TESTIMONY OF PHYLLIS ARTHUR, SENIOR DIRECTOR FOR VACCINES, IMMUNOTHERAPEUTICS AND DIAGNOSTICS POLICY, BIOTECHNOLOGY INDUSTRY ORGANIZATION (BIO)

Good morning Chairman Harkin, Ranking Member Enzi, Members of the Committee, ladies and gentleman. I am Phyllis Arthur, Senior Director for Vaccines, Immunotherapeutics and Diagnostics Policy at the Biotechnology Industry Organization (BIO). BIO represents more than 1,100 companies, academic institutions, state biotechnology centers and related organizations in all 50 states.

In the area of biodefense, BIO represents a broad mix of small, medium and large companies involved in the research, development and manufacture of medical countermeasures or MCMs. These companies develop and manufacture biological products for the detection, diagnosis, treatment, prevention and delivery of countermeasures in response to chemical, biological, radiological and nuclear (CBRN) events.

One of the goals of the Department of Health and Human Services' (HHS) review of the Public Health and Emergency Medical Countermeasures Enterprise (PHEMCE) was to identify and solve those issues limiting companies of all sizes from successfully engaging in the countermeasure process. In its input on both the HHS PHEMCE review and reauthorization of the Pandemic and All-Hazards Preparedness Act (PAHPA) of 2006, BIO has stressed one overarching principle: the biopharmaceutical industry wants to be an integral partner with the U.S. government in the development and stockpile delivery of these vitally important countermeasures to protect the American people. Therefore BIO has focused its recommendations on changes that are essential to both attract *and retain* companies of all sizes to the Enterprise. Maintaining the skills and know-how of companies that have already weathered the complicated MCM development and contracting process must be as important to the U.S. government as attracting new companies to the MCM development space.

BIO has identified three key priorities to improve preparedness, accelerate approvals and reduce the time needed to develop essential MCMs. We urge the Committee to address these areas in the reauthorization of PAHPA. These include: (1) providing greater transparency and clarity in the MCM market establishment, the contracting process, and in advanced research and development activities; (2) improving the clarity, consistency and integration of FDA in the development and approval of MCMs; and (3) ensuring that the future of the PHEMCE is adequately funded by simultaneously reauthorizing Project Bioshield and the Special Reserve Fund (SRF) with PAHPA.

Investments have yielded success

Over the last ten years, bipartisan Congressional efforts have created and funded an Enterprise that has begun to show success. Some of the most important accomplishments involve pandemic influenza preparedness. Not only did government agencies and

industry partners mount a well thought out response to the 2009 H1N1 pandemic, they also invested in products to prepare for a possible avian/bird (H5N1) pandemic and conducted a comprehensive review of influenza vaccine production issues. This review resulted in the President's Council of Advisors on Science and Technology (PCAST) report in August of 2010[1]. This report made important and attainable recommendations for both existing and future technology to meet the challenges of responding to future pandemics. Some of these are currently being implemented, but all should be fully considered and supported with adequate resources.

Currently, there are more than 50 biotechnology companies conducting research and development in new seasonal and pandemic influenza vaccines in over seven different novel technologies and platforms. Other companies are developing new antivirals and diagnostic tools as well. While the Biomedical Advanced Research and Development Authority (BARDA) has invested in new manufacturing facilities and issued new contracts for several of these innovative platforms, more investment at every phase of development is vital from both the public and private sectors if America wants to realize our full potential.

Developing countermeasures to respond to bioterrorism threats is even more complex than influenza. First, the targeted diseases are less well characterized and studied, especially in special populations such as children and pregnant women, and the study of these diseases often relies on complicated animal models. Second, how the MCM will be used in response to an attack determines how it should be designed and clinically studied. Thus, determining the best development pathway to demonstrate safety and efficacy requires a great deal of scientific collaboration between industry and the key federal agencies. Third, for each unique biothreat, the goal is to have a diagnostic tool to identify the threat as well as countermeasures to prevent illness and others to treat those who become infected. Lastly, many of the technologies being applied for medical countermeasures are relatively new themselves. They hold great promise as methods to solve the pivotal clinical issues that these threats pose, but they also require more significant investment at every research stage to help increase the probability of success.

Despite these challenges there have been some successes in the development and procurement of MCMs for the treatment and prevention of lethal biothreats, such as anthrax, botulinum toxin and smallpox. In the past 2 years, key countermeasures to vaccinate against smallpox and treat exposure to anthrax have been delivered to the Strategic National Stockpile (SNS). Furthermore, several key procurement and advanced development contracts have been issued that will lead to the final development of novel technologies for smallpox, new broad spectrum antibiotics and innovative treatments for the side effects associated with acute radiation syndrome (ARS).

Recommended actions

BIO has identified three challenges that limit industry's participation in PHEMCE and we urge Congress to address them in the PAHPA reauthorization: (1) defining a viable

[1] Executive Office of the President, President's Council of Advisors on Science and Technology, Report to the President on Reengineering the Influenza vaccine Production Enterprise to Meet the Challenges of Pandemic Influenza, August 2010.

market value for MCMs versus the opportunity cost of investing in alternative therapeutic areas; (2) management of cost and risk, especially in the regulatory process; and (3) the sustainability of the market over time.

(1) Defining a Viable Market Value for MCMs

The Project BioShield Act of 2004 accomplished several important goals, but the most significant was the creation of the Special Reserve Fund. BioShield is designed to guarantee companies that the government will purchase new, successfully developed countermeasures for placement in the Strategic National Stockpile. The existence of the SRF and the annual appropriations to BARDA, which support MCM advanced development and CDC procurement funding, define the marketplace for MCMs. Companies consider the amount of resources available through BARDA and the SRF when comparing the opportunity cost of pursuing the development of a specific countermeasure. The time and company resources allocated for these products diverts R&D and manufacturing resources away from commercial products and must be subjected to the same rates of return analysis. In addition, private investors place little to no value on this type of research as the market is difficult to calculate, development and contract award projections are seldom met, and the guarantee of government purchase is not always clear. Therefore, there are very limited external private funds to support companies in the MCM space.

Another part of the opportunity cost assessed by industry is the time required to achieve success. While industry, particularly small biotechnology companies, finds BARDA a good and effective partner, the acquisition and contracting functions to acquire new countermeasures are viewed as lengthy, opaque, and unpredictable. The trigger to transition a program from advanced development to procurement is unclear. Target dates to complete contract awards are typically not met and some acquisitions are delayed by months, years, or even canceled. The negotiation process is lengthy and the rationale and potential triggers for contract options are unclear. The signal to industry is that despite the enormous risks of development, new drugs and vaccines developed as countermeasures have far less value than commercial products.

BIO recommends that HHS be required to provide bi-annual reports to Congress outlining BARDA advanced development activities and the status of achieving key milestones, the length of time to BioShield procurement award, and other BioShield procurement activities. BIO also recommends greater transparency in BARDA/BioShield contract requirements including the early establishment of required product characteristics.

(2) Management of Cost and Risk and the Regulatory Process for MCMs

The development of countermeasures is a unique, resource-intensive and complex process that is costly and fraught with risk. One of the most significant risks is that countermeasures are approved via a convoluted regulatory pathway. Similar to commercial biologicals, new countermeasures can take 8-12 years to develop at a cost of $800 million to $1 billion, and failure is common at all stages of development. Yet in

most other ways MCM development and approval is much more complicated. Testing and clinical trial design requirements are less well established, requiring the use of multiple animal models to prove efficacy, which adds an extra dimension of risk and uncertainty to this process.

One of the most significant recommendations from the PHEMCE review was to invest significantly in the FDA review and regulatory science processes. BIO and its members strongly support this recommendation, and have worked to ensure FDA was allowed a transfer of money for such purposes as part of the FY 2011 FDA appropriation. The FDA has tremendous expertise in the science of drug development and the manufacturing of complex drugs, diagnostics and biologics. The lack of full integration across the Enterprise, especially as it pertains to the approval process for countermeasures, has in several instances, led to significant delays and the need for unexpected regulatory actions by companies in order to achieve licensure for a product. Effectively integrating FDA into the MCM development efforts will ensure that the government can have more rapid access to fully licensed medicines, devices and diagnostics for national security threats in a cost-effective manner.

To meet this goal FDA needs to be given an affirmative role in solving the scientific and regulatory hurdles, not just the review and approval, of MCMs. This can best be accomplished by encouraging the FDA to work collaboratively with company sponsors throughout the entire MCM development process to design development plans and associated studies, especially those requiring use of animal models. The current structure and resources provide a disincentive for FDA to spend time on these complex issues in partnership with industry. Additionally, BIO recommends that FDA funding targeted to improving MCM efforts should be linked to measurable metrics.

BIO recommends that the FDA become more involved in the development of MCM's through a combination of planning and coordination activities and implementation of specific measurements for MCM initiatives.

(3) Sustainability of the MCM Market

The Project BioShield Act and PAHPA helped to build processes to advance clinical and manufacturing infrastructure to protect against a multitude of biological threats. While there have been successes in several strategic portfolios within HHS, currently the U.S. is decades away from having an adequate arsenal of countermeasures to safeguard our citizens. In addition to developing and stockpiling countermeasures against currently anticipated threats, it is critical that the U.S. build the capability to respond to novel threats such as newly emerging diseases and genetically-modified pathogens. The U.S. government can help increase the nation's preparedness by undertaking several other key actions.

First, the reauthorization of PAHPA and the BioShield SRF are critical to these efforts. Therefore BIO strongly urges Congress to reauthorize the Special Reserve Fund simultaneously with the reauthorization of PAHPA. The SRF should be funded at a level that incentivizes private industry to actively participate in the MCM process.

Furthermore, Congress should clearly articulate that development of MCMs is a national security priority and that funding for these efforts be treated as national security and/or homeland security spending.

Second, BIO recommends that Congress formally establish a process by which HHS and its relevant agencies (NIH, CDC, FDA and ASPR) develop an integrated five-year plan that can be shared with all stakeholders. Ineffective coordination and collaboration between the various government agencies involved in the Enterprise adds to the overall uncertainty surrounding MCM's. The prioritization of threats is not transparent so it is not clear which pathogens, platforms, indications and target populations are the most important. Indeed one government agency may view these threats in different ways from the others, thus leading to conflicting, or overlapping, programs with differing priorities.

The PHEMCE review highlighted the importance of a 5-year plan for the Enterprise with goals tied to measurable outputs and outcomes. Due to the long development timelines for biological products, industry partners need to be able to plan and communicate with their investors on the anticipated value and impact of MCM projects with some increased level of certainty. A systematic, transparent vision from the U.S. government will help companies assess the viability of both their existing and future countermeasures' programs. This multi-year strategic plan, coupled with modifications to the contracting processes, would encourage increased industry participation.

Third, BIO recommends the continued investment in distribution and public health infrastructure. Both the PHEMCE review and the PCAST report on Pandemic Influenza considered the breadth of the preparedness continuum – surveillance, rapid manufacturing of MCMs, diagnosis, and ultimate delivery to the public. In order to benefit the public, the U.S. government must know when and how to deploy and administer countermeasures. Some of the PHEMCE and PCAST recommendations will require longer-term investments, such as training public health and medical first-responders, while others can be implemented in the near-term through more effective planning and with modest resources. For example, stockpiling strategies for products that are applicable to many different emergencies – such as needles, syringes, and critical assay compounds, can ensure rapid availability and avoid supply chain disruptions.

Lastly, one of the most critical elements of responsiveness involves the nation's ability to detect and identify these threats to best mount a proper and timely response. BIO members are also concerned that the U.S. government makes the right investments in global and U.S. surveillance testing and reporting networks. Efforts should be made to extend the network and to invest in and explore common platforms and design tools that can increase efficiency and reduce costs. Improving interagency coordination within the U.S. national network, while striving to modernize its technical and technological capabilities, would increase speed and accuracy in detecting emerging diseases and threats.

Improving the MCM process requires sustained partnership

Because there is no viable commercial market for most MCMs, it is essential for federal, state and local governments to be involved in the detection of threats and the development and dissemination of the products in the event of an emergency. As is true with typical biologics development, it takes many products in development to arrive at one successfully licensed vaccine, antimicrobial or diagnostic test. If our collective goal is to use innovative technology to help solve vital national security issues, then everyone must be willing to acknowledge the higher degree of risk and uncertainty inherent in MCM development. Future plans and investments are pivotal to sustain current successes and further strengthen and improve the nation's preparedness.

BIO commends the Committee for holding this important hearing and stands ready to work with Congress on these important issues. BIO strongly encourages the Committee to improve preparedness and accelerate development and approval of essential MCMs by: (1) providing greater transparency and clarity in the MCM market establishment, the contracting administration process, and in advanced research and development activities; (2) improving the clarity, consistency and integration of FDA in the development of MCMs; and (3) ensuring that Project Bioshield and the Special Reserve Fund are simultaneously reauthorized with PAHPA.

Over the last ten years, bipartisan Congressional efforts have created and funded a public health emergency medical countermeasure enterprise (PHEMCE) that has begun to show success. It is critical that future plans and investments be made that will build upon this success.