

# Alliance for Biosecurity

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## *Via Email*

Dr. Nicole Lurie  
Assistant Secretary for Preparedness and Response  
Department of Health and Human Services  
Room 6-638G, 200 Independence Avenue, SW  
Washington, DC 20201

Dear Dr. Lurie,

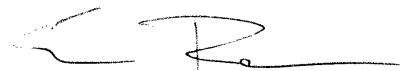
The Alliance for Biosecurity greatly appreciated the opportunity to meet with you and your colleagues on January 28<sup>th</sup>. We believe that this is a critical juncture for government, industry and other stakeholders in our shared mission to identify, create, and obtain medical countermeasures that will protect citizens against bioterrorist attacks and potentially destabilizing emerging infectious diseases. Therefore, we welcome your energy and commitment for sustaining and enhancing the medical countermeasure enterprise, and your efforts to seek detailed feedback from the biopharmaceutical industry.

As promised, attached please find a white paper that summarizes our views on the aspects of the existing programs that are working well and details specific recommendations for areas that will improve the countermeasure enterprise. We look forward to discussing the white paper with you in detail on March 16th.

Respectfully submitted on behalf of the Alliance,



Susan Berger, Ph.D.  
Senior Director, Risk Management Strategy  
Pfizer Inc.  
Co-Chair, Alliance for Biosecurity



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**WHITE PAPER**

**FEEDBACK ON**

**END TO END REVIEW OF COUNTERMEASURE ENTERPRISE**

**ALLIANCE FOR BIOSECURITY**

2 March 2010

ALLIANCE FOR BIOSECURITY WHITE PAPER:  
*Feedback on End to End Review of Countermeasure Enterprise*

**EXECUTIVE SUMMARY**

Companies require robust incentives to compensate them for the high cost and risk associated with developing medical countermeasures (MCMs). The Tufts Center for the Study of Drug Development estimates<sup>1</sup> that the discovery and development of a pharmaceutical product, including a MCM, typically takes an average of 10-12 years and costs roughly \$800 million. The significant costs for research and development are in part due to the reality that of thousands (in some cases hundreds of thousands) compounds initially screened, only one becomes an approved drug. Companies must pay for these failures out of the profits of successful medicines. Adding to the financial pressures is the fact that even those compounds that become approved medicines often don't recoup their R&D investments. Furthermore, the pursuit of bioterrorism countermeasures would require pharmaceutical companies to divert resources from research and development efforts in drugs for diseases affecting millions of Americans today, such as AIDS, cancer, heart disease, and diabetes.

The development and licensure of biological, chemical, radiological and nuclear countermeasures will entail the same costs as developing other pharmaceutical products (and perhaps greater costs due to the expense of regulatory approval under the animal efficacy rules). Access to the capital required to fund the development of these products is largely driven by the prospect of attractive economic returns. For the MCM sector, the inability to accurately understand and forecast the behavior of the sole purchaser – i.e., the US Government has prevented industry from making sound predictive assessments, of the unmet medical need.

The difficulty in predicting market demand, the reality of lengthy timelines and the inherent risks and uncertainties associated with the research and development of MCMs present unique challenges and hurdles. Under these circumstances, the primary drivers to spur industry and capital investments in medical countermeasure development will be policies and concomitant budget requests that signal a firm commitment by US government to procure medical countermeasures – i.e., (i) sufficient and timely funding for advanced development and (ii) predictable, transparent, and meaningful signals from the US government on its intent to procure MCM. These actions should create a sufficiently robust business model to motivate companies to invest in MCM.

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<sup>1</sup> Study published in December 2001. Lead author: Joseph DiMasi. See, for example, <http://enews.tufts.edu/stories/1208/2001/12/04/BallooningCosts/>

The Alliance for Biosecurity's core recommendations to advance the countermeasure enterprise are:

- Improve the predictability and ensure the availability of consistent, robust funding for the development of MCMs. Independent analysis has recommended annual funding of \$1.7 billion for BARDA. In addition, it is critically important to replenish Project BioShield's Special Reserve Fund (SRF). The government's plans for replenishment should be included in the recommendations/report of the PHEMCE review and funding should be included in the Administration's FY 2012 budget.
- Articulate a comprehensive long-term US strategy for the development of a sustainable MCM enterprise. This long-term strategy should include among other things: desired product characteristics and technological improvements, planned investments in manufacturing capacities, and anticipated infrastructure investments. It is important for BARDA to finalize its Strategic Plan and ensure that it clearly articulate priority MCMs for advanced development and provide specific details on what quantities are needed and in what timeframes. These clear signals will provide greater transparency and certainty and help drive investment and action in MCM development.
- Accept that drug development is a risky and expensive proposition and insist that BARDA must be willing to take on some risk and operate within a framework that allows for late stage MCM candidates to fail.
- Create a viable market by ensuring that market-based commercial prices are paid for MCMs. The key to increasing and sustaining the engagement of private industry in the MCM enterprise is creating a viable market for MCMs. Additional financial, intellectual property and other potential incentives (we suggest several herein) will support industry engagement, but will be insufficient on their own in the absence of fair commercial pricing and a viable market.
- Improve the procurement and contracting process to more effectively promote development of MCMs. With the delinking of advanced development and procurement contracts, and the lack of any market guarantee, advanced development contracts should include a higher fee.
- Improve the speed and efficiency of regulatory interactions between private industry and the US government. FDA, CDC, BARDA and other relevant agencies must improve coordination and ensure that they are collaborating closely and effectively to develop MCMs. In particular, the Alliance

recommends that FDA and CDC be provided with adequate resources that are coupled to performance metrics that can ensure timely and appropriate responses to regulatory submissions and inquiries – perhaps by direct transfer of funds from BARDA advanced development funds or creating a Medical Countermeasures User Fee Program. We also strongly urge that the role of FDA’s advisory committees be clarified and limited to the appropriate scope. Advisory committees should not consider questions of need and/or product specifications which are defined prior to contract award.

**I. POSITIVE ASPECTS OF THE CURRENT COUNTERMEASURE ENTERPRISE**

In response to your request, we are pleased to share our views on the aspects of the existing government policies and infrastructure that are working well:

- We strongly supported the creation of BARDA as a centralized biodefense authority to direct the advanced development and procurement of medical countermeasures (MCMs). We have been impressed with BARDA's commitment to partnering with the biopharmaceutical industry and the sense of urgency that Dr. Robinson and others bring to their core mission. In our view, the overarching structure of the PHEMCE is generally well-organized and operating effectively. We provide some specific thoughts below on suggested focused improvements.
- The Alliance strongly supports the PHEMCE Strategy's<sup>2</sup> goals of increasing transparency and predictability, as well as DHHS's stated commitment to expand its advanced development program, increase staff levels, and strengthen and streamline the execution of Project BioShield procurements. By providing greater transparency to the decision-making process, DHHS will help the private sector to direct its research and development efforts in a manner that will allow it to be a more effective partner with PHEMCE.
- The new BAA process is an improvement over previous solicitations – the process allows and encourages interaction with BARDA staff, it identifies current priorities, adding transparency into near-term BARDA interests. In addition, the timeframe for response is open-ended, eliminating years of waiting for a relevant solicitation. Finally, BARDA has targeted a six month timeline for BAA awards – a significant improvement over historical award timelines, if met.
- The Alliance believes that significant strides have been made during the past few years in terms of increasing openness and cultivating opportunities for substantive and constructive dialogue between industry and government. For example, the BARDA Industry Day organized as part of the annual PHEMCE Stakeholders Conference has been a positive development. We provide below some more detailed comments on how to continue this positive trend and further enhance communication and transparency.

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<sup>2</sup> [http://www.hhs.gov/aspr/barda/documents/federalreg\\_vol72no53\\_032007notices](http://www.hhs.gov/aspr/barda/documents/federalreg_vol72no53_032007notices).

## II. ALLIANCE RECOMMENDATIONS

The Department of Health and Human Services has made considerable progress in the past few years to improve the MCM enterprise and it is unnecessary to “reinvent the wheel” at this stage. Rather, focused initiatives to improve the enterprise are needed. We provide below some specific recommendations for areas of focus and action in order to evolve and improve the countermeasure enterprise.

### *Ensuring Adequate Funding*

Improving the predictability and ensuring the availability of consistent, robust funding by the US Government for the development of MCMs is essential to ensuring that the MCM enterprise is successful. We wish to share the following feedback on existing challenges and propose specific improvements to the procurement and contracting process:

- Funding for early stage development (e.g., via NIH) is relatively robust and provides sufficient impetus for companies to initiate research into MCMs. (That said, there can be difficulty in accessing NIH funding for emerging pathogens.)
- Funding for advanced development is insufficient to achieve PHEMCE/BARDA’s objectives. While the Alliance is somewhat encouraged by the level of advanced development funding included in the FY 2011 budget request, we note that \$476 million falls well short of the \$1.7 billion estimated to be required annually to ensure the development of countermeasures for identified biological threats. We were also encouraged to see the request for additional flexibility for the Secretary to transfer additional funds for advanced development, as needed and after notification of Congress.<sup>3</sup>
- It is essential that this MCM review outline a process for restoring funding to the Project BioShield Special Reserve Fund (SRF) or for otherwise providing long-term and stable funding for the procurement of MCMs. While the Alliance is supportive of increased funding for advanced development activities it is

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<sup>3</sup> “Funding in FY 2011 will be targeted to countermeasure development in the high priority areas of anthrax, enhanced biothreats, and acute radiation syndrome. BARDA also manages pandemic influenza and Project BioShield, and the request consolidates the associated management costs. Additionally, the Budget will permit the Secretary to make additional BioShield funds available for advanced research and development activities after notification of Congress. This flexibility would enable BARDA to target resources to the most promising countermeasure candidates whether through advanced development or through acquisition using Project BioShield.” See <http://www.hhs.gov/asrt/ob/docbudget/2011budgetinbrief.pdf> at page 105.

difficult to overstate the destabilizing impact of continued depletion of the SRF to support non-procurement activities, including the FY 2010 transfer to NIH. Without ample funding for procurements there can be no guarantee of a market for these products.

### *Procurement and Contracting*

Improving the ease and efficiency of interactions between private industry and the US government is essential to ensuring that the MCM enterprise is successful. We wish to share the following feedback on existing challenges and propose specific improvements to the procurement and contracting process:

- A recent delinking of advanced development and procurement contracts has delayed the potential for a procurement contract until very close to the time of BLA/NDA submission. This places companies, particularly small ones, in a tenuous financial situation, and it presents a very different business paradigm than that originally envisioned under Project BioShield. Project BioShield allowed, for the first time, the procurement of non-approved products if the Secretary determined that there was a reasonable chance that FDA approval would occur within eight years. The possibility of a procurement contract at an early stage of development was the carrot that enticed many small companies to enter the biodefense market, and made the biodefense business model attractive to investors. Without early procurement contracts the biodefense business is viewed by biopharmaceutical companies and investors as very high risk with little reward.
- It is critical that contracts reflect market-based commercial pricing for MCMs.
- In order to be fully successful in developing MCM, the US government must understand and accept that drug development is a risky and expensive proposition, and BARDA specifically must be willing to take on some risk. The reality is that not all technologies selected for funding are going to be successful. BARDA has increased its technical staff considerably and has a number of consultants assisting program personnel, but in some cases there has been a lack internal support with adequate drug development and commercial experience. This may well have led to program guidance that is overly conservative and also chilled progress in initiating projects. This is a fundamental and pervasive issue that must be addressed in order for the countermeasures enterprise to succeed.
  - Establishment of an advisory board or panel of external advisors with an ombudsman type function that could weigh in on critical program issues where BARDA and the sponsor have reached an impasse.

- BARDA should hire high-level staff (not external consultants) who have experience with developing and commercializing biologics.
- The existing practice of short-term contracts (typically 1 year with annual renewals) does not fit well with the model of MCM development, and creates uncertainty and disruption that often contributes to development delays. For example, it may force a company to postpone animal studies while awaiting confirmation of the extension or renewal of a contract. The execution of longer-term contracts (e.g. 4-6 years) would represent a significant improvement.
- Over the past four years there have been just two large procurement contracts awarded: one for rPA anthrax vaccine and one for a smallpox vaccine. The rPA contract was awarded and subsequently terminated; the smallpox vaccine award is progressing and is anticipated to result in delivery of product to the Strategic National Stockpile in the near future. Two other major solicitations: one for a radiation therapy and a second rPA anthrax vaccine were terminated after nearly two years of deliberations. It appears as though BARDA has elected to reduce risk associated with procurements and instead support advanced development of promising technologies until very late stage development before considering a procurement opportunity. In the Alliance's view, this approach does not maximize the opportunities to grow a viable market. Some proposed solutions:
  - One option is to follow the DoD path, i.e., support a small number of programs at an early stage and perform a downselect to one or two programs for advanced development and procurement. This would require a number of changes to current operations and would require BARDA to commit to fully fund the one or two programs selected. A small number of winners would allow for more meaningful contracts, but also shrink the market over time. This approach would also allow those companies not selected to put resources elsewhere at an early stage of development, thereby limiting their risk.
  - Another option would be to maintain the current paradigm but allow a much larger fee on advanced development contracts. Right now the fee cap is 15%, and often is negotiated lower. A fee in the 25%-30% range might make development contracts more attractive from an economic perspective since they are no longer tied to a procurement, and there is no guarantee that developed products will ever be purchased.
  - A third option would take advantage of Defense Production Act Title III authorities available to HHS that allow grants and loans for the development of technologies that meet national security needs. This

program uses a Technology Investment Agreement contracting instrument rather than the FAR. Oversight and management of the program is also much less cumbersome than current contract vehicles. DPA does focus on strengthening the US economy and technological competitiveness so it would likely only be applicable to US-based companies.

- A fourth option would be to work with Congress to allow BARDA to budget prospectively as does DoD so that programs selected for development can be fully funded. Additionally, since advanced development funding needs to be flexible to allow changes in the development plan based on new data and FDA guidance, work with Congress to allow BARDA funding to be “no year” money. This will reduce program delays due to the annual appropriations process and allow for the acceleration of programs whenever possible.
- Contract awards should be granted in a more reliable and timely manner. Procurement contracts have taken over two years and advanced development contracts targeted for a six month award timeline have not been met. Companies have not been able to give accurate guidance to investors, who view BARDA as unreliable and unpredictable.
  - A potential solution would be to add contracting staff to enable faster negotiation of contracts. Another solution would be for the agency to consider taking advantage of existing authorities under FAR 12-102(f)(1) that allows CBRN contracts to be executed using commercial terms and using authorities in the PAHPA legislation that allow contracts to be awarded using other methods than the FAR, such as OTA (other contracting authorities).
- Improvements in billing and invoicing are necessary. Specifically, invoicing should be limited to documentation regarding reimbursement for cost incurred or for milestone achieved. BARDA’s requirement for providing “Estimate to Complete” (ETC) or “Estimate at Complete” (EAC) and variance should be removed from the billing process. This is problematic as issues with ETCs or EACs can hold up payment for legitimate costs, which is a particular issue for small businesses. Having an ETC/EAC can be worthwhile, but it should be a program management requirement and not a billing factor for legitimate work performed. DoD delinks the ETC/EAC from billing and consequently has a much more effective and efficient billing process.

- The appropriate use of Earned Value Management (EVM) should be assessed. EVM is a new and novel tool for tracking schedule and cost. While it can be useful if applied appropriately, it is only one of many tools that can be used to track program progress and identify cost and budget issues. While it is routinely applied to contracts over \$25 million, it is only applicable to cost plus contracts. It is not an appropriate tool for fixed priced contracts. Most biodefense vendors in the commercial drug development space are not familiar with EVM and do not have established rates with the government. Thus, they must provide fixed priced bids – even though the prime may be operating under a cost-plus contract from BARDA. If a subcontractor provides a fixed priced bid, the prime can only track the amount paid based on the negotiated task at completion as the prime only has limited visibility into the costs that underlie the fixed price bid. In order to use EVM more effectively and as intended, BARDA should consider the following:
  - Evaluate the nature of individual contracts and for those that are mostly fixed price eliminate the EVM requirement or only apply it to those portions of the contract that are cost plus.
  - For those contracts where application of EVM is appropriate, ensure the EVM activities are funded sufficiently. The resources required to develop an EVM system and/or execute it correctly are not trivial and adequate reimbursement should be budgeted.

### *Regulatory Improvements*

In order to meet the product development targets set by the Federal government, the departments and agencies that comprise the MCM enterprise must prioritize interactions with companies developing products for identified national security priorities. Below are several suggestions for affecting specific improvements to the regulatory process:

- Provide clear, consistent and transparent regulatory requirements surrounding emergency use of unlicensed products. Licensure requirements under the animal rule need to be consistent across the varying centers, especially for diseases where countermeasures under development are regulated by multiple centers. Furthermore, the US government must ensure that guidance developed by the FDA regarding licensure using the animal rule is adhered to (*e.g.* no requirement to provide meaningful therapeutic benefits to patients over existing treatments; no requirement for lack of existing treatment). It would be beneficial to have roadmaps for the following: approval under the animal rule, Emergency Use Authorization, and delivery to and purchase by SNS.

- Provide clear, consistent and transparent requirements for delivery of unlicensed and licensed products to the Strategic National Stockpile. In particular, clear delineation of the responsibilities of CDC as consignee and responsible party for products delivered to the SNS is required.
- Ensure that contracting agencies are effectively coordinating with the agencies responsible for licensure and storage of MCMs. Incomplete or ineffective communications between the agencies responsible for procuring, regulating and storing medical products can produce delays, cause duplicative efforts and introduce avoidable errors. For instance, in several instances advice offered by BARDA reveals a lack of understanding of FDA regulations and requirements and is sometimes contradicted by the FDA. Improving coordination and communication between FDA and BARDA regarding regulations and requirements associated with licensure and/or delivery allowance is needed.
- Prioritize regulatory interactions for companies that are developing MCMs. In many respects, the FDA given its critical regulatory responsibilities, has become the *de facto* arbiter of contract compliance for countermeasure development. This has caused tension between the contracting office, BARDA, and the FDA creating delays, introducing uncertainty and hampering effective program management efforts by the US government and companies. In order for biodefense companies to meet the aggressive product development timeframes established by BARDA, interactions with FDA on regulatory matters and the CDC on stockpiling matters must be prioritized. In order to accomplish this, FDA and CDC must be provided with adequate resources to ensure timely and appropriate responses to all regulatory submissions and inquiries. Associated with these resources would be commitments by FDA (and the CDC where applicable) to accelerate review times for all pre-NDA and pre-BLA interactions related to licensure and delivery of MCMs. Direct transfer of funds from BARDA or DOD to the FDA and CDC could be connected to the issuance of contracts for research and development of medical products. Alternatively, the creation of a Medical Countermeasures User Fee program could provide the necessary resources to ensure timely responses by FDA. Under either system, the provision of these resources would include commitments by FDA (and the CDC where applicable) to accelerate review times related to regulatory issues surrounding the products. This would be similar to the goals and timelines associated with Prescription Drug User Fee Act but would include all pre-NDA and pre-BLA interactions with FDA (and CDC where applicable).
- Clarify the role of FDA's advisory committees in the approval of MCMs. The role of FDA advisory committees should be limited to assessing product safety and

efficacy in the context delineated by the procurement contract or the data required to demonstrate efficacy under the animal rule. Questions of need and/or product specification are all defined prior to contract award and are inappropriate topics to be considered during the final stages of licensure. Advisory committees should not consider these matters in their deliberations and the FDA should ensure that it delimits the charge to the Advisory Committee appropriately.

### *Industry Incentives*

As noted above, one of the primary ways to engage industry in the research and development of MCMs is to create a robust market by: (i) ensuring adequate advanced development funding and (ii) clear and concrete messages from the US government on procurement of MCMs. Ensuring that commercial prices are paid for MCMs is imperative. Additional market-based incentives that do not require direct Congressional appropriations could also support industry engagement, particularly involvement by large pharmaceutical companies. Below are some suggestions for additional market-based incentives:

- Orphan Drug-Like Exclusivity. Bioterrorism countermeasures are somewhat analogous to drugs intended for diseases that afflict very few people (so-called “orphan” drugs) in that neither class of medicine has a sufficient market to adequately encourage development. Congress recognized that market-based incentives such as additional marketing exclusivity could provide an efficient means of encouraging drug development when it enacted the Orphan Drugs Act, and that Act has been undeniably successful in encouraging the development of new drugs for orphan diseases. Since it was signed into U.S. law in 1983, more than 2,000 products in development have been designated by the FDA as orphan drugs and the FDA has approved for marketing 350 drugs and biologics. In fact, during the 2000s, orphan products constituted 22% of all new molecular entities and 31% of all significant biologics receiving U.S. marketing approval. In the same way, marketing exclusivity may prove to be an efficient means of encouraging the development of bioterrorism countermeasures.
- “Wild card” patent extension. Over the years, Congress has considered a range of incentives designed to encourage biopharmaceutical companies to participate in development of biodefense and public health (i.e., pandemic and epidemic) countermeasures. One such incentive, which became known as the “wild card” patent extension, provided an extended patent term for a specific, designated

non-countermeasure product, in exchange for development of a MCM.<sup>4</sup> The Infectious Disease Society advocated for the “wild card” patent incentive in its report “Bad Bugs, No Drugs.”<sup>5</sup>

- BPCA-Like Exclusivity. The Best Pharmaceutical for Children Act (BPCA) has dramatically increased the number of pharmaceutical products for which pediatric information is available. In return for conducting clinical trials to establish potential pediatric dosing and indications, BPCA offers an additional period of marketing exclusivity in which the sponsor retains exclusive marketing rights to all forms of a drug product line containing the active ingredient. This incentive has been largely responsible for increasing the number and quality of pediatric indications for therapeutics. A similar type of exclusivity could encourage research into new or alternative biodefense applications of licensed pharmaceutical products.
- Patent Extensions on Older Drugs. The Alliance supports patent term extensions that encourage a sponsor to work on products that are at or near the end of their patent life. An example of such an incentive is if a company that has a drug with only two years left in its patent life initiates work that demonstrates the efficacy of that drug against a specifically-identified bioterrorism threat, then the company would receive a significant patent extension on the composition of matter patent for that drug. The legislation should pertain to un-marketed compounds as well as marketed ones. In determining the exact length of the extension, one approach would be to award a patent extension of x years, with a cap so that it supplies no more than y years of additional exclusivity. This type of formulation serves to ensure standardization of the patent award and is successfully employed in Hatch-Waxman patent restoration. However, patent extension on a MCM is not useful for a drug that is stockpiled but never used. Furthermore, such an incentive likely will be of benefit only for those products for which there other profitable commercial applications (dual use).
- There is some interest on the part of the U.S. government in finding “flexible defense” MCMs, i.e., multi-purpose countermeasures. In order to encourage large biopharmaceutical firms to participate in the development of such “flexible defense” products, such products should not explicitly exclude products with commercial purposes, and the countermeasure potential of the product should not affect the firm’s ability to sell the product at market rates for commercial

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<sup>4</sup> Biological, Chemical and Radiological Weapons Countermeasure Research Act of 2002, S. 3148, §203.

<sup>5</sup> “Bad Bugs, No Drugs,” Infectious Disease Society of America, 2004, p. 6. Available at: <http://www.idsociety.org/badbugsnodrugs.html>.

(non-countermeasure) purposes. However, even with such incentives it is unclear whether the “one drug for many bugs” approach is advisable or viable. First, it may be difficult to find a single MCM that is as effective against a range of biothreats as would be separate MCMs each targeted for a specific threat. Research and development approaches that are “known-to-the-industry” versus “new-to-the-world” drive dramatically different technical risks. Technical risk should be quantified and managed across a portfolio. “One drug, one bug” is often a cost effective solution since it carries a lower risk posture than “one drug for many bugs”. Second, in the case of antibiotics, broad-spectrum products are likely to kill more normal microorganisms in the body than would narrow-spectrum antibiotics. Thus, broad-spectrum antibiotics pose a greater risk of superinfection. Third, broad-spectrum antibiotics pose a greater risk of causing antibiotic resistance than do narrow-spectrum antibiotics, and hence experts in antibacterial resistance have advocated limitations on the use of broad-spectrum antibiotics.<sup>6</sup>

### *Promoting Communication and Collaboration Among Government & Stakeholders*

As noted above, there has been a positive trend toward increased communication and dialogue between government and industry during the past few years. Sustaining this dialogue and identifying fresh and creative ways to increase the lines of communication and encourage collective thinking remains an important goal. This is particularly needed in the federal contracting process, during which a significant amount of the communication between industry and government occurs and many real or perceived constraints exist. The following proposed initiatives are aimed at strengthening the public-private partnership for MCM development:

- Increase appropriate communication between industry and government. Industry communication should not be limited to written responses to Requests for Information (RFIs) or Requests for Proposal (RFPs). Appropriate prohibitions on the discussion of products under review should be maintained, but it would be suitable and productive to have discussions related to products that are not under review. Company input during the pre-requirements and requirements phase should be encouraged to inform the requirements development process. The length and formality of the current RFI process virtually assures that government will not be in a position to issue an RFP until one year after the RFI

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<sup>6</sup> For example, see “Bad Bugs, No Drugs” report from the Infectious Disease Society of America. For example, on page 8 the report advocates an increase in the number and size of grants for new drugs that treat targeted pathogens. Report available at: <http://www.idsociety.org/badbugsnodrugs.html>

issuance. This long lag time often dates and sometimes renders irrelevant the information collected through the RFI. We urge the government to establish other mechanisms (for example, a standing Advisory Board), through which companies can update DHHS of significant developments in real time in order to obtain helpful input, and to inform guidance and funding decisions in a timely manner.

- Allow industry to present data on its technologies to inter-agency working groups. The decision-making process for biodefense products is fragmented and involves many different agencies and departments. It is difficult for companies to identify all of the parties involved and present information or seek guidance. DHHS could provide an opportunity for companies with promising technologies to regularly engage in discussions with interagency working group members. These types of interactions would help industry to develop medicines and vaccines that better meet the government's needs.
- Institute a consistent mechanism at DHHS to alert industry to key activities and developments, such as the issuance of an upcoming RFI, RFP, or other notice. Other agencies do this effectively. For example, NIH often contacts interested parties by e-mail or phone if the release of a relevant notice is imminent or has just occurred. DOD staff also alerts interested parties prior to the issuance of a relevant notice.
- Encourage involvement of industry scientists and others with explicit expertise in the development and production of vaccines and medicines in the review of NIH contracts and grants related to development projects. It is critical to have a robust connection between the basic science undertaken by NIH (and funded through NIH grants) and the identification of viable approaches that the pharmaceutical and biotechnology industries can bring forward to develop new countermeasures. In this regard, it would be constructive to develop a more formalized mechanism by which NIH, DHHS, and industry could exchange information on the types of basic research most likely to aid in the development of countermeasures appropriate for stockpiling and administration. This would result in the funding of better designed projects, leading to higher degrees of success.
- Allow industry access to data on relevant animal models, potentially useful biomarkers, genomic data, and assays that allow for efficient study design. Developing acceptable animal models, biomarkers, etc. is a key factor in the success of MCM development and is critical to the acceptance of company data by the FDA. Currently, each company is proceeding with its own interpretation

of the published literature; this could lead to inconsistencies in study design and, ultimately, more difficulty in evaluating the potential of one medicine versus another. Furthermore, promoting open communications on animal models, etc. would provide opportunities for industry to more consistently and effectively design successful animal studies to determine the efficacy of medicines/vaccines. A number of agencies and departments are involved in the development of animal models (including, to varying degrees, FDA, NIH, CDC, and DOD). DHHS could take the lead in establishing a mechanism to work more closely with industry, particularly for countermeasures identified in RFPs for which there are no current animal models, biomarkers, etc. to speed product development. This mechanism could take the form of regular public workshops in which relevant government agencies and stakeholders could participate. Output could include information for guidance or points to consider documents and publications submitted to peer-reviewed journals.

### *Alliance Commitments*

The Alliance's member companies are firmly committed to promoting the success of the medical countermeasures enterprise by investing in the research and development of MCMs and serving as a collaborative and constructive partner to the US Government in this critically important endeavor. We wish to highlight recent and ongoing activities:

- The Alliance has established an animal model working group that engages several different federal agencies and is focused on creating a collaborative database to facilitate the sharing of animal model data. This is an ambitious and important undertaking and the kind of collaboration that could have a significant positive impact on the development of MCMs.
- As noted above, the Alliance has strongly advocated that Congress secure and allocate sufficient funding to BARDA and other elements of the countermeasure enterprise. We will continue these efforts in the future. The Alliance is also committed to educating appropriators about the risks inherent in the process of developing MCMs, as well as to foster a realistic understanding of the significant challenges that BARDA and the industry face.
- The Alliance has and continues to be willing to serve as a resource for technical expertise and pragmatic advice on processes, programs and initiatives designed to support the countermeasures enterprise. We understand that HHS is considering a number of scenarios for the development, approval and manufacture of MCM, including a new public-private partnership that would establish a centralized, dedicated multi-product manufacturing facility. The Alliance believes that there are areas where multiproduct and/or flexible

manufacturing process might be successfully deployed and we look forward to engaging with HHS as they explore these opportunities. We are particularly interested in engaging on the strategic implications of such investments - including such questions as:

- What is the fundamental problem the facility is meant to solve?
- Who would own, manage, run the operations, and make decisions as to priorities in terms of which products would go into the facility?
- What would be the timing of building and developing this type of facility?
- Would the facility be for vaccines, small molecules, monoclonals, and/or recombinant proteins?
- Would it be dedicated to certain phases of development and manufacturing?
- Where would the funding come from for such a facility? What is the estimated cost?
- How would the FDA be involved with such a facility?
- How would regulatory matters be handled for such a facility?

The answers to these questions directly relate to the feasibility of such an endeavor. The member companies of the Alliance for Biosecurity have technical expertise that could be of assistance in exploring the feasibility of a flexible manufacturing facility for MCMs. The Alliance urges HHS, BARDA, the FDA and other relevant agencies to engage in a robust dialogue with industry and other stakeholders to evaluate the technical and regulatory hurdles of this option and carefully consider whether this would be an appropriate allocation of resources at this time.

### Conclusion

The Alliance is grateful for the opportunity to provide this feedback and looks forward to the opportunity to discuss these topics and recommendations with you and your colleagues in early March. In the meantime, please do not hesitate to contact us with any questions or other feedback.

**Members:** Bavarian-Nordic • Cangene Corporation • Dynport Vaccine Company LLC, a CSC Company • Elusys Therapeutics  
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