

DEVELOPING MEDICAL COUNTERMEASURES FOR BIODEFENSE

HHS IS RESPONSIBLE FOR researching, developing, manufacturing, and stockpiling the medicines, vaccines, and other medical products, also known as medical countermeasures (MCMs), that will be needed to care for the sick and protect the healthy in the wake of bioterrorist attacks (as well as nuclear, radiation, and chemical attacks) against the U.S. population. The nation currently lacks MCMs against many biological threats. Other MCMs exist only in limited quantities. For example, there are no FDA-approved vaccines or therapeutics to counter an Ebola infection, and no FDA-approved, rapid, point-of-care diagnostics exist for any of the biothreat agents of greatest concern. These products do not have traditional commercial markets, so private-sector biotech and pharmaceutical companies have little incentive to develop them without significant government support. HHS has thus far determined 8 MCMs are required to defend Americans against biological attacks, with at least 3 more required to defend against chemical, radiological, and nuclear attacks.

The transformation of a promising drug candidate into a licensed product typically takes 10 or more years from basic research to approval by the FDA, at a cost of hundreds of millions of dollars. These costs and timelines are driven by the uncertainties and risks associated with drug development. It is estimated that of every 5,000 “candidate” drugs that look promising on the lab bench, only 5 enter clinical trials, and only 1 of those achieves FDA licensure.

While funds have been provided to HHS for MCM development, they have been far from sufficient given the costs of drug development and the number of MCMs needed. NIH has received approximately \$1.6 billion per year since FY2004. BARDA was created by Congress in December of 2006 (Pub. L. No. 109-417) and received \$201 million in FY2007–FY2008. For FY2009, BARDA received \$275 million, which was transferred to it from the BioShield Special Reserve Fund. The BioShield program was created by law in 2004 (Pub. L. No. 108-276). Its Special Reserve Fund (SRF) for procurement has a \$5.6 billion multiyear appropriation (FY2004 to FY2013); to date \$1.9 billion has been spent or obligated. The Department of Defense (DoD) also has an MCM program; in FY2008, the

“medical systems” component of this program for research, development, and procurement of new medicines and vaccines was \$341.9 million.

The enterprise dedicated to developing new MCMs has the potential to improve national security as well as to be an engine of innovation for battling all infectious disease threats. Since 2001, HHS has worked to develop effective programs, hire staff with relevant expertise, and build partnerships with the private-sector developers of medical products. HHS is now in a position to successfully move forward on its mission to catalyze research and develop and manufacture MCMs for the civilian population. But this vision will remain unfulfilled if the enterprise is not appropriately funded, staffed, and empowered by effective leadership from the White House.

Recommendations

► **The Administration should ensure that funding for basic science research in biodefense remains steady and that this work is linked to an overall strategy and to biodefense needs and requirements.**

Basic science funding for biodefense has led to fundamental discoveries that lay the foundation for early development efforts leading to vaccines, medicines, and diagnostic technologies. This work also focuses on critical scientific challenges that underpin these efforts, such as adjuvant science, immunology, and microbial pathogenesis. As an example of the value of the basic science biodefense effort, the NIH Regional Centers of Excellence have been highly productive, as measured by the number of new faculty drawn into this field, the quality of the collaborations, the papers published, and the patents filed. This basic science research enterprise should continue to be supported in the new Administration. To the maximum extent possible, the basic science efforts for biodefense should be linked to the other elements of the countermeasure development and procurement process. The more effectively these efforts can be connected, the more efficient the government management of the enterprise, and the

more transparent and clear the process for the private sector companies who are developing new biodefense medicines and vaccines.

► **The President should make full funding for BARDA a top priority.**

Since its creation in December 2006, BARDA has received approximately \$100 million per year. The failure to fund BARDA adequately means that the investments made in NIH to advance basic science cannot be translated into effective medicines or vaccines, which means that there are no products to purchase for the Strategic National Stockpile using BioShield funds. BARDA was designed to provide “advanced development” support for MCMs that have no commercial market. Without federal support for this crucial phase of development, private sector biopharma companies are unlikely to participate in biodefense and the country will be without MCMs. HHS’s successful pandemic influenza MCM development program illustrates that BARDA can successfully manage ambitious advanced development projects. However, BARDA does not have sufficient funding to accomplish its mission for CBRN MCM development. The Center for Biosecurity estimated, based on publicly available industry data, that to have a 90% chance of successfully developing MCMs for the 8 biodefense requirements already determined by HHS, BARDA would need \$14 billion through FY2015. The Center has recommended \$1.7 billion for FY2010.

► **The President should direct HHS to provide funding and personnel to foster collaborative public-private partnerships to establish paths to regulatory approval for biodefense MCMs.**

Currently, there is not a clear regulatory path to FDA approval of biodefense MCMs, since most cannot ethically be tested for efficacy in humans. The FDA’s Animal Efficacy Rule establishes a pathway for biodefense MCMs to be proven effective using validated animal models; however, for many biodefense diseases of concern, animal models have yet to be developed and validated.

Public-private partnerships among government, industry, and academia could focus on sharing animal models and precompetitive model validation data and on encouraging dialogue between developers and regulators. In a related issue, it is unclear what standards for safety and efficacy will make products that are in late-stage development, but not yet FDA approved, eligible for use in a crisis via an Emergency Use Authorization (EUA). These regulatory risks are major barriers to private sector engagement in MCM development.

► **The President should request funding and provide leadership for a partnership between MCM developers and HHS, DoD, and other federal agencies to develop one or more facilities that aggregate expertise and infrastructure for MCM advanced development, manufacturing, and regulatory affairs. This partnership would work to improve all MCM development—lowering risk, reducing costs, and accelerating timelines.**

Specialized technical expertise (eg, medicinal chemistry, analytics development, bioprocess engineering, animal study development) is needed in each stage of MCM development for it to be successful. However, much of this expertise is distributed throughout industry and is frequently treated as proprietary. To meet the government’s MCM development requirements, this expertise must coalesce and become available to a wider array of the partners in the MCM development enterprise. This is especially true of process development, manufacturing skills, and regulatory expertise. Much of this know-how resides in “big pharma,” which currently does not participate in biodefense. Government-sponsored public-private partnerships, combined with dedicated facilities or centers of excellence that concentrate the necessary combination of development expertise, should be initiated to support biodefense MCM development requirements. These partnerships and innovations can and should be used to catalyze medicine and vaccine development for a range of naturally occurring infectious disease threats as well.

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