diseases, including 13 for Malaria, 12 for Tuberculosis, and 10 for Ebolavirus. This is supported by the larger overall trend observed in venture (private company) investment in infectious disease, which has seen a 220% increase between 2012 and 2015, and is presumed to include a significant increase in investment in neglected tropical diseases.

Regarding pediatric rare diseases, as a recent GAO study noted, it is still "too early to gauge the effectiveness" of the rare pediatric disease priority review voucher program. The rare pediatric disease voucher program was created in 2012 with the passage of the Food and Drug Administration Safety and Innovation Act (FDASIA). Unlike the neglected tropical disease voucher program, which is permanent, the authority of the Secretary to award vouchers was set to terminate one year after the award of the third voucher under this program (which was awarded in March 2015). Though the program received an extension through September 2016 in last year's Omnibus package, the unclear future of the program and lack of permanence introduces significant uncertainty and unpredictability for sponsors who are considering the risky, long, and costly investment into a clinical development program for rare pediatric condition. For this reason, BIO has supported and continues to work with Congress to make the program permanent, so the full potential of the program can be realized in stimulating new drug development of new therapies for devastating childhood diseases.