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## U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

ON

# THE PUBLIC HEALTH EMERGENCY MEDICAL COUNTERMEASURES ENTERPRISE REVIEW

## **BEFORE THE**

## SUBCOMMITTEE ON LABOR, HEALTH AND HUMAN SERVICES, EDUCATION, AND RELATED AGENCIES

## **COMMITTEE ON APPROPRIATIONS**

## UNITED STATES SENATE

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Chairman Harkin, Senator Cochran, and Members of the Subcommittee, thank you for the opportunity to discuss my department's recent review and recommended initiatives to improve our medical countermeasures enterprise<sup>1</sup>.

Our greatest responsibility in government is keeping the American people safe. We have always maintained a powerful military that can guard against conventional threats. But in today's world, the range of threats is ever-widening to include biological, chemical, nuclear, and radiological hazards in addition to the conventional threats. The next public health emergency could be a dirty bomb set off in a subway system. It could be a biological weapon we've never seen before, assembled by a terrorist in a lab. And, as we have seen, it could be naturally-occurring novel strain of influenza virus.

### 2009 H1N1 Pandemic Influenza

Right after I was sworn in as Secretary of HHS, I was briefed by John Brennan, the President's Advisor for Homeland Security and Counterterrorism, on 2009 H1N1 influenza, and immediately found myself immersed in the national need to respond to this new threat. Fortunately, HHS was already in the process of rapidly responding to 2009 H1N1, working in close partnership with virtually every part of the federal government under a national preparedness and response framework. We characterized the new virus, disseminated the information to researchers and public health officials, and developed and began shipping to states a new test to diagnose cases of the infection. We distributed antiviral drugs to the states from the Strategic National Stockpile. We also completed key steps in the vaccine development process – preparing a virus strain for vaccine production, contracting with manufacturers for vaccine, performing necessary clinical trials, and licensing multiple 2009 H1N1 influenza vaccines. After close collaboration with state and local authorities and healthcare providers, we began the voluntary national vaccination program in October. HHS was in constant communication with state health officers and hospital administrators to monitor stress on the healthcare system and to be prepared in case federal medical assets were necessary to augment state and local surge capabilities.

We responded as quickly as possible to the H1N1 emergency, and the speed of these efforts was due in large part to the prior investments in pandemic preparedness. I would like to thank this Committee for its support in this area over the past four years. We did, however, experience challenges with the vaccine manufacturing and availability. No matter how quickly we responded, we were still dependent on vaccine technology from the 1950s, relying on the virus to grow in eggs. We also had to depend in part on foreign vaccine manufacturers, which meant there were two instances in which our vaccine deliveries were delayed in order to meet another country's vaccine needs first. HHS had already taken steps to expand domestic vaccine manufacturing with the opening of a new cell-based influenza vaccine manufacturing facility in North Carolina in November 2009. But, further action was needed to provide a more robust and nimble domestic manufacturing surge capacity. We continue the process of that investment today.

<sup>&</sup>lt;sup>1</sup> The Public Health Emergency Medical Countermeasure Enterprise Review is available online at: http://www.phe.gov/Preparedness/mcm/enterprisereview/Pages/default.aspx

### Medical Countermeasures (MCMs)

The success of a response to a public health crisis depends on many factors, including the expertise of our health care workforce, the capacity of our nation's hospitals, the ability of federal, state, local, tribal, and community partners to coordinate, and the engagement of the public. The success of a response also greatly depends on medical countermeasures. These are the medical treatments, vaccines, diagnostics, personal protective equipment, and non-pharmaceutical aids like ventilators that help reduce the spread of infections, reduce health consequences, and ultimately save lives. In a public health crisis, medical countermeasures are typically our most direct and often our most effective response.

Medical countermeasures take years to develop, are very expensive, and must follow the rigorous development and regulatory pathway to demonstrate safety and efficacy. Unlike the drugs destined for everyday or frequent use, the countermeasures needed for biodefense threats in many cases may have greater development risks, due largely to the absence of significant commercial markets and the difficulty in demonstrating efficacy in the absence of human clinical trials.

The federal government has invested considerable resources over the past ten years in expediting the development of these products. However, it was apparent from both the 2009 H1N1 experience and the paucity of medical countermeasure candidates moving from early to advanced development that we needed a better understanding of how the federal government and industry are generating new products. We realized that the greatest danger we may face is a microbe that we have never seen before and for which we do not yet have a medical countermeasure. We clearly need the capacity to develop a medical countermeasure quickly.

### MCM Review

Recognizing this need, with the encouragement and strong support of President Obama, I called for a comprehensive review of our entire medical countermeasure enterprise in order to transform these efforts into the highly responsive and flexible system we know we need. In order to get the 21st-Century products essential for our national security, we understood that we must invest in 21<sup>st</sup>-Century technical approaches as well as 21st-Century financial, legal, and regulatory frameworks that nurture a viable commercial sector and create incentives for companies to build these advanced countermeasures. In his 2009 State of the Union address, the President called for a renewal of our national capability to respond to bioterrorism and infectious disease.

The review was led by our Department's Assistant Secretary for Preparedness and Response (ASPR), Dr. Nicole Lurie. She was joined by representatives from across HHS (the Office of the ASPR, the Centers for Disease Control and Prevention (CDC), the National Instituties of Health (NIH), the Food and Drug Administration (FDA), the Office of the Assistant Secretary for Financial Resources (ASFR), the Office of the Assistant Secretary for Planning and Evaluation (ASPE), the Office of the Assistant Secretary for Legislation (ASL), and the National Vaccine Program Office (NVPO)); federal interagency partners (the Department of Agriculture (USDA), the Department of Defense (DOD), the Department of Homeland Security (DHS), and the Department of Veterans Affairs (VA)); and the Executive Office of the President to dissect the issues, identify critical gaps, and respond to the challenges that would be uncovered as the review proceeded.

The review was conducted in multiple stages. First, we analyzed a large body of work on medical countermeasure development, financial and market incentives, and procurement of science. We looked at how the needs of the medical providers are considered in the design of MCM products, and which mechanisms are employed to get products to those providers. Second, the successes and failures of the MCM enterprise were examined in order to identify the critical components for success and impediments to realizing our goals. In addition, we interviewed numerous opinion leaders, representatives from the pharmaceutical and biotechnology industry, members of the investment community, and leaders in state and local public health for their views on the role of HHS in MCM development. A series of meetings and workshops were conducted, including: a two-day workshop hosted by the Institute of Medicine's Forums on Public Health Preparedness and Drug Development, a town hall meeting at the National Association of County and City Health Officials Preparedness Summit, and a meeting with leaders of the President's Council of Advisors on Science and Technology. Finally, the Assistant Secretary for Preparedness and Response, on my behalf, asked the National Biodefense Science Board, an HHS Federal Advisory Committee, to convene a workshop to review the overall strategic management, leadership, and accountability structure of the MCM enterprise.

I released the review, *The Public Health Emergency Medical Countermeasures Enterprise Review: Transforming the Enterprise to Meet Long-Range National Needs,* last month. This review highlights the need for the MCM enterprise to adopt a new strategy that incorporates our ability to rapidly and flexibly respond to a new or unknown threat balanced against our longstanding requirements for producing MCMs to counter identified threats. This new strategy is articulated through the following vision statement: Our Nation must have the nimble, flexible capacity to produce MCMs rapidly in the face of any attack or threat, known or unknown, including a novel, previously unrecognized, naturally occurring emerging infectious disease.

The principle at the heart of this strategy is that our public health response is only as strong as its weakest link. So, using it as a guide, we have worked to upgrade our entire end-to-end response, from how we assess and identify threats to how we distribute and administer products to counter those threats in cities and towns across the country. That is why we will continue to look for ways to build – not just a stronger countermeasures enterprise with a solid base of discovery, a clear regulatory pathway, and agile manufacturing – but also a stronger public health response all the way from disease surveillance to administering countermeasures to people in our cities and towns.

#### **Recommendations**

The MCM review recommends five new infrastructure initiatives as well as other enhancements to the MCM enterprise. The review found that the unique products required by the public health emergency medical countermeasure enterprise are not of general commercial interest to the major pharmaceutical companies, due to the risks and opportunity costs to produce and receive approval for products with very limited commercial market value. The federal government often partners with smaller pharmaceutical or biotechnology companies, many of whom would benefit from additional resource or management investments to become successful and reliable entities. We came to realize that we need to provide a variety of supports to ensure the viability of these partners. In the end, if a product fails to make it into our national response capability, it should only be based on its failure to meet our stringent standards for safety, efficacy or quality, and not because we failed to provide the needed business, regulatory and technical support for success. We also realized that the approach to the threats of the future requires building a "capability-based" system that can quickly adapt to a rapidly emerging or sudden, novel threat.

#### 1. 21<sup>st</sup>-Century Regulatory Science

The first infrastructure investment, which enjoyed nearly universal support, is the strengthening of regulatory science at the FDA.

We heard from stakeholders that one of the greatest risks to successfully developing a product was the uncertainty associated with the complex regulatory process that governs the approval of these particular drugs, vaccines and diagnostics.

FDA has been testing and producing cutting-edge products using science that's decadesold and it is prudent to invest in providing the FDA with the tools, models, methods and knowledge necessary to 21st-Century technologies and assist industry in reviewing and regulating these new products.

As part of this initiative, FDA is launching a new program entitled, Advancing Regulatory Science for Public Health, designed to augment the tools used to assess the safety, efficacy, and quality of medical products, with a particular focus on MCMs. The FDA will create new Action Teams to work with those manufacturers who are developing the high priority products and platforms. This strategy is based on an approach that worked well several years ago when the U.S. licensed its vaccine for smallpox, ACAM 2000. The Action Teams, composed of experts from across the FDA, will work with sponsors to identify and help resolve scientific issues as early and efficiently as possible, and to facilitate more rapid evaluation of these high-priority candidate products. Finally, the FDA will launch a collaborative project with other HHS and interdepartmental members of the MCM enterprise to resolve several of the real challenges that have been identified for these types of products. For example, one of these challenges is the difficulty in using the Animal Efficacy Rule. This rule allows appropriate studies in animals in certain cases to provide substantial evidence of effectiveness in humans of new MCMs against biological threats. These initiatives will both give our world-class FDA scientists the cutting-edge resources they need to analyze promising new discoveries faster as well as help industry navigate the complex regulatory processes to ensure that safe, effective, and high quality products are ready for our use. The FDA has already begun to identify areas of needed scientific investment via internal discussions with science leaders from among its various centers, as well as the processes and metrics they will use to track return on this investment.

2. Flexible Manufacturing and Advanced Development Core Services Partnerships The second initiative we are investing in is the development of flexible manufacturing capable of producing the next generation of medical countermeasures.

As noted previously, the federal government often partners with smaller pharmaceutical or biotechnology companies in the development of medical countermeasures. Many of these companies would benefit from technical expertise and guidance in scaling up from small to large production and in the approval of an MCM product. Further, many of these innovators do not have the capital or experience to construct and operate commercial-scale manufacturing facilities.

To fill this need, HHS will establish Centers for Innovation in Advanced Development and Manufacturing. These centers will provide a variety of core services to lessexperienced innovator companies with federally-supported medical countermeasure candidates through public-private partnerships with fully-integrated pharmaceutical partners. HHS will coordinate these core services with regulatory science assistance and other services already provided by the federal government, such as clinical studies and animal-challenge model development. In addition, these centers will be expected to fill the remaining gap in domestic pandemic influenza vaccine manufacturing and surge capacity, utilizing new recombinant and molecular platform technologies. Last, the manufacturing output from these centers will be coordinated by HHS with a domestic network of fill-finish manufacturers to ensure that the first and last doses of vaccine or other medical countermeasure become available as soon as possible. These centers are expected ultimately to aid in controlling the costs of developing and procuring medical countermeasures in emergencies and of stockpiling. The centers will provide development and pilot-manufacturing activities for vaccine candidates, allowing their associated costs to be absorbed into the center's operating budget and thereby reducing the total amount of the R&D contract. Similarly, the costs for commercial-scale manufacturing of MCMs destined for stockpiling in the Strategic National Stockpile will be lower than the costs under the current fixed-price contracts.

The centers will be managed by the Biomedical Advanced Research and Development Authority (BARDA) within ASPR in coordination with other HHS agencies and the Department of Defense. BARDA issued a draft solicitation earlier this month to seek public comment and engagement in this envisioned public–private partnership capability. We expect that the final solicitation will be available by the end of the year, and that competitive contracts will be awarded in 2011.

### *3. Accelerating Discovery and Translation of Product Concepts* The third initiative we will invest in is nurturing discoveries in their earliest stages.

The federal government has invested heavily in a strong, vibrant basic research and discovery program with the ultimate goal of translating important scientific discoveries into licensed medical countermeasures. However, most individual scientific discoveries do not lead directly to an identifiable product. Scientists may make a discovery without realizing that it could be turned into a useful countermeasure, or, if they do see its potential, they may have trouble attracting private investment with an uncertain commercial development path to market. The Conception Acceleration Program at NIH's National Institute of Allergy and Infectious Disease (NIAID) aims to change that dynamic.

A key component of this initiative will be Early Development Teams, that will work closely with partner agencies and programs (NIH, CDC, DOD, ASPR/BARDA, and FDA) and with academic researchers, biotechnology companies, and large pharmaceutical companies. NIH, and especially NIAID, has a broad capability to scout the emerging science that comes from its investments. These teams will be responsible for scouring grant portfolios for discoveries that could have applicability to medical countermeasure development. They will be empowered to leverage both additional funding and access to a wide range of NIH core services to foster these potential solutions into promising medical countermeasure candidates. Where necessary, staff could even play a matchmaking function with other investment organizations, the Centers for Innovation in Advanced Development and Manufacturing, or biotechnology and pharmaceutical firms. Such an approach represents a new and potentially transformational model of advancing our science investments at NIH, and could enable benefits far beyond the realm of MCMs. NIAID is in the process of identifying the number and level of skilled personnel that need to be dedicated to this effort.

#### *4. Modernizing Pandemic Influenza Vaccine Manufacturing* Fourth, we will invest in our domestic manufacturing surge capacity.

The emergence of a novel pandemic strain of influenza virus is a continuous threat to human health. In addition to the experiences of 2009, we are ever vigilant to the possibility that avian influenza H5N1 or other circulating virus strains may become highly transmissible and virulent in humans. Our experience with 2009 H1N1 taught us that we need to respond even faster to an emerging pandemic. Although we were able to manufacture and distribute a safe vaccine faster than in previous years, domestic manufacturing surge capacity needs to be expanded and accelerated.

The MCM Enterprise review, along with a parallel study conducted by the President's Council of Advisors on Science and Technology to improve influenza vaccine manufacturing, identified immediate needs and opportunities to shorten vaccine production timelines. We need better methods for potency assays and sterility testing, optimized virus seed strains, additional development of diagnostic devices, and expanded capacity to fill and finish vaccine. The review also recommends that HHS support the

development of at least three new influenza vaccine candidates whose manufacture does not depend on virus grown in eggs or cells. This initiative is already underway through collaborative efforts by ASPR/BARDA, NIH, FDA, CDC, and the industrial and academic communities.

#### 5. Strategic Investor Fund

The fifth initiative we have identified is a strategic investment fund for new medical countermeasure technologies.

Biotechnology companies are often founded with a promising novel technology, but without the resources and business acumen necessary to fully develop and license their idea into a marketable product. As I described above, the large manufacturers in the private sector often choose to not invest the needed capital and management expertise in these entrepreneurial endeavors due to the many risks inherent in medical countermeasure development, especially with firms or technologies whose products have no market outside that currently needed for federal government stockpiles. We discovered that this same set of problems led the intelligence community and the Department of the Army to each establish "strategic investor" organizations, In-Q-Tel and On Point, respectively, which help in partnering federal government needs with companies that are developing technical approaches that match those needs, and which are also capable of producing commercially viable spinoffs, or multi-use products, based on that technology.

The Administration's FY 2011 Budget Amendment transmitted to Congress in August included authorization for HHS to use an independent strategic investor that would nurture biotechnology companies by providing the needed capital and business expertise to yield a successful product for government needs. The mission of the envisioned MCM Strategic Investor (MCMSI) would be the development of novel technologies that have the potential for sustainable commercial applications to the commercial market and the MCM public health enterprise. In addition to its own investments, the MCMSI could potentially leverage other private capital, provide expert consultation, and link promising companies with potential partners in the private sector. The MCMSI is envisioned as a private, not-for-profit corporation operating outside the federal government, but it would still work closely with NIH, BARDA, DOD, and our other federal partners.

#### Management, Administration, and Accountability

The review also found that while some program management components are working quite well, better management and administration would provide more clarity and predictability, as well as less risk to development partners. These include: improving coordination across the agencies involved in the MCM enterprise, speeding up the contracting process or using more flexible transaction authorities, clearly setting and prioritizing broad enterprise goals, and coordinating the process of product development itself, from initial concept development to product use.

### **Implementation of the Recommendations**

We have re-allocated \$1.9 billion in funding already appropriated for pandemic influenza and the procurement of medical countermeasures under Project BioShield to begin implementing these recommendations. This includes:

- \$170 million to promote regulatory innovation and investment in regulatory science at the FDA;
- \$678 million to build domestic flexible manufacturing infrastructure and advanced development core services;
- \$33 million to support promising efforts and translation of concepts and research at NIH;
- \$822 million to address immediate development needs related to pandemic influenza vaccines, antiviral drugs, and diagnostics; and
- \$200 million to explore alternative capital market mechanisms.

The Administration has submitted an amendment to the FY 2011 President's Budget to provide new authorities where needed. Specifically, new authority is required to support the efforts at FDA, the efforts at DOD, and the MCMSI.

HHS has begun developing implementation plans for each of the initiatives and enhancements described above. Some have progressed more than others, based on the complexity and novelty of the new efforts. The HHS senior leaders from CDC, FDA, NIAID and ASPR, working with colleagues at DOD, have conducted strategic reviews of our major product portfolios for smallpox, anthrax and radiological/nuclear threats. They have identified priority actions to further enhance the production and eventual distribution of these medical countermeasures, looking as well at economies that can be realized so we may be better stewards of the public funding for this capability. As previously noted, BARDA released a draft solicitation to support Centers of Innovation for Advanced Development and Manufacturing.

BARDA has also awarded new contracts recently for the development of products that could be used as medical countermeasures to known or unknown threats as well as having a possible commercial market. BARDA awarded a contract to develop an antibiotic that could be used against two possible types of bioterrorism (plague and tularemia) as well as common infections that are becoming resistant to antibiotics. BARDA also awarded a contract to continue developing a new way to treat an illness caused by exposure to a nuclear blast; this treatment potentially could be used for other blood disorders and complications of cancer. BARDA is also expected to award a contract for the development of a next-generation ventilator as part of all-hazards preparedness generally, and pandemic influenza specifically.

As we transition to this improved approach to medical countermeasure development, we see opportunities for advances in other areas of public health—new vaccines for neglected diseases, rapid response for emerging naturally-occurring infectious diseases, and new approaches to treating drug-resistant bacteria in hospitals or other settings. This

strategy aligns with our concepts under the National Health Security Strategy,<sup>2</sup> which was developed to galvanize efforts to minimize the health consequences associated with significant health incidents and achieve a national vision of health security. The advances coming out of the medical countermeasure enterprise may ultimately address day-to-day needs as well as the ever-widening threats of biological, chemical, nuclear, and radiological hazards.

### **Conclusion**

I called for a review of the MCM enterprise recognizing that we need to incorporate 21stcentury technology along with 21st-century financial, legal, and regulatory frameworks in order to have the medical countermeasures necessary to defend against the diverse threats we face. The review focused primarily on our ability to take an idea or concept in research and move it quickly to producing an approved medical countermeasure. But, we recognize that our ability to respond begins with the rapid identification of a new event through public health or medical surveillance and the ability to identify the requirements of an MCM—how much we will need, for what part or parts of the population. A medical countermeasure is successful only if it reaches the right population at the right time. We must rely on surveillance capabilities and feedback from end-users incorporated at the beginning of development cycle.

The review identifies a variety of initiatives and opportunities to accomplish these intended goals with the ultimate vision of a nimble, flexible capacity that the nation can rely on to produce medical countermeasures rapidly in the face of any attack. As I mentioned earlier, in the end, if a product fails to make it into our national response capability, it should only be based on its failure to meet our stringent standards for safety, efficacy or quality, and not because we failed to provide the needed business, regulatory and technical support for success. By moving toward a 21st-century countermeasures enterprise with a stong base of discovery, a clear regulatory pathway, and agile manufacturing, we will be able to respond faster and more effectively to public health threats.

Thank you for this opportunity to speak with you today on this important subject. I look forward to answering your questions.

<sup>&</sup>lt;sup>2</sup> Available online at: http://www.phe.gov/Preparedness/planning/authority/nhss/Pages/default.aspx