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The Role of NIH Biomedical Research in Preparing for Public Health Emergencies

Statement of

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Mr. Chairman and members of the Committee, thank you for the opportunity to appear before you today to describe the NIH role in countering emerging and re-emerging public health threats, including bioterrorism and pandemic influenza. I will first briefly discuss the nature of the multiple threats we face and outline the NIH role within the broader framework of the Department of Health and Human Services and other Federal activities. I will then turn specifically to the NIH biodefense and influenza research programs.

EMERGING THREATS TO PUBLIC HEALTH

Despite advances in medicine and public health such as antibiotics, vaccines, and improved sanitation, infectious diseases continue to exact a substantial toll of morbidity and mortality in the United States and throughout the world. Moreover, because the threats we face are not static, we must be prepared to respond quickly and effectively to new microbes as they emerge and to familiar pathogens that re-emerge with new properties or in unusual settings. Examples of recent emerging and re-emerging public health threats include naturally emerging infectious diseases such as Severe Acute Respiratory Syndrome (SARS), West Nile Virus, extensively drug resistant tuberculosis (XDR-TB) and pandemic influenza. They also include threats posed by the deliberate release of pathogenic organisms, biological toxins, chemical poisons, or radioactive substances in a terrorist attack.

The National Institutes of Health (NIH) is the Nation's premier agency for the conduct and support of biological and medical research. As such, it is the lead agency within the Department of Health and Human Services (HHS) for basic scientific research and concept development that leads to the creation of the vaccines, therapeutics and other medical countermeasures needed to address new threats to public health. The National Institute of Allergy and Infectious Diseases (NIAID) is the component of NIH assigned primary responsibility for the conduct of research concerning emerging and re-emerging infectious diseases, including the deliberate use of infectious biological agents and toxins that directly affect human health. At NIH, NIAID is a key component of the NIH Biodefense Research Coordinating Committee, the focal point for trans-NIH coordination and planning of NIH medical countermeasure research activities.

NIH carries out its research mission within a larger framework of Federal activities. Within HHS, several other agencies and offices are charged with major responsibilities. Among them, 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 emergencies, and trains and advises local public health response teams, in addition to many other roles. The Food and Drug Administration (FDA) is responsible for regulatory approval of new medical countermeasures. The Office of the Assistant Secretary for Preparedness and Response (ASPR) coordinates research and preparedness activities both within HHS and with other Federal

agencies, including the Department of Homeland Security and the Department of Defense. At the highest level, coordination of medical countermeasures research is carried out by the White House, and in particular, the Homeland Security Council and the National Security Council. It is important to note, however, that in addition to the formal structure through which the Nation's biodefense research programs are coordinated, NIH collaborates daily with the other Federal agencies and is party to a large number of interagency programs, informal contacts, and communication mechanisms that significantly contribute to the efficiency and effectiveness with which medical countermeasures research is carried out across the U.S. government.

NIH BIODEFENSE RESEARCH

The possibility that terrorists will use a biological, chemical, radiological, or nuclear agent to mount an attack is a serious threat to the citizens of our nation and the world. Research to mitigate these threats is a key focus of NIH, and complements the NIH role in meeting the challenges of naturally emerging and re-emerging infectious diseases. The President's fiscal year (FY) 2008 budget requests $1.723 billion to support NIH biodefense research activities. Strategic planning to guide the NIH biodefense research program has been extensive and includes three essential pillars: 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 development of medical countermeasures to create the

vaccines, therapeutics and diagnostics that would be needed in the event of a bioterror attack. These efforts enhance not only our preparedness for a bioterrorism attack, but for naturally occurring endemic and emerging infectious diseases as well.

NIH is currently in the midst of a substantial expansion of the Nation's biodefense physical 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. They include two National Biocontainment Laboratories and thirteen Regional Biocontainment Laboratories; in addition, three intramural biocontainment labs—on the NIH campus, on the National Interagency Biodefense Campus at Fort Detrick in Fredrick, Maryland, and at the NIAID Rocky Mountain Laboratories in Hamilton, Montana—are operational or nearing completion. In addition to these facilities, NIH has strengthened the Nation's intellectual infrastructure by establishing a network of ten Regional Centers of Excellence (RCEs) for Biodefense and Emerging Infectious Diseases Research, which conduct research and development activities and provide training for future biodefense researchers.

NIH efforts already have yielded substantial dividends; many of these have been described in our periodic progress reports, the latest of which was issued in January 2007. For example, new or improved candidate vaccines and therapies

against anthrax, smallpox and Ebola virus have shown great promise. Among these is ST-246, a promising smallpox drug candidate that has protected both rodents and nonhuman primates from what would otherwise be a lethal exposure to live smallpox virus. Basic scientific discovery is proceeding as well. For example, NIH-funded researchers recently determined the structure of botulinum toxin—a Category A bioterror threat and the cause of botulism—as it binds to its receptor protein on nerve cells. This advance opens new possibilities for creating new drugs to treat botulism.

NIH also is responsible for the conduct and coordination of research to develop medical countermeasures against a range of radiological and chemical threats. To that end, we have 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, through the NIH medical countermeasures program, more than 40,000 compounds have been screened for potential radioprotective benefits and animal model screens have been developed to test the most promising of these candidates.

NIH continues to coordinate and collaborate on these important components of national security within HHS and with our interagency partners, including the Departments of Defense, Energy, and Homeland Security. The research and development process for new medical countermeasures against biological,

chemical, and radiological threats, especially in its later stages, will be substantially enabled by the advanced development tools provided in the Biomedical Advanced Research and Development Authority (BARDA) and the purchase capability of Project BioShield, both within the Office of the ASPR.

NIH INFLUENZA RESEARCH

Influenza is a classic example of a re-emerging infectious disease. Seasonal outbreaks of influenza occur almost every year in the United States, but because circulating human influenza viruses continually undergo small genetic changes a new vaccine must be formulated each year. These seasonal epidemics cause an annual average of about 200,000 hospitalizations and 36,000 deaths in this country, mostly among seniors, infants and people with chronic health conditions. Globally, an estimated 250,000 to 500,000 influenza-related deaths occur each year with seasonal influenza. This is a substantial toll; however, when an influenza virus emerges that has undergone a major genetic shift such that the global population has limited natural immunity and the virus can be easily transmitted among people, a worldwide pandemic may result.

Historically, pandemic influenza is a proven threat. In the 20th century, influenza pandemics occurred in 1918, 1957, and 1968. The pandemics of 1957 and 1968 were serious infectious disease events that killed approximately two million and 700,000 people worldwide, respectively. The 1918-1919 pandemic, however, was catastrophic: epidemiologists estimate that it killed more than 50 million

people worldwide, including more than 500,000 people in the United States, and caused enormous social and economic disruption. In each of these pandemics, for reasons that remain unclear, a much greater proportion of young adults died than is typical of seasonal influenza. Given this history, we can expect that a new influenza virus will emerge and another pandemic will occur at some point in the future. Although it cannot be predicted precisely when the next pandemic virus will appear, a pandemic strain is likely to spread rapidly through our highly mobile society once it emerges. The consequences of the next pandemic could be severe throughout the world, especially in poor countries that do not have adequate public health capacity.

Of known influenza viruses, the highly pathogenic H5N1 avian influenza virus that has been found in domestic and migratory birds in Asia, Africa, Europe and the Middle East is of greatest concern. Although the H5N1 virus remains primarily an avian pathogen, 277 people are known to have been infected, usually from direct contact with infected poultry; 167 of the people diagnosed with H5N1 avian influenza infection have died. At this time, the virus does not spread efficiently from birds to humans, and transmission from one person to another is rare. However, if the H5N1 virus mutates further or exchanges genes with a human influenza virus to acquire the ability to spread from person to person as efficiently as the viruses that cause seasonal influenza epidemics, a human pandemic could become a reality. The degree of threat from such a virus would

depend on the extent to which the virus retained its current virulence and how transmissible it became.

It is imperative that we prepare for the possibility that a new influenza virus will emerge to cause a 1918-like pandemic. How well we do that, however, depends to a large extent on improving how we cope with seasonal influenza. Control of both seasonal and pandemic influenza requires development of—and access to—a sufficient supply of effective vaccines and antiviral drugs, effective infection control measures and diagnostics, and clear public communication. To this end, the FY 2008 President's budget requests $268 million to support NIH influenza research programs.

NIH research has laid the foundation for improved influenza vaccine manufacturing methods, new categories of vaccines that may work against multiple influenza strains, and the next generation of anti-influenza drugs. Certain of these goals will be accomplished through basic research projects intended to increase our understanding of how animal and human influenza viruses replicate, interact with their hosts, stimulate immune responses, and evolve into new strains. Other goals will be accomplished through targeted projects, such as a program to screen compounds for antiviral activity against influenza viruses.

To better understand the varied and ever-changing genetic blueprints of influenza viruses, NIH launched the Influenza Genome Sequencing Project in the fall of 2004. The goal of this collaboration between NIH (NIAID and the National Library of Medicine, NLM), St. Jude Children's Research Hospital, the Wadsworth Center, the Institute for Genomic Research, the CDC, and several other organizations is to determine the complete genomic sequences of the large number of influenza viruses from around the world and to rapidly provide these sequence data to the scientific community as well as to other government agencies, including CDC, which supplies viruses it collects for sequencing. At this point, we have sequenced 100 viruses for the CDC. To date, the project has determined genomic sequences of more than 2,000 animal and human influenza viruses, all of which are freely available to researchers and government agencies through GenBank, an Internet-accessible database of genetic sequences maintained by the National Center for Biotechnology Information (NCBI) at NLM. We have the capacity to sequence more than 200 new viruses every month. The data flowing from this program will enable scientists to track how influenza viruses evolve as they spread through their host populations and across geographic regions, and to match viral genetic characteristics with virulence, ease of transmissibility, and other clinically relevant properties. The end result will be a clearer understanding of how influenza epidemics and pandemics emerge, which will support the HHS priority goal of influenza pandemic planning and preparedness.

During the past year, we have made substantial progress in influenza vaccine research. The inactivated-virus H5N1 vaccine currently stockpiled by HHS has been shown in NIAID-sponsored clinical trials to be well-tolerated and capable of inducing immune responses predictive of protection against the H5N1 virus at similar levels in healthy adults, children, and seniors. Although immune responses to the vaccine alone are noted over a range of doses, the highest response rate occurred at such high doses that would make it challenging to provide vaccine for the entire population. Studies on enhancing the immune response to lower doses by employing immune enhancers called adjuvants are showing promising preliminary results. NIAID also is collaborating with industry to pursue several other vaccine strategies in addition to inactivated virus H5N1 vaccines. For example, trials of cold-adapted, live-attenuated H5N1 vaccine candidates are underway, as is a Phase I clinical study of a novel DNA H5N1 vaccine candidate developed at the NIAID Vaccine Research Center.

We also have made progress in antiviral drug and diagnostic test research over the past year. An NIAID program that screens both licensed drugs and new drug candidates—first in cell culture systems and then in animal models—has identified several promising anti-influenza candidates that are now being further developed in partnership with industry sponsors. These include FluDase, which prevents viral entry into host cells; T-705, which inhibits replication of viral RNA; and Peramavir, which inhibits an influenza enzyme called neuraminidase. Research into influenza diagnostics is being vigorously pursued. For example,

NIAID-supported researchers, working in collaboration with scientists at the CDC, have reported encouraging results with a potentially revolutionary diagnostic device called the MChip, which is capable of quickly and accurately identifying many influenza viruses, including H5N1.

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 and treatment of infectious diseases. However, it is now clear that naturally emerging, re-emerging infections will perpetually challenge us, and deliberately disseminated infectious diseases will continue to challenge us for the foreseeable future, as will the possibility of chemical or radiological terrorist attacks. The task for NIH is not only to continue building the strong foundation of basic and applied research and development we need to counter these threats, but 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 ASPR and CDC colleagues to protect the health and safety of our Nation.

Thank you for the opportunity to appear before you today, and I would be happy to answer any questions you may have.