Testimony
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NIH Implementation of Project BioShield in the Research and Development of Defense Countermeasures

Statement of

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Introduction

Mr. Chairman and Members of the Committee, thank you for the opportunity to speak with you today concerning the role of the National Institutes of Health (NIH) in implementing the Project BioShield Act of 2004 (Public Law 108-276). This critical legislation, signed in to law by President Bush in July 2004, provided the Department of Health and Human Services (DHHS) with new authorities to develop and procure medical countermeasures that will protect the Nation in the event of a terrorist attack with a biological, chemical, nuclear, or radiological agent or device. The National Institute of Allergy and Infectious Diseases (NIAID) is the lead NIH Institute for infectious diseases research, including research and development of countermeasures against potential agents of bioterrorism. In addition, the NIAID coordinates NIH research toward the development of medical countermeasures against chemical, radiological and nuclear agents. Today, I will discuss with you the substantial progress that has been made in medical countermeasures research and development, and how Project BioShield has facilitated this progress. In addition, I will discuss some of the challenges that remain.

Components of Project BioShield

The Project BioShield Act of 2004 provided DHHS with several new authorities to facilitate a three-pronged program to expedite the development and deployment of medical countermeasures against biological, chemical, nuclear, and radiological agents. Project BioShield enabled NIH to expedite the research and

development of critical medical countermeasures, established a secure funding source at DHHS for the purchase of critical medical countermeasures, and established a Food and Drug Administration (FDA) Emergency Use Authorization for critical medical countermeasures. My testimony today will focus on the implementation of NIH's BioShield authorities.

First, Project BioShield provides NIH additional flexibility in awarding contracts, cooperative agreements, and grants for research and development of critical medical countermeasures. These new authorities allow NIH to use expedited peer review procedures to obtain an assessment of the scientific and technical merit and potential contribution to the relevant field of a grant, contract, or cooperative agreement for countermeasure research. The normal NIH review and award process averages eighteen months from initial concept clearance to award; the BioShield mechanism significantly shortens this timeframe to six to eight months.

Thus far, NIAID has used Project BioShield authorities to award $29 million in grants and contracts. The activities supported by these awards will advance development of countermeasures toward possible future procurement with Project BioShield funds. These initiatives also follow recommendations in the NIAID Biodefense Research Agenda. Twelve grants have been awarded to support research and development of therapeutics directed against the CDC Category A agents that cause anthrax, smallpox, tularemia, plague, botulism,

and viral hemorrhagic fevers. These grants have the potential for making a broad impact in developing therapies against the most serious agents of bioterrorism. Additionally, a contract for the development and production of monoclonal antibodies against botulinum toxin type A and a contract for the production of a recombinant vaccine candidate against botulinum toxin type E have been awarded using BioShield authorities. With each of these awards, the science already had progressed sufficiently so that NIAID is now able to undertake specific developmental activities toward possible procurement.

NIAID also has solicited applications for grants and contracts to support research on medical countermeasures against radiological or nuclear terrorist attacks, including countermeasures to protect the immune system against radiation and improved treatments for the elimination of internal radionuclide contamination that can be given by mouth rather than intravenously.

The BioShield Act also provides NIH with streamlined personnel authority. This authority allows NIH to hire individuals to fill key positions related to product development more quickly than traditional hiring processes. To date, NIAID has used Project BioShield authorities to hire two highly qualified individuals with significant product development expertise. NIAID has appointed Dr. Michael Kurilla to the dual positions of NIAID Associate Director for Biodefense Product Development and Director of the Office of Biodefense Research Affairs in the Division of Microbiology and Infectious Diseases; Dr. Bert W. Maidment, Jr. to

the position of Associate Director for Product Development in the Division of Allergy, Immunology, and Transplantation; and Dr. Richard Hatchett to the position of Associate Director for Radiation Countermeasures Research and Emergency Preparedness, in the Division of Allergy, Immunology, and Transplantation,.

Project BioShield also provides NIH with additional authority for the construction of research facilities. Since the law was enacted, NIAID has used this authority to solicit applications for grants for construction of four to five additional Regional Biocontainment Laboratories (RBLs), which will support biomedical research on the NIAID Category A, B and C priority pathogens and emerging infectious diseases. These RBLs will join two National Biocontainment Laboratories (NBLs) and nine additional RBLs, the construction of which was authorized and funded in fiscal year 2003, to conduct research, train investigators, and to assist National, State and local public health efforts in the event of a deliberately released (bioterrorism) or naturally occurring infectious disease emergency.

As noted above, Project BioShield provides DHHS with the authority and funding to procure promising countermeasures for the Strategic National Stockpile (SNS), which is administered by the Centers for Disease Control and Prevention (CDC). It also provides the authority to grant emergency authorization for the use of unapproved countermeasures if, among other things, the FDA

Commissioner determines that there is no adequate approved alternative available.

Certain pharmaceutical and biotechnology companies have proven to be willing and eager to help in the development of biodefense countermeasures, but they need a reasonable assurance that a market for these products will in fact exist should they invest the resources necessary to fully develop them. To help provide these incentives, Project BioShield established a Special Reserve Fund for the purchase of biodefense countermeasures for the SNS for use in an emergency. Through these authorities, Project BioShield has given us new ways to both "push" and "pull" science toward needed countermeasures; NIH-supported basic research provides the "push", and guaranteed funding for procurement of these countermeasures provides the "pull" needed to attract industry.

Advanced Development

NIH historically has supported research that generates new knowledge about disease and has worked to translate these findings into vaccines, therapeutics, and diagnostics that protect public health. Working in close collaboration with industry, NIAID supported the advanced development of a next-generation anthrax vaccine that has since been procured by DHHS using BioShield funds. NIAID also is supporting trials of a next-generation smallpox vaccine, which would be eligible for future BioShield procurement.

NIAID played a major role in the rapid development of the next-generation anthrax vaccine known as recombinant protective antigen, or rPA. The applied research and advanced development of rPA were supported by the NIAID with contracts awarded in September 2002 and 2003, respectively. These were milestone-driven contracts with well-defined goals including the manufacture of clinical-grade vaccine, the conduct of Phase I and Phase II clinical trials, and consistency lot manufacturing of vaccine. Clinical trials to evaluate rPA are currently underway. To date, the immune responses elicited in humans are similar to those elicited in animal studies, which have demonstrated that the rPA vaccine protected animals against aerosol challenge with anthrax spores. Last November, DHHS awarded a contract for the acquisition of 75 million doses of rPA vaccine to be held in the SNS. NIAID's rPA product development initiatives were instrumental in making the SNS initiative possible.

NIAID-supported researchers also are developing and testing a new smallpox vaccine, modified vaccinia Ankara (MVA), which causes fewer side effects than the traditional "Dryvax" vaccine because it does not replicate effectively in human cells. NIAID has supported the advanced development of MVA through milestone-driven contract awards in 2003 and 2004. Early clinical trials in small numbers of human volunteers have demonstrated the MVA vaccine to be safe and immunogenic, and animal studies by the developers are confirming earlier studies by NIAID and Department of Defense (DoD) scientists showing that MVA

protects monkeys and mice from smallpox-like viruses. Based on these results and the demonstration of the feasibility of large-scale manufacturing capacity, DHHS has moved forward with the initial stages of an MVA acquisition program.

NIAID's support for the advanced development of the rPA and MVA vaccines was a unique commitment that was begun prior to the BioShield legislation. The advanced development of these two vaccines was enabled by a substantial research base developed by the DoD and NIAID.

Biodefense Research Priorities

The NIH biodefense research agenda was developed through a comprehensive and systematic strategic planning process. In February 2002, NIH convened the Blue Ribbon Panel on Bioterrorism and Its Implications for Biomedical Research, with membership composed of distinguished researchers from academic centers, private industry, government civilian agencies, and the military. Three key documents were developed based on this panel's advice and on extensive discussions with other Federal agencies: the *NIAID Strategic Plan for Biodefense Research*, the *NIAID Research Agenda for CDC Category A Agents*, and the *NIAID Research Agenda for CDC Category B and C Agents* (agents whose biological properties make them more difficult to deploy or less likely to cause widespread harm than a Category A agent). It is important to note that NIAID maintains an NIAID list of Category A, B and C Priority Pathogens which closely follows the CDC list of Category A, B and C Biological Diseases/Agents. The

NIAID list highlights specific pathogens identified as priorities for additional research efforts as part of the NIAID biodefense research agenda. The Strategic Plan provides a blueprint for the conduct of basic research on microbes and host immune defenses, as well as targeted, milestone-driven development of drugs, vaccines, diagnostics and other interventions that would be needed in the event of a bioterror attack. The two biodefense research agendas describe short-term, intermediate, and long-term goals for research on the wide variety of agents that could be used to conduct such an attack.

We developed the *Strategic Plan* and the two research agendas based on an overall threat assessment formulated by CDC in close cooperation with the intelligence community. Category A agents are the most dangerous microbes and toxins; these agents cause diseases that include anthrax, smallpox, plague, botulism, tularemia, and hemorrhagic fevers. These agents were given the highest priority because they: (a) are relatively easily disseminated or transmitted from person to person; (b) result in high mortality rates with the potential for major public health impact; (c) would likely cause significant social disruption; and (d) require special action for public health preparedness. Category B agents are in the second tier of priority. They are agents that: (a) are moderately easy to disseminate, (b) result in moderate morbidity and low mortality, and (c) require specific enhancements of national diagnostic capacity and disease surveillance systems. Category C Agents have the next highest priority. They include emerging pathogens that could be engineered for mass dissemination in the

future because of their availability, ease of production and dissemination, and potential for high rates of morbidity and mortality and major health impact.

NIAID also recently completed a Strategic Plan to accelerate the development and deployment of new medical countermeasures against ionizing radiation for the civilian population, and DHHS has tasked NIAID with drafting a strategic plan and research agenda to guide development of medical countermeasures against chemical threats. Input from several expert panels will be incorporated into a Strategic Plan and Research Agenda for countermeasure research against the leading chemical threats of concern to public health. Both the plan and agenda are expected to be complete by the end of this calendar year. I would note that efforts are underway, in partnership with other research institutes of the NIH and the DoD, to address medical countermeasures against chemical threats.

To obtain information about new threats that may arise, DHHS relies heavily on the Department of Homeland Security (DHS) to provide a prioritized list of threats along with Material Threat Determinations (MTDs) that will provide reasonable estimates of population exposure. DHS has issued MTDs for attacks with the agents that cause anthrax and smallpox, attacks with botulinum toxin, and nuclear and radiological attacks; MTDs against additional agents are underway. This information is critical for strategic decision-making on how best to focus our future efforts in countermeasure development. Because new infectious diseases emerge naturally on a regular basis, NIH has considerable experience in rapidly mobilizing research resources to confront new infectious disease threats. This

experience serves us well when we are called upon to adjust our research priorities in response to new intelligence information. In addition, this information is necessary to fully engage the pharmaceutical and biotechnology industries in countermeasures development; without MTDs, industry has no way of knowing which high-priority products are being considered for procurement for the SNS.

NIAID's long experience with infectious disease research allowed us to take on a greatly expanded role in civilian biodefense after the terrorist attacks in the fall of 2001, and I am confident that we are making good progress. Project BioShield has provided us with some of the tools necessary to accelerate and expand the basic and applied research, advanced development, and ultimate procurement of safe and effective vaccines, therapeutics, and diagnostics against biological, chemical, nuclear, and radiological agents. We have already begun using these tools to support important research for our nation's defense. I look forward to working with you, Mr. Chairman, and with this Committee, to continue to address the challenges involved in the research and development of biodefense countermeasures.

I appreciate this opportunity to testify before you today, and I would be pleased to answer any questions that you may have.