



May 4, 2018

Chairman Greg Walden
Committee on Energy and Commerce
U.S. House of Representatives
2125 Rayburn House Office Building
Washington, DC 20515

Ranking Member Frank Pallone, Jr.
Committee on Energy and Commerce
U.S. House of Representatives
2322A Rayburn House Office Building
Washington, DC 20515

Chairman Lamar Alexander
Committee on Health, Education, Labor and Pensions
428 Dirksen Senate Office Building
U.S. Senate
Washington, DC 20510

Ranking Member Patty Murray
Committee on Health, Education, Labor and Pensions
428 Dirksen Senate Office Building
U.S. Senate
Washington, DC 20510

Re: Transforming medical countermeasure technology and partnerships

Dear Chairman Walden, and Ranking Member Pallone, Chairman Alexander, Ranking Member Murray:

The Blue Ribbon Study Panel on Biodefense recently moderated two roundtables to identify ways to overcome some of the most vexing medical countermeasure (MCM) technology, business, and policy challenges across the biological threat domain. Private sector pharmaceutical, scientific, academic, and governmental affairs representatives attended and were joined at the second meeting by federal officials from the Department of Agriculture (USDA), Department of Defense (DOD), Department of Health and Human Services (HHS), and the White House.

The MCM assets now available to civilians and to military personnel have grown substantially in the last decade. The partnerships needed to continue to build these assets to meet persistent and advancing biological threats, however, are now at considerable risk. Real and perceived under-investment, unsustainable investment, process uncertainty, and strategic disparity undermine what must be a vibrant enterprise. We maintain that advancing the national MCM infrastructure needed for research, development, and procurement will reduce the risk associated with biological warfare, bioterrorism, emerging infectious diseases, and biological accidents. We urge you to demonstrate your commitment to this core national security function by advancing the following recommendations.

1. **Integrate animal health into the national security approach to medical countermeasures.** The gross inequality between human and animal funding levels and the segregation of research between the two sectors constitute a national security liability. Many material threats, select agents, and emerging infectious diseases are human diseases with veterinary counterparts, some of which regularly cause outbreaks elsewhere in the world in livestock and wildlife. Yet conversations about the protection of human health by controlling emerging infectious diseases in animal hosts have been extremely limited, and the authority of animal health agencies to regulate has been based on animal health, not public health.
 - a. ***Establish a framework for combatting emerging infectious diseases.*** Most emerging infectious diseases in people originate in animals. No MCM were ready when the largest Ebola outbreak the world had ever seen – likely caused by a spillover from bats to humans – occurred. In the preceding years, the government had not sufficiently determined what to fund with its limited resources. At present, HHS prioritizes efforts to address biological threat agents via Department of Homeland Security material threat determinations (MTDs), but the U.S. government has not instituted and budgeted for an analogous process for emerging infectious diseases. In accordance with Blue Ribbon Study Panel Recommendation 7c (*A National Blueprint for Biodefense*, 2015), HHS, in coordination with DOD and USDA, should create a similar

prioritization framework for emerging infectious disease threats. This framework should address pathogens and pathogen families with the potential to cause a catastrophic public health emergency and include agents known to infect wildlife and domestic animals. It should drive funding for MCM development and other areas (e.g., biosurveillance, response planning) and engage and motivate the private sector to develop and manufacture MCM. Funders must establish a vision for an emerging infectious disease MCM enterprise, define what constitutes successful emerging infectious disease MCM, and communicate this vision along with specific product requirements to industry partners.

- b. ***Make USDA part of the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE):*** BARDA was envisioned to be part of – not the entire – MCM enterprise. USDA should also participate in PHEMCE. Many diseases that could necessitate USDA MCM acquisitions are the same for DOD and HHS. USDA also has lessons to share about how it works with industry to develop effective MCM for production animals, a market in which the cost must be low and efficacy must be high. Some veterinary companies are already using platforms to develop their animal products, and the veterinary development timeline is much shorter. This means animal health pharmaceutical companies get products to market earlier. These companies also possess extensive experience in areas like animal models and manufacturability that can help inform human MCM endeavors. These experiences are relevant and should not be ignored.
- c. ***Require animal disease risk assessment.*** USDA should develop a risk assessment for animal diseases and work with HHS to assess the risk of diseases with zoonotic potential. USDA should assess the ability of the National Veterinary Stockpile to deploy sufficient MCM to combat high-consequence animal diseases within 24 hours of request. USDA should also use these risk assessments to prioritize the pathogens identified on the USDA *High-Consequence Foreign Animal Diseases and Pests* list. USDA should use the findings to inform its budget request; drive federal priorities for MCM innovation; and incentivize public-private partnerships to develop, transition, approve, license, and procure these products.

2. **Reduce market and process uncertainty at BARDA.** Variability and lack of certainty are two of the foremost hurdles to expanding industry participation in MCM advanced development and manufacturing. Indeed, these hurdles may prove so significant for some companies, even those that have successfully delivered MCM, that they may exit the market entirely. Although all biopharmaceutical ventures carry risk, larger companies can manage this risk through a balanced portfolio of projects, the most successful of which can yield a high return on investment. Pervasive market uncertainty in the far less profitable MCM enterprise makes business endeavors unattractive and unsustainable.

- a. ***Create fiscal certainty.*** In order to develop national security MCM, industry partners forego potential profit margins orders of magnitude higher than for commercial products. These companies need certainty in procurement to convince them and their investors that engaging in MCM development makes reasonable business sense. The annual appropriations process for advanced development and procurement, and dependency on emergency supplemental appropriations for unanticipated threats, make doing business with companies that base their operations on multi-year outlooks and planning unsustainable. In accordance with Blue Ribbon Study Panel Recommendation 28b (*A National Blueprint for Biodefense*, 2015), Congress must reinstate the advanced appropriation for Project BioShield for ten years at a minimum of \$7.1 billion. Additionally, in accordance with Blue Ribbon Study Panel Recommendation 28c, Congress and the HHS Assistant Secretary for Preparedness and Response (ASPR) should address prioritization and the need for guaranteed, sustained funding for pandemic influenza preparedness. The appropriation levels must be tied to rigorously established MCM requirements based on risk analysis.
- b. ***Create process certainty:*** In the last several years, the HHS Biomedical Advanced Research and Development Authority (BARDA) noticeably shifted away from process and partnership toward product. Prioritizing products over partnerships has damaged partnerships and preparedness. The rules governing BARDA and DOD processes for advanced development and manufacturing should be defined with industry partners up front and with far greater clarity and commitment. Companies need to understand when and how much of their proposed product the government will procure, as the frequent moving of goalposts throughout development and procurement creates an untenable business environment. For projects in which the government is not interested, federal public health security leaders need to relay that quickly (i.e., white papers should be reviewed and comment provided within 45 days). The BARDA process at this stage of

review should be more like that of the Defense Advanced Research Projects Agency (DARPA), for which program managers, not contracting officers, are the central deciding figures.

3. **Accelerate platform technologies.** One way to create MCM quickly, safely, and effectively for unpredictable emerging infectious diseases and outbreaks is to develop a suite of platform technologies. Generally, platform technologies rely upon a common manufacturing process backbone that uses a standard process to insert foreign genes. By relying upon a well-established manufacturing process and customization through standardized processes, platform technologies can reduce the risk associated with development. These production platforms may be based on, but not limited to, RNA expression systems; DNA cloning vectors; various virus, plant, or bacterial expression vectors; and viral-vectored vaccines. With targeted government and industry investments, these technologies could come to fruition within three to four years, especially for vaccines and diagnostics. To mature the technology, however, the government must mature the way it invests in the technology and ensure that partnership and business plans accompany technical plans for leveraging any platform capability. There is presently no business model in place that addresses how the government can work with industry to develop MCM platforms. At a minimum, elements of certification, expedited review, and the role of the HHS Centers for Innovation in Advanced Development and Manufacturing must be addressed.
 - a. **Certify platforms:** The Food and Drug Administration (FDA) approves products, not platforms. FDA, in consultation with DOD, BARDA, and other PHEMCE partners, should establish an MCM platform certification process. A regulatory construct that allows for the consideration of a company's novel platform as a basis for future MCM products would serve as an industry incentive. Its establishment would effectively reduce the risk of future product development using that platform. Determining what constitutes a platform will be difficult, but the definition should include a regularized chemistry, manufacturing, and controls (CMC) process and standardized general release criteria. The USDA Center for Veterinary Biologics policy, "Licensing Guidelines for Production Platform-Based, Non-Replicating, Nonviable Products," allows for rapid swapping of closely related immunogenic determinants, and could provide a starting point from which FDA could build a platform certification process for human products.
 - b. **Priority review platforms:** The platform certification process described above is likely to be extensive and should result in a thorough FDA understanding of the platform technology (e.g., CMC, clinical experience). This advanced understanding will enable subsequent review by the FDA under the expedited Priority Review process of other products based upon that certified platform. FDA commitment to the accelerated approval times associated with Priority Review for subsequent products utilizing a certified platform would provide significant incentive for industry to utilize appropriate platform technologies.
 - c. **Leverage CIADMs:** The HHS CIADMs and the DOD MCM Advanced Development and Manufacturing facility (ADM) were envisioned to make such platform-based products a reality. They could enable advanced development and manufacturing of platform technologies if aggressively integrated into the product development process. They should become places where companies want to go to advance their promising technologies. They should shrink development schedules and address significant business difficulties. At present, two major challenges prevent this: small companies are concerned about protecting their intellectual property when handed over to a privately owned ADM with its own MCM interests, and large companies are concerned about risks to their commercial business during regulatory review. The Salk Institute, a private nonprofit organization, was essentially the forerunner of what we think of as an ADM today, and BARDA should consider Salk's example as it revisits the business model for these kinds of facilities. DOD and BARDA should undertake planning for CIADM reconfiguration immediately. Planning should include industry and all federal agencies with MCM responsibility. Considerable thought must be given to contracting reform (discussed below) as the Federal Acquisition Regulation (FAR)-based, cost-reimbursable contract system in place does not work. An independent assessment (outside of DOD and HHS) of the existing CIADM model is needed to support this reconfiguration. This planning must consider the role of the USDA and its industry partners in using the CIADMs to enable mutually beneficial technologies and to keep the facilities in use.
4. **Reform FDA process to develop products faster.** We can get closer to on-demand MCM in just a few years and investments to improve production cycling by days or weeks are possible. These kinds of advances, however, will not provide the same near-term relief that FDA could achieve on release testing. Investment in enabling technologies must go, therefore, hand in hand with reform of regulatory process. FDA needs to be part of the

advanced development process early on, describing what it wants to see in a product or an investigational new drug. Advances in the speed with which products are marketed should not compromise the FDA's high safety and efficacy standards.

- a. **Standardize and clarify regulatory process.** The FDA, in collaboration with its upstream development government partners, must address development and standardization of regulatory processes that will provide needed transparency to MCM developers. The MCM industry needs to understand all elements of the process, and the government needs to mitigate the inherent risk. Several areas of regulatory reform should be considered – for example, reducing risk associated with clinical trials, and allowing companies to focus their resources on development. Through P.L. 115-92, Congress authorized DOD to request, and FDA to provide, assistance to expedite the FDA review process for MCM for military personnel. DOD and FDA have now put a work plan in place to coordinate planning for this process. FDA and BARDA should develop a parallel plan. Expedited release testing and a plan for increased usage of emergency use authorizations (EUAs) should be addressed as part of this plan.
- b. **Expedite release testing:** Even with a vaccine platform, the response time to produce a vaccine for the foreseeable future will be 6-12 months for mass-produced product. While maintaining safety and efficacy standards, acceptable FDA release testing during an outbreak might be different from acceptable release testing at other times. FDA should consider options. For instance, FDA might release products for use on an interim basis with final release testing to follow. FDA might identify suitable surrogates in place of full toxicology panels – or at least utilize a process to pre-identify what those surrogates would be. FDA should describe what an accelerated schedule would look like in an emergency. This will be especially important for platforms that could address multiple infectious diseases. Once in place, manufacturers could then propose specific schedules for a given MCM.
- c. **Examine increased usage of Emergency Use Authorizations:** EUAs are designed for those MCM that are sufficiently well characterized to be of likely clinical benefit in an emergency. FDA essentially certifies that a given MCM fulfills EUA requirements. FDA should determine when more aggressive utilization of EUAs would be appropriate.

5. Improve contracting authorities. BARDA must be empowered to make decisions in the best interest of fulfilling its mission. This means ensuring that the contracting process is as smooth, flexible, and transparent as possible. Other Transactional Authority (OTA) is most prominent among the existing contracting authorities that would incentivize MCM partnerships, yet it is utilized very rarely and limited by the statute that provided OTA authority to BARDA.

- a. **Amend the OTA statute.** Congress modeled the OTA authority addressed in the *Pandemic All-Hazards Preparedness Act (PAHPA)* after DOD's OTA statute. In its reauthorization of *PAHPA*, Congress should customize OTA authority to fit BARDA's needs. Congress should also remove references to DOD and the need for approval by the senior executive for projects above \$20 million (as it did previously for DOD). OTA contracts should become far more common than they are now, perhaps as common if not more than FAR-based contracts.
- b. **Adopt OTA for the CIADMs:** FAR-based contracting does not work for rapid response procurements. Using OTA for the ADMs is critical to prevent abandonment of partnerships when rapidity is imperative, when the science does not go as planned, and when intellectual property and FAR-based requirements arise. DOD has adopted this OTA-based model for its ADM.
- c. **Move contracting authority back to BARDA.** In accordance with Blue Ribbon Study Panel Recommendation 29a (*A National Blueprint for Biodefense*, 2015), and the *21st Century Cures Act* Section 3082, contracting authority should be the exclusive responsibility of BARDA, not the office of Acquisition, Management, Contracts and Grants in the Office of the ASPR. This move must be finalized.

6. Foster innovation and new capabilities. The government often bases MCM-related plans on budgets instead of basing budgets on need. A similar mindset is seen with the government's approach to industry, often issuing solicitations to assess existing capabilities, rather than fostering new capabilities to meet national security needs. At the time of its authorization in *PAHPA*, Congress envisioned BARDA to be on the leading edge of MCM

innovation. Over the past decade, BARDA has focused on more, well-established, product development technologies and investments in technologies closer to full maturity. This approach certainly justified much of the development portfolio. Live viral vaccine platforms and therapeutics based on monoclonal antibodies may well provide near- to medium-term solutions. Yet BARDA needs to devote sufficient resources to novel and high-risk product development activities in parallel with their less risky investments.

- a. ***Invest in novel and high-risk products.*** Meeting emerging national security threats will require BARDA to employ a high-risk, high-reward model for at least a portion of its investments. Instead of issuing solicitations to assess current industry capabilities, agencies should aggressively work with the private sector to build capabilities to meet national security needs. While investment in tried-and-true technologies will remain important, aggressively pursuing technologies that fall outside BARDA's comfort zone is imperative. The *21st Century Cures Act* authorized the Director of BARDA to engage an independent, non-profit innovation partner. BARDA should leverage this opportunity to dedicate additional resources to high-risk, high-reward outputs. It should further consider the role of the animal sector in providing needed technological advancements. The animal sector has existing markets for certain pharmaceuticals (for instance, with respect to coronaviruses and influenza viruses, which happen to be the most significant viral pandemic threats to the human population) that are lacking in the human sector. A shared interagency approach to planning for, and funding in, such areas could lead to needed innovative breakthroughs. Precedence for interagency funding mechanisms can be found in the funding HHS provided to USDA in 2009 to conduct domestic biosurveillance for swine influenza virus, a pathogen with minimal health impacts on the animal carrier but large potential impacts on public health.
- b. ***Invest in rapid diagnostics.*** The nation needs to invest far more in patient-side, point-of-care diagnostics. Diagnostics can guide prioritization of MCM resources, but MCM conversations often refer only to vaccines and therapeutics, omitting diagnostics altogether. Rapid diagnostics cannot continue to be an afterthought. In accordance with Blue Ribbon Study Panel Recommendation 30a (*A National Blueprint for Biodefense*, 2015), DOD and BARDA need to invest in rapid diagnostics as a core element of their MCM portfolios. This work should identify generalized biomarkers that would enable such technologies.
- c. ***Drive decision-making with early warning and predictive tools.*** Leadership has yet to embrace predictive science as a core capacity that can support traditional and transformative MCM development. Advances in genomics and proteomics, risk mapping, and biosurveillance data analytics should all be leveraged to create early warning that could both inform and spare the stockpile. Budget requests and corresponding appropriations should support these efforts and ensure that they are an integral part of the federal MCM development and procurement strategy by aligning MCM investments with the threats identified through early warning programs.

7. **Establish end-to-end enterprise coordination.** Although PHEMCE was envisioned as a coordinating body for the federal MCM enterprise, it has been too HHS-centric to do this effectively. Development of a far more forward-looking process – from idea to procurement to dispensing – is needed. As the Office of the ASPR reimagines the end-to-end nature of the enterprise, it has an opportunity to address some specific challenges in the current construct.

- a. ***Improve interagency product transitions.*** Successful research projects at the National Institutes of Health, DARPA, or other agencies, must begin competition anew for advanced development – if advanced development funding is even available or prioritized. This creates major bureaucratic hurdles to product advancement. The National Biodefense Strategy should direct the creation of more streamlined interagency transition mechanisms. Awards can be structured to assume transition from one agency to the next.
- b. ***Transfer management of the Strategic National Stockpile under specific conditions.*** In the President's Budget Request for FY 2019, the Administration moved management responsibility of the Strategic National Stockpile (SNS) from the Centers for Disease Control and Prevention (CDC) to the ASPR. CDC management of the SNS has been inadequate, resulting in industry confusion and losses when the agency suddenly decided to remove elements from the stockpile that it had previously approved. The Administration made this move, in part, to better enable HHS leadership to direct acquisition for, and deployment of, the SNS. The move has the potential to create a more cohesive development-to-

distribution structure and apply more process certainty to procurement decisions. Concerns about how BARDA and the SNS will interact once the move is finalized, and whether investments made by BARDA will inadvertently or intentionally force the SNS to acquire those MCM it developed, must be addressed. Congress should authorize the transfer of management of the SNS to the ASPR only if it also requires the ASPR to fix SNS-related problems that the CDC and state, local, tribal, and territorial (SLTT) partners previously encountered or created, and to put controls in place to prevent automatic uptake of BARDA products by the SNS just to demonstrate BARDA success. Congress should also direct the ASPR to establish a meaningful SNS training program for SLTT partners that focuses on more than just anthrax, takes SLTT ability to distribute SNS pallets upon receipt into consideration, and does not assume distribution will occur the same as in the military.

- c. **Produce an MCM response framework.** In accordance with Blue Ribbon Study Panel Recommendation 22a (*A National Blueprint for Biodefense*, 2015), the Office of the ASPR, CDC, and the Federal Emergency Management Agency should, together with non-federal partners, identify requirements and capacities needed to achieve successful distribution and dispensing of MCM from the SNS as well as from local caches. The framework they develop must address unresolved issues. A progressive and innovative approach should push beyond what a given agency might devise and the bureaucratic impediments associated with a federal-only distribution system. If implementation exceeds funding available through current grant allocations, additional funding must be requested.

Thank you for considering these findings and recommendations. Please contact Dr. Asha M. George, Panel Executive Director, at (202) 974-2416 or Asha.George@BiodefenseStudy.org with further questions.

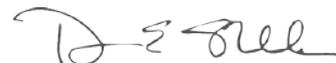
Sincerely,



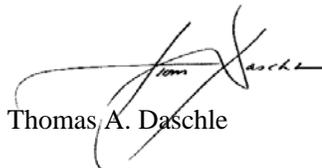
Joseph I. Lieberman, Chair



Thomas J. Ridge, Chair



Donna E. Shalala



Thomas A. Daschle



James C. Greenwood



Kenneth L. Wainstein