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The Role of NIH Biomedical Research in Preparing for Emerging Public Health Threats

Statement of

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INTRODUCTION

Mr. Chairman and Members of the Committee, thank you for the opportunity to speak with you today about the role of the National Institutes of Health (NIH) in preparing the Nation to respond effectively to emerging public health threats. In my testimony today, I will describe NIH research that is leading to new and effective countermeasures against these threats. I also will discuss the NIH role in the implementation of the Project BioShield Act of 2004 and the Biomedical Advanced Research and Development Authority (BARDA), established by the Pandemic and All-Hazards Preparedness Act of 2006.

As a Nation, we must be prepared to respond quickly and effectively to any threat to public health. The threats we face include new microbes that might emerge naturally, such as the virus that caused Severe Acute Respiratory Syndrome (SARS), and familiar pathogens that re-emerge with enhanced properties or in unusual settings, such as bacteria that cause extensively drug-resistant tuberculosis (XDR-TB) and influenza viruses with pandemic potential. As was made clear by the terrorist attacks of 2001—including the anthrax attacks in the eastern United States—we must also be prepared for the deliberate release of pathogenic organisms, biological toxins, chemical poisons, or radioactive substances. The primary role of the NIH in confronting these diverse threats is to carry out basic and applied scientific research and early-stage development of potential products, upon which late-stage advanced product development and

ultimately approval of vaccines, therapeutics and other medical countermeasures can be based.

NIH RESEARCH ON EMERGING PUBLIC HEALTH THREATS

Research to mitigate emerging threats to public health is a key focus of the NIH. The National Institute of Allergy and Infectious Diseases (NIAID) is the component of the NIH assigned primary responsibility for research on emerging and re-emerging infectious diseases, including the deliberate use of infectious biological agents and toxins that directly affect human health. The NIAID also coordinates NIH research into medical countermeasures against chemical, radiological and nuclear agents; this research is supported by several NIH institutes, including the NIAID, the National Cancer Institute, and the National Institute for Neurological Disorders and Stroke.

Strategic planning to guide the broad NIH biodefense and emerging infections research effort has been extensive, and has involved substantial consultation with outside experts in academia, private industry, civilian government agencies, and the military. The overall strategy encompasses three components of NIH biodefense and emerging infections research: the infrastructure needed to safely conduct research on dangerous pathogens; basic research on microbes and host immune defenses that serves as the foundation for applied research; and targeted, milestone-driven, early-phase development of medical countermeasures to create the vaccines, therapeutics and diagnostics that will be

needed in the event of a public health crisis. These efforts enhance the Nation's preparedness for both potential bioterrorism attacks and naturally occurring infectious disease outbreaks.

The NIH is substantially expanding the Nation's biodefense research infrastructure, which will greatly enhance our ability to safely and efficiently conduct research on infectious agents. Facilities currently or soon to be under construction will be capable of safely housing research on the most deadly pathogens, as well as microbes that are more familiar and less virulent, but nonetheless deleterious to human health. These facilities include two National Biocontainment Laboratories (BSL-4 - the highest level of containment) and thirteen Regional Biocontainment Laboratories (BSL-3 – one level down from highest level of containment). In addition, three intramural biocontainment labs—on the NIH campus in Bethesda, Maryland (BSL-3), on the National Interagency Biodefense Campus at Fort Detrick in Fredrick, Maryland (BSL-4), and at the NIAID Rocky Mountain Laboratories in Hamilton, Montana (BSL-4)—are operational or nearing completion.

In addition to building new facilities, the NIH has strengthened the Nation's intellectual infrastructure by establishing a network of ten Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research. These Centers conduct research and development activities and provide training for future biodefense researchers. Most recently, the NIH announced awards to

create six Centers of Excellence for Influenza Research and Surveillance; these centers will bolster influenza research in key areas, including understanding how animal viruses can adapt to cause human disease and how the human immune system responds to infection with the virus.

The NIH role in biodefense research is similar to its role in biomedical research in general; namely, to support basic scientific discovery, applied research and early-stage development activities that start new vaccines and drugs down the pathway toward approval. Early-stage development activities that the NIH often supports include preclinical testing, animal model development, and establishment of pilot lot-scale manufacturing processes. Late-stage advanced product development, such as commercial-scale process development and validation, is usually left to industry. On rare occasions, however, the NIH has supported late-stage medical countermeasure development activities. For example, in 2003, the NIH awarded milestone-driven contracts to two companies, Avecia and VaxGen, Inc., for late-stage advanced development of second-generation anthrax vaccines. These contracts predated the Project BioShield Act of 2004.

The vaccines are based on a purified, recombinant (r) anthrax protein called Protective Antigen (PA), against which the body generates a strong antibody response; studies conducted in the 1990s showed that rPA vaccines could protect animals exposed experimentally to airborne anthrax spores from

developing anthrax disease. The Avecia and VaxGen contracts supported activities such as advanced manufacturing process development, Phase II clinical trials, and advanced assay development. As noted above, NIH funding of late-stage advanced development for biodefense countermeasures is the exception rather than the rule.

RESEARCH PROGRESS

NIH research has yielded substantial scientific advances in the effort to counter emerging public health threats. For example, new or improved candidate vaccines and therapies against smallpox and Ebola virus have shown great promise. Among these is ST-246, a promising smallpox drug candidate that has protected nonhuman primates from what would otherwise be a lethal exposure to live smallpox virus, and that is now in human clinical trials. Basic research also has proceeded rapidly. NIH-supported researchers recently determined the structure of botulinum toxin—a Category A bioterror threat agent and the cause of botulism—as it binds to its receptor protein on nerve cells; these findings may lead to the development of new drugs to treat botulism. Further, an NIH program that screens both approved drugs and new drug candidates has identified several promising anti-influenza drug candidates, including FluDase (which binds host cell receptors to prevent viral entry), T-705 (which inhibits replication of viral RNA) and Peramavir (which inhibits an influenza enzyme called neuraminidase). All three of these influenza drug candidates are undergoing further development in partnership with industry sponsors.

With regard to the development of medical countermeasures against radiological, nuclear, and chemical threats, the NIH has established eight Centers for Medical Countermeasures against Radiation, and four Centers for Countermeasures against Chemical Threats. Basic and applied research conducted in these centers and elsewhere is moving forward rapidly. For example, researchers supported by one of these Centers recently characterized changes in gene activity in mice exposed to different doses of ionizing radiation and in cancer patients undergoing radiation therapy; these results may lead eventually to a diagnostic test to distinguish people who have suffered serious radiation exposure from those who have not prior to the onset of clinical illness. That capability would allow treatments to be efficiently directed early on to those who need them most following a radiological incident.

NIH ROLE IN BIOSHIELD AND BARDA

Two landmark pieces of legislation designed to speed the development, approval, and acquisition of biodefense and emerging infections countermeasures have been enacted in recent years: the Project BioShield Act (Public Law 108-276), which became law in July 2004, and the Pandemic and All-Hazards Preparedness Act (Public Law 109-417), which became law in December 2006.

The BioShield legislation provided HHS and its constituent agencies with several new authorities regarding medical countermeasures against a terrorist attack with

a biological, chemical, nuclear, or radiological agent or device. Three of these authorities were of particular relevance to the NIH. First, BioShield provided the NIH additional flexibility in awarding contracts, cooperative agreements, and grants for research and development of critical medical countermeasures. Second, BioShield gave the NIH streamlined personnel authority that has allowed expedited hiring to fill key biodefense positions. Third, BioShield provided the NIH with additional authority for the construction of research facilities. The NIH has used all three of these authorities in carrying out its biodefense and emerging infections research and development responsibilities.

Perhaps the most important provision of BioShield was the establishment of a secure funding source at HHS for the purchase of critical medical countermeasures. Many pharmaceutical and biotechnology companies have been willing to help in the development of biodefense countermeasures, but they needed reasonable assurances that a market for these products would, in fact, exist should they invest the resources necessary to fully develop them. To provide these incentives, BioShield established a Special Reserve Fund for the purchase of biodefense countermeasures to be placed in the Strategic National Stockpile for use in an emergency.

Procurement contracts under BioShield are developed and awarded by the HHS Office of the Assistant Secretary for Preparedness and Response (ASPR). As is the case with other scientists within the Federal government and particularly

within HHS, NIH personnel often serve as subject matter experts, consultants, and members of committees and boards that participate in the planning and execution of the HHS preparedness activities, including the development of contracts for BioShield acquisitions. Ultimately, however, the decisions regarding acquisitions are made by the Office of the ASPR.

Title IV of the Pandemic and All-Hazards Preparedness Act established BARDA within HHS. When BARDA is fully implemented, the Office of the ASPR will administer the Biodefense Medical Countermeasure Development Fund to support late-stage advanced product development. Because the NIH is likely to have played a role in earlier phases of development of some of the products that BARDA might support, the NIH will coordinate with BARDA staff. However, all decisions concerning products to be supported by BARDA will be made in the Office of the ASPR.

CONCLUSION

Emerging and re-emerging public health threats pose a perpetual challenge. At one time, some in public health thought it might be possible eventually to "close the book" on the study of infectious diseases because of advances in therapies and vaccines. However, it is now clear that naturally emerging and re-emerging infections will challenge us for the foreseeable future, as will threats from deliberately disseminated infectious diseases, chemical, or radiological terrorist attacks. The task for the NIH is to continue building a strong foundation of basic

and applied research and development that is needed to counter these threats, and also to be nimble enough to respond with speed and precision to new threats as they arise. NIH efforts to address these challenges complement those of our colleagues in ASPR, CDC, FDA and other agencies in the Federal government to protect the health and safety of our Nation.

Thank you for the opportunity to appear before you today. I am happy to answer any questions you may have.