Biodefense: Next Steps
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Testimony

Mr. Chairman and Members of the Subcommittee, thank you for the opportunity to speak with you today. I will discuss our national biodefense research program, with particular emphasis on recent progress toward the development of medical countermeasures against a bioterrorist attack. I am particularly honored to appear at the very first hearing of this Subcommittee, and I look forward to working with you to continue to improve our biodefense capabilities which are essential to protecting our Nation's health.

The destruction of the World Trade Center, the attack on the Pentagon and the downing of an airliner over Pennsylvania on September 11, 2001, clearly exposed the vulnerability of the United States to brutal acts of terrorism. The anthrax attacks in Florida, New York and Washington that followed only a few weeks later made it very clear that the threat of bioterrorism with pathogens or biological toxins represents a serious threat to our Nation and the world. The Administration and Congress responded forcefully to this threat, and biodefense has become a top national security priority for which funding has increased substantially. The Department of Defense, the Department of Health and Human Services (HHS), the Department of Homeland Security (DHS), the Department of Agriculture (USDA) and other federal agencies each have been given important roles to play in biodefense preparedness.

The National Institute of Allergy and Infectious Diseases (NIAID), of which I am Director, is a component of the National Institutes of Health (NIH) and the lead agency within HHS for the conduct of research concerning potential agents of bioterrorism that directly affect human health. Three other components of HHS also are charged with major biodefense responsibilities. Among many roles, the Centers for Disease Control and Prevention (CDC) carries out disease surveillance and detection, maintains the Strategic National Stockpile of medicine and medical supplies for use in an emergency, and trains and advises local public health response teams. The Food and Drug Administration (FDA) is responsible for regulatory approval of new biodefense countermeasures. The Office of Public Health Emergency Preparedness (OPHEP) coordinates all HHS biodefense activities. The President's FY 2006 budget proposal calls for $4.2 billion in funding for HHS bioterrorism preparedness activities, an increase of $154 million over FY 2005.

NIH Biodefense Research

In the wake of the 2001 terrorist attacks, NIH embarked on a systematic strategic planning process by convening the Blue Ribbon Panel on Bioterrorism and Its

Implications for Biomedical Research, comprised of distinguished researchers representing academia, private industry, civilian government agencies, and the military. Based on the panel's advice and extensive discussions with other Federal agencies, NIH developed three key documents to guide its biodefense research program; these are the NIAID Strategic Plan for Biodefense Research, the NIAID Research Agenda for Category A Agents (covering agents that pose the gravest threat to human health, such as those that cause smallpox, anthrax, botulism, and plague), and the NIAID Research Agenda for Category B and C Agents (for agents whose biological properties make them more difficult to deploy or less likely to cause widespread harm than Category A agents).

The Strategic Plan provides a blueprint for the construction of three essential pillars of the biodefense research program: infrastructure needed to safely conduct research on dangerous pathogens; basic research on microbes and host immune defenses, which serves as the foundation for applied research; and targeted, milestone-driven medical countermeasure development to create the vaccines, therapeutics and diagnostics that we will need in the event of a bioterror attack. The two Biodefense Research Agenda documents present detailed descriptions of short-term, intermediate, and long-term goals for research on the wide variety of potential bioterrorism threat agents. NIH also conducts research into ways to mitigate harm to civilians from chemical, nuclear, and radiological weapons. Meeting the goals delineated in the research agendas required a significant expansion of NIH programs already in place that study human pathogens and the immune system. To implement the biodefense agendas, Congress increased NIH appropriations for biodefense research from $53 million in FY 2001 to $1.5 billion in FY 2003 and approximately $1.7 billion in FY 2005; the President has requested $1.8 billion for FY 2006.

The Nation’s investment in a strengthened, accelerated and expanded biodefense research program has already begun to return substantial dividends in all three aspects of biodefense research outlined in the Strategic Plan, which has been described in two recent progress reports. Some of the funds are devoted to intramural research, which is work carried out in NIH-owned and operated laboratories; most, however, goes to extramural research funded through grants and contracts awarded to researchers throughout the country at academic institutions and in the private sector.

Infrastructure. Perhaps the most tangible signs of the increased priority for biodefense research are the integrated research facilities under construction to safely contain and study pathogens. In terms of intramural facilities, construction is well under way for new biodefense laboratories. NIAID also is supporting the construction of National Biocontainment Laboratories (NBLs) which will include facilities built to Biosafety Level 4 standards and will therefore be capable of safely containing any pathogen. Nine Regional Biocontainment Laboratories (RBLs), with Biosafety Level 3 facilities, also are planned or already under construction. All of these high-level research laboratories will provide the secure facilities needed to carry out the nation's expanded biodefense research program in a setting of safety for both workers and the surrounding communities. NIAID also has funded eight Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research (RCEs). This nationwide network of multidisciplinary

academic centers will conduct wide-ranging research on infectious diseases that could be used in bioterrorism, and will develop diagnostics, therapeutics and vaccines needed for biodefense. These Centers will develop the human infrastructure that biodefense research will require in the years ahead by serving as a training ground for biodefense researchers, and the Centers will partner with State and local public health agencies to help ensure a strong, coordinated response in a time of crisis.

Basic Research. Advances in the field of medicine rest on a foundation of basic research into the fundamental properties and mechanisms of life. In biodefense, these studies include the sequencing and understanding of microbial genes (genomics), how microbes cause disease (pathogenesis), and how the human immune system and pathogens interact (immunology). NIH-funded basic researchers have made significant progress since 2001 in each of these areas. For example, researchers have determined the genetic sequence of at least one strain of every Category A, B, and C pathogen; in many instances multiple strains have been sequenced, allowing researchers to better understand the factors that determine virulence. NIH has established the Pathogen Functional Genomics Resource Center to help researchers apply and analyze the large new database of genome sequence information. In pathogenesis, NIH researchers recently determined the three-dimensional structure of anthrax toxin bound tightly to a target cell surface receptor, and thus have gained a detailed snapshot of a crucial step in the pathway that allows anthrax to kill. This work provides important new leads for the development of novel antitoxins that could save lives late in the disease when large amounts of toxin are present and antibiotics alone are no longer sufficient to save the patient. Finally, immunological studies of the human innate immune system, which is comprised of broadly active "first responder" cells and other mechanisms that are the first line of defense against infection, have been moving forward rapidly. These advances suggest new ways to boost innate immune responses and suggest that it will be possible to develop fast-acting countermeasures that mitigate the effects of a broad spectrum of bioterror pathogens or toxins. Manipulation of the innate immune system also could lead to the development of powerful adjuvants that can be used to increase the potency and effectiveness of vaccines.

Medical Countermeasure Development. The new emphasis placed on biodefense as a national priority has led NIH to develop an expanded paradigm with respect to biodefense product development. NIH has always supported research that generates new knowledge about disease and has worked to translate these findings into vaccines, therapeutics, and diagnostics that protect public health. But to develop safe and effective products for biodefense as quickly as possible, we needed to intensify and accelerate this process. Thus, we have sought creative ways to modify NIH’s traditional process of research and development to move ahead more rapidly while continuing to preserve the excellence in basic research that is a hallmark of NIH . Working in close collaboration with industry and academia, we have taken a much more pro-active role in moving promising concepts into advanced product development.

The Project BioShield Act of 2004 signed into law last July provides powerful new mechanisms that will expedite the development and deployment of medical countermeasures for bioterrorism. For example, BioShield gives NIH additional

flexibility in awarding contracts, cooperative agreements, and grants for research and development for critical medical countermeasures, and streamlines the scientific evaluation of biodefense research proposals. The pharmaceutical industry has proved to be willing and eager to help in the development of biodefense countermeasures, but it needs a reasonable assurance that a market for these products will in fact exist should industry invest the resources necessary to fully develop them. To help provide these incentives, BioShield establishes a secure 10-year funding source for the purchase and stockpiling of new vaccines and drugs for use in an emergency. To put it another way, BioShield has given us new ways to both "push" and "pull" science toward needed countermeasures—basic research provides the push, and new incentives to industry for product development provide the pull. NIH works vigorously with both.

Much has been accomplished. With respect to medical countermeasures against attack with biological agents, we are already in a far stronger position today than we were only a few years ago. For example, in September 2001 we had 15.4 million doses of smallpox vaccine available; today we have more than 300 million doses. We also have a next-generation safer smallpox vaccine called modified vaccinia Ankara (MVA) in clinical testing and others under pre-clinical development. In addition, a new oral form of an antiviral drug cidofovir is in advanced product development for use in the event of a smallpox attack, as well as to treat the rare but serious complications of the classic smallpox vaccine. For anthrax, NIAID has aggressively pursued a new vaccine called rPA; HHS has contracted with VaxGen, Inc. to purchase 75 million doses of rPA under BioShield. This vaccine is produced using modern vaccine manufacturing techniques and may require fewer doses than the currently licensed vaccine. New anthrax therapies that can neutralize the anthrax toxin are being developed, such as monoclonal and polyclonal antibodies. Candidate antibody treatments for the toxin that causes botulism are in development, as is a new vaccine to prevent the disease. Finally, an Ebola vaccine based on a new strategy is in human clinical trials at the NIAID Vaccine Research Center. I expect the coming years to be at least as productive.

In addition, HHS is pursuing research, development and acquisition of medical countermeasures to address radiological and nuclear threats. These efforts include an acquisition programs for a pediatric formulation of potassium iodide under Project BioShield and acquisition of Prussian blue by the Strategic National Stockpile. HHS is also seeking information from industry about capabilities for developing medical countermeasures to treat acute radiation syndrome and exposure to nerve agents.

Conclusion

I would close with one last point. Infectious diseases have afflicted humanity since its inception, and they will always be with us. The viruses, bacteria, and parasites that cause infectious diseases do not remain static, but continually and dramatically change over time as new pathogens emerge and as familiar ones re-emerge with new properties or in unfamiliar settings. Emerging infections such as HIV, Ebola and SARS and re-emerging infections such as plague and influenza have shaped the course of human history while causing incalculable misery and death. Fortunately, the knowledge and products that will

flow from the NIH biodefense research program, including research results, intellectual capital, laboratory resources, and countermeasures in the form of diagnostics, therapeutics, and vaccines, will help us cope with naturally emerging, re-emerging, and deliberately released microbes alike. Recent experience tells us that knowledge developed to understand one pathogen invariably applies to others. When HIV first emerged, for example, antiviral drug development was in its infancy. Now, new technologies have led to the development of more than 20 antiretroviral drugs that can effectively suppress HIV replication and dramatically reduce AIDS morbidity and mortality. These same technologies, and the lessons learned about antiviral drug development, are being applied to the development of new generations of drugs against many viruses, including influenza, SARS, smallpox, and Ebola. Even if we are never confronted with another bioterror attack, the biodefense research and preparations being carried out now will without question prove to be very valuable.

HHS/NIH has a strong mandate from the President and Congress, robust funding, and a detailed and vigorous plan to carry out needed biodefense research. Our long institutional experience with infectious disease research allowed us to seamlessly take on a greatly expanded biodefense role when it became a priority, and I am confident that we are making good progress. Again, Mr. Chairman, I look forward to working with you and the members of the Subcommittee to address the challenges of bioterrorism preparedness and its impact on public health.

I am pleased to answer any questions that you may have.