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MEETING REPORT

BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY (BARDA) ROUNDTABLE

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ON MARCH 22, 2007, the Center for Biosecurity of the University of Pittsburgh Medical Center (UPMC) convened an invitational meeting to discuss the implementation of Title IV of the Pandemic and All-Hazards Preparedness Act (P.L. 109-417, passed in December 2006), which seeks to improve the development of medical countermeasures for national security threats. The Act requires the Department of Health and Human Services (HHS) to develop a strategic plan, and deliver it to Congress on June 19, 2007, to integrate biodefense and emerging infectious disease requirements with advanced research and development, strategic initiatives for innovation, and the procurement of qualified countermeasures.

The goals for the meeting were to provide ideas for improving the research, development, and procurement of countermeasures; to provide concrete suggestions for building an effective partnership between HHS and the biopharmaceutical industry for developing countermeasures; and to facilitate communication among HHS, industry, Congress, and all other parties interested in the development of medical countermeasures for the nation. The Center for Biosecurity will offer, in a separate report, suggestions for how HHS might develop strategic, flexible defense initiatives in BARDA.

The meeting participants included present and former U.S. government officials, members of the biopharma industry, and academic experts (participants are listed in the sidebar). Participants were not asked to reach consensus on the topics discussed; rather, the intention was to spur an open discussion of key issues related to medical countermeasure development and to seek proposals for constructive actions. Individual comments made during the meeting were not for attribution. In advance of the meeting, the Center for Biosecurity interviewed more than 40 people from the biopharma industry, including the members of the Alliance for Biosecurity;[1] current and former officials from HHS, the Department of Defense (DoD), the National Institutes of Health (NIH), and Congress; and academics with knowledge and experience in this area. The results of the interviews were distilled and presented during the meeting.

The meeting agenda roughly followed the provisions of Title IV of the Pandemic and All-Hazards Preparedness Act, as well as the obligations that HHS has under the Act. It included the following topics:

1. The role of the Biomedical Advanced Research and Development Authority (BARDA), which was created by the legislation;
2. Improving the Request for Information (RFI), Request for Proposals (RFP), and procurement processes for medical countermeasures within HHS;
3. Effective implementation of new authorities granted to HHS in the legislation;
4. Leadership and staff of BARDA; and
5. Roles of the National Biodefense Science Board and working groups, as created in the legislation.

Participants in the March 22, 2007, BARDA Roundtable

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Background on Title IV of the Pandemic and All-hazards Preparedness Act (P.L. 109-417)

This legislation, signed on December 19, 2006, established the Biomedical Advanced Research and Development Authority (BARDA) within HHS. Under the Act, the Secretary of HHS is required to coordinate the acceleration of countermeasure and product advanced research and development under BARDA by facilitating collaboration between the U.S. government and stakeholders in the biopharmaceutical industry, promoting countermeasure advanced research and development, facilitating communi-

cation between stakeholders and the FDA, and promoting innovation to reduce the time and cost of countermeasure and product advanced research and development.

The Act established the Biodefense Medical Countermeasure Development Fund to fund BARDA activities and authorized $1.07 billion over FY2006 to FY2008 for the fund. The authorization includes the monies that had been committed to ongoing advanced development programs, such as pandemic influenza preparedness and medical countermeasure development at the National Institute of Allergy and Infectious Diseases (NIAID). As of this writing, no funds have been appropriated for the BARDA development fund in FY2006 or FY2007. The President's FY2008 budget requests $189 million for the BARDA development fund, but Congress has just begun the FY2008 budget process, and it is not yet clear what will be appropriated.

The Role of BARDA in HHS

Meeting participants held a wide range of views about the role BARDA should play in medical countermeasure development. Depending on which model is chosen by HHS, BARDA could either be a mechanism for awarding government funding for areas of countermeasure research and development that currently do not qualify for any government funding, or it could significantly change the responsibilities, processes, and contracting authorities of government in developing medical countermeasures.

The BARDA Mission: Limited vs. Broad

Some participants felt that BARDA should be limited to bridging the "valley of death," the term commonly used to describe product development that falls between NIH-funded research and end-stage procurement by the BioShield program. NIH could continue to fund products through early development, called Phase I, while BARDA could fund candidates for further development until they are eligible for BioShield procurement. Transitions from NIH funding to BARDA funding to BioShield procurement would be made through distinct RFP processes made at different points in the research and development timeline. There would be no guarantee that a product funded by NIH would be selected by BARDA for further development, and no guarantee that a BARDA-funded product would be selected for BioShield procurement. Both NIH and BARDA might choose to support multiple products for a specific countermeasure need, with opportunities to down-select products throughout the development cycle. In this model, the BARDA director could participate in strategic planning for countermeasure development within HHS, but he or she would not have authority over NIH or BioShield decision making on countermeasures.

Other meeting participants conceived BARDA authorities and responsibilities as broad and flexible and not limited to filling the gap between NIH funding and BioShield procurement. In this view, BARDA could be the "conductor of the medical countermeasure orchestra," used to manage the development of countermeasures throughout the entire development process. BARDA would manage early-stage NIH investment into countermeasures, as well as BioShield procurement. This approach may effectively encourage companies to partner with the government, if their involvement in early-stage research is seen as part of a continuum. Developing a seamless process between early-stage research and late-stage procurement was seen by many biopharma participants as an incentive for their participation.

Tolerance for Risk

How BARDA, and by extension HHS, manages risk was seen as crucial to the success of the medical countermeasure development effort. Developing drugs or vaccines is an inherently risky endeavor: More than 80% of pharmaceutical drugs in Phase I development will eventually fail.[2] Given these realities, it would be reasonable to conclude that most countermeasures that BARDA will fund will fail.

Some participants felt that a low tolerance for risk in the development of countermeasures would not succeed: A reliance on safe investments would result in a dearth of suitable countermeasures for procurement, a lack of innovation, and a lack of interest on the part of the biopharma industry in being involved as a partner with government. Under this view, the best bet would be to make small-scale investments in many different medical countermeasures in hopes of increasing the odds of successful products for procurement.

However, many participants felt that accepting the building of high failure rates into this government program will be a serious challenge. Without Congressional tolerance for risk-taking (which was perceived by most meeting participants to be low), BARDA would be unlikely to develop the risk-tolerant culture or receive the necessary funding it would need to accomplish its mission. Many agreed that a concerted effort is needed to inform Congressional leaders both about the necessary risks associated with countermeasure development and the necessary scale of investment in the nation's medical countermeasure enterprise. As one participant explained, BARDA should be comparable to the Apollo program that put a man on the moon: Great rewards could come from taking risks, but there are inevitable failures along the way to reaching that lofty goal.

Venture-Capital and DARPA Models

Some participants conceived of BARDA as a venture capital firm with a public mission. Like venture capitalists, BARDA could scan for new technologies and fund a portfolio of projects at varying levels of development and risk. As projects meet defined milestones, they would qualify for additional rounds of funding.

Other participants viewed BARDA as a biomedical equivalent of the Defense Advanced Research Projects Agency (DARPA), with autonomous program managers. A BARDA program manager could be responsible for a given threat, with a portfolio of countermeasures in various stages of development. Autonomous program managers could help smaller biotech companies, which do not have the capital to wait through long delays and can be "killed by slow committee decisions."

One participant suggested that program managers fund some products up to an advanced stage, but not fully to licensure. These advanced-stage products would then be "mothballed" for future use during an emergency, or if other products selected for further development fail in later-stage testing.

Improving RFIs, RFPs, and Procurement of Medical Countermeasures

Meeting participants made specific recommendations to improve HHS's procurement processes for contracting with developers of medical countermeasures. There was wide agreement from industry participants on the following major points:

- *HHS should signal what they want to procure as early as possible.* Since medical countermeasure development can take ten or more years, HHS should signal their priorities for procurement as soon as possible, well before the release of an RFP. Industry participants said it would be useful if HHS could outline priorities soon after completing medical consequence assessments of national security threats if it is logistically possible; this would be an early indicator of what countermeasures are sought. Some participants suggested that HHS use DoD's "advanced planning briefings for industry"[3] as a model for communicating these early intentions for procurement. It was hoped that the HHS Public Health Emergency Medical Countermeasures Enterprise (PHEMC) Implementation Plan, scheduled for release in April 2007, would list HHS's longer-term priorities for procurement.
- *Communicate early and often with companies.* Companies would like more face-to-face meetings before, during, and after an RFP has been awarded. Medical countermeasures for national security threats are for the most part seen as a market with only one real customer—the U.S. government. Better communication of requirements by the customer would lead to more useful products and more successful outcomes. Many meeting participants suggested that these barriers to communication resulted from an overly conservative interpretation by HHS of the Federal Acquisition Regulation (http://www.acqnet.gov/FAR/). These issues should be resolved.
- *Actively seek companies that might respond to RFPs.* Most biotech companies do not currently contract with government, so they do not typically monitor government websites for RFP announcements and will not know of the opportunities to respond to them. Thus, the government should actively seek companies who may have the technical capacity to respond to RFPs. HHS does have a "tech watch" program, but it is unclear whether it is sufficiently broad and well-staffed to capture the breadth of biotechnologies in development.
- *RFIs and draft RFPs can improve the quality of RFP responses.* HHS should issue more RFIs and draft RFPs to establish the technical feasibility of countermeasure requirements. RFIs also can be a helpful market signal of government interest in a particular technology. Some meeting participants felt that without HHS feedback on individual RFIs, however, the request disappears "into a black hole." Similarly, draft RFPs were thought to be valuable for communication, particularly when HHS publishes its answers to industry questions, which helps all companies in their replies to final RFPs.
- *RFPs should be specific.* Many participants felt that RFPs should be more specific, clarifying minimal and ideal product requirements. Some participants recommended that HHS "write the label" of a product, or even the product insert, in its RFP. Others recommended that an RFP contain FDA guidance on what body of data is required to satisfy the Emergency Use Authorization (EUA) for a countermeasure, which is required to meet the "usable product" threshold for BioShield procurement. It was also suggested that RFPs include a description from CDC on their concept of operations for how a countermeasure will be used. For example, CDC input could help companies know whether a countermeasure can be delivered by syringe or whether a multidose vial is acceptable, or whether the product will be used in healthy adults or specific populations. These details affect whether and how a company responds to an RFP. Meeting participants suggested that HHS examine the DoD countermeasure procurement contracts as a model for specificity.
- *The RFP should define the market in doses.* Companies need to know the volumes of countermeasures HHS will procure. The anthrax therapeutic RFP called for between 10,000 and 200,000 doses.[4] Such a wide range makes it

difficult for a developer to know how much manufacturing capacity is required and also complicates the developer's economic feasibility analysis. It might be profitable or feasible for a company to develop a high-volume product, but unprofitable or completely infeasible to develop a low-volume product. Moreover, as some participants pointed out, certain products are more scaleable than others. Without more market certainty, a company may not be able to convince its board of directors to pursue an RFP; HHS should set a narrower volume range. Another suggestion was to allow companies to respond to specific dose ranges.

- *The first phase of an RFP should be a technical proposal, without a budget or economic analysis.* It is not uncommon for companies to spend up to $400,000 responding to an RFP. This cost can be especially prohibitive for small biotech companies. Meeting participants suggested that RFPs have a first phase that includes only a technical proposal. From these proposals, HHS could select the most promising candidates and request a full proposal. Some participants suggested these full proposals could be funded by the government, similar to challenge grants issued by NIH.[5]
- *Faster decision making on contract awards.* Meeting participants thought that HHS should respond to companies within 60 to 90 days after an RFP deadline to notify them as to whether they are in the competitive range of a contract. HHS should then award the RFP within 3 to 6 months. With predictable timelines, companies could project their work in the future and to their boards, increasing their likelihood of responding to RFPs.
- *RFPs should be binding.* Investors react negatively to delayed, altered, or cancelled RFPs, which can hamper company participation. Some meeting participants felt that HHS should guarantee that, as long as development milestones are met, "if you make it, we will buy it."

New HHS Authorities under P.L. 109-417

The Act gives the Secretary of HHS several new authorities under BARDA to promote the development and procurement of medical countermeasures. These authorities include the ability to award procurement contracts, grants, and cooperative agreements; to select "other transactions" authority as well as to expedite procurement authorities; to expedite peer review; to offer personal service contracts; to waive advance payment and advertising requirements that normally govern U.S. government contracts; to use milestone payments; and to establish research centers. In addition, the Act specifies new BioShield contract authorities to make milestone payments, to enter into exclusive sales contracts, and to establish warm-base manufacturing capacity for a countermeasure, which may need to be brought online quickly during a crisis. The Secretary of HHS was also granted some limited antitrust exemption authorities to facilitate communication to improve the development of medical countermeasures.

Meeting participants recommended that HHS dedicate a team of attorneys in the Office of the General Counsel (OGC) to interpret and use these new authorities. Alternatively, attorneys could be hired by the Office of the Assistant Secretary for Preparedness and Response (ASPR) and dedicated to this project. The barriers to communication between the biopharma industry and HHS after an RFP is issued are especially important to resolve, and the new authorities should make this possible. Many felt that HHS should clarify how milestone payments will be used and begin using them.

Some cautioned that some of these expedited authorities, such as the ability to award sole source contracts, may be politically controversial. If BARDA were modeled on DARPA, it could award $30 million contracts in less than a week; however, BARDA, unlike DARPA, has a clear mission to produce countermeasures and may need to be more accountable in its contracting.

Leadership of BARDA and Staff

It was widely believed by meeting participants that the success of BARDA and the medical countermeasure effort will depend on who is selected to lead it. Some participants felt that hiring the BARDA director should be the first priority, before other staffing or strategic planning decisions are made.

Participants made a number of suggestions for hiring the BARDA director. Of prime importance was that he or she should have experience in the biopharma industry. The position will require aggressive recruitment beyond the normal government job postings, and rules on divestment and financial disclosure will have to be resolved and clarified. While HHS has hired a recruitment firm, it was suggested that HHS also set up a search committee that would include industry participation to find qualified candidates. In addition, the tenure of the job should be made explicit; it should be clear to candidates whether the position will last beyond the end of the present administration.

Participants agreed that more full-time employees at HHS would be needed to accomplish BARDA's mission. Some participants felt that the new director should be able to pick his or her staff. Others noted that BARDA staff will need to be given special incentives to work in a fast-paced and risk-filled environment. For example, DARPA program managers have a 4-year tenure to encourage innovation and risk-taking; they are not tied to "career-safe" decisions.

National Biodefense Science Board and Working Groups

Under the Act, the National Biodefense Science Board will "provide expert advice and guidance to the Secretary on scientific, technical, and other matters . . . regarding current and future chemical, biological, nuclear, and radiological agents, whether naturally occurring, accidental, or deliberate. The board will consist of US government officials, 4 representatives of the biopharma and medical device industry, 4 academic representatives, and 5 others including at least one practicing healthcare professional and one representative of healthcare consumers." The Act directs HHS to convene the first meeting of the board in December 2007.

Meeting participants thought that the board could educate members of Congress about the costs and risks of medical countermeasure development and procurement, defend the BARDA mission to Congress and other stakeholders, and assess the success of the program. Some participants believed that, in addition to the Act's requirements for board expertise, some board members should have broad policy experience.

HHS also is authorized to create working groups. Several working group topics were suggested, including emergency use authorization, the use of milestones for development, setting RFP specifications, the use of animal models for development, and the promotion of innovation in biodefense countermeasure development.

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