Testimony
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Protecting the Public Health: The Importance of NIH Biodefense Research Infrastructure

Statement of

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Mr. Chairman and members of the Subcommittee, my name is Hugh Auchincloss and I am the Deputy Director of the National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health (NIH), an agency of the Department of Health and Human Services (HHS). I am pleased to have the opportunity to discuss the NIH biodefense research program, including the expansion of the Nation's biodefense research infrastructure and the need to ensure that biodefense research is conducted safely.

The anthrax attacks in 2001 were a sobering reminder that the threat of deliberately released microbes can be used as a form of terrorism. Moreover, naturally occurring microbial outbreaks pose a serious threat to domestic and global health. The experience with SARS in 2003 and the ongoing outbreaks of H5N1 avian influenza and extensively drug-resistant tuberculosis have reminded us that defense against naturally emerging microbes must be a top national priority. Congress has recognized the urgency of improving our defenses against emerging public health threats and has supported funding for such research. Within the broad Federal effort against emerging threats to public health, the role of the NIH is to conduct and support basic and applied research that will lead to new vaccines, drugs, and diagnostic tools.

Expanding the Nation's Biodefense Research Capability

In February 2002, the NIH embarked on a systematic planning process for its biodefense research program. It first convened the Blue Ribbon Panel on

Bioterrorism and Its Implications for Biomedical Research, made up of distinguished scientists representing academia, private industry, and government. Based on the panel's advice and extensive discussions with other Federal agencies, the NIH developed three key documents to guide its biodefense research program: the NIAID Strategic Plan for Biodefense Research, the NIAID Research Agenda for Category A Agents, and the NIAID Research Agenda for Category B and C Agents.

As a result of the strategic planning process, a clear consensus emerged that meeting the goals of the biodefense Research Agendas would require additional research infrastructure, especially research laboratories built to modern Biosafety Level 3 (BSL-3) and Biosafety Level 4 (BSL-4) standards. BSL-3 laboratories are used to study contagious agents that can be transmitted through the air and cause potentially lethal infection. BSL-4 laboratories are used to study agents that pose a high risk of life-threatening disease for which no vaccine or therapy is available; they incorporate all BSL-3 features and occupy safe, isolated zones within a larger building.

There has been considerable discussion of how best to assess the extent of high-containment facilities that would be required in the United States in the public, academic and private sectors and for what purposes these varied facilities are used. Published estimates range from as few as 200 to as many as 1400 BSL-3 laboratories. (Many institutions maintain multiple facilities.) The

explanation for this wide discrepancy is that an assessment of laboratory capacity depends on the definitions and sources of information used. Estimates at the high end, for example, include the many hospitals that maintain small areas that meet BSL-3 standards that can be used for testing clinical samples that might contain infectious agents. These are not "research laboratories." Some hospitals, pharmaceutical companies, biotechnology firms, private reference laboratories and State public health laboratories also have facilities that meet BSL-3 standards, but these are not generally available for NIH-sponsored research. Finally, many BSL-3 facilities constructed before the mid-1990s cannot support research on select agents and on associated animal models. In 2002, NIAID determined that very little usable BSL-3 or BSL-4 research space was actually available for its academic scientists in the extramural research program.

The Blue Ribbon Panel of 2002 noted the shortage of BSL-3 and BSL-4 laboratory space as a significant rate-limiting obstacle in accomplishing the objectives of the NIAID Biodefense Research Agendas. In response, NIAID estimated the new BSL-3 and BSL-4 facilities that would be required to accomplish the Research Agenda. Congress also recognized the critical need for new BSL-3/4 laboratories and responded quickly to supply the necessary resources to fulfill this need. In 2002, the Department of Defense and Emergency Supplemental Appropriations for Recovery from and Response to Terrorist Attacks on the Unites States Act, Public Law (P.L.) 107-117,

appropriated $70 million for the construction and renovation of NIH intramural biocontainment facilities. The Consolidated Appropriations Act of 2003, P.L. 108-7, provided $372.6 million to NIAID for construction of extramural biocontainment facilities and $291 million for construction of additional intramural biocontainment facilities. Further, the Project BioShield Act of 2004 (P.L. 108-276), amended the Public Health Service Act to provide ongoing authority to NIAID to award grants and contracts for construction of research facilities. An additional $150 million was appropriated for NIAID in the 2005 consolidated appropriations act (P.L. 108-447) for extramural facilities construction grants.

The NIH is now implementing a construction program that will complete 14 new BSL-3 facilities and 4 new BSL-4 facilities within the next several years. During this process, the NIH or its funded institutions have participated in literally hundreds of public forums on the nature and safety of the new facilities, and have submitted reports to Congress annually, along with periodic updates on our strategic plans. In addition, NIH leadership has discussed the infrastructure expansion with Congress on many occasions. And because NIH does not fund or conduct classified research, the title and substance of every research project funded by the NIH is publicly available.

Another important aspect of the biodefense research infrastructure is a network of ten NIH-funded Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research (RCEs). Created in 2003, these multidisciplinary

academic research programs are located at institutions across the country and provide the scientific expertise for a wide-ranging biodefense research program, directed against deliberate and naturally-occurring threats, that will be pursued in the new facilities.

NIH Role in Ensuring Safety

The NIH is committed to helping ensure that all biodefense research facilities provide maximum protection for public health. The NIH is committed to the highest quality in the design and construction of these facilities, the rigorous training of the personnel that operate them, and the safe conduct of the research undertaken within them.

To ensure that the new laboratories are designed and constructed to the highest standards, the NIAID works closely with each grantee institution. Highly experienced NIAID staff architects and engineers, with extensive experience in design of biocontainment facilities, are assisted by a Construction Quality Management group of contracted consultants with additional expertise. Together, these teams make certain that the finished projects will meet the regulations of HHS's Centers for Disease Control and Prevention (CDC) and the Department of Agriculture's Animal and Plant Health Inspection Service (USDA/APHIS) for facilities that conduct research on select agents.

The NIH also supports a vigorous biosafety and biocontainment training effort that has expanded substantially over the past five years. The National Biosafety and Biocontainment Training Program (NBBTP) is a partnership between the NIAID and the NIH Division of Occupational Health and Safety (DOHS), managed by a not-for-profit education and research foundation. The mission of this program is to prepare biosafety and biocontainment professionals of the highest caliber. The program offers two-year post-baccalaureate and post-doctoral fellowships at NIH's campus in Bethesda, Maryland, with both academic and hands-on training. The NBBTP has also provided training for containment laboratory operation and maintenance personnel across the country. In addition to this program, NIAID funds 28 Institutional Training Grants in Biodefense, and the RCEs conduct extensive training in biosafety and biocontainment. At the RCE at Emory University in Atlanta, for example, trainees from across the country regularly participate in BSL-3 and BSL-4 training in mock laboratories, constructed specifically for training purposes.

When these new facilities are ready for operation, NIH is committed to ensuring that the research conducted within them is performed safely. The most widely used guidance on the safe conduct of this research is the Biosafety in Microbiological and Biomedical Laboratories Manual (BMBL), which was first produced jointly in 1984 by the NIH and CDC and which is now in its fifth edition and available online.

Monitoring adherence to good laboratory practices is a complex process because multiple agencies are involved. Much of the research in BSL-3 and BSL-4 facilities involves pathogens that have been designated as select agents. CDC and APHIS have the responsibility for regulating the possession, use, and transfer of select agents. For research that involves recombinant DNA, the select agent regulations incorporate the NIH Guidelines for Research Involving Recombinant DNA Molecules (Recombinant DNA Guidelines) as a consideration in the entity's development of its biosafety plan. The NIH Office of Biotechnology Activities (OBA), with advice and guidance from the NIH Recombinant DNA Advisory Committee (RAC), is responsible for implementation of the Recombinant DNA Guidelines, which outlines biosafety and containment standards for research involving recombinant DNA. Also, the select agent regulations require that restricted experiments, such as the deliberate transfer of a drug-resistant trait to a select agent, must be approved by CDC or APHIS prior to initiation. However, some research conducted in BSL-3 facilities involves neither select agents nor recombinant DNA.

Local institutional bodies play a very important role in oversight of many aspects of biomedical research. For example, oversight to protect human subjects in clinical studies is provided by local Institutional Review Boards (IRBs), and in the case of animal research, oversight to ensure humane treatment is provided by the Institutional Animal Care and Use Committees (IACUCs). The NIH Guidelines mandate that Institutional Biosafety Committees (IBCs) oversee

recombinant DNA research, but many institutions have gradually broadened IBC responsibilities to include oversight of research involving all pathogens studied at BSL-3 and BSL-4 levels. At this time there is no federal body that sets national standards or policies for this function of local IBCs, and adherence to BMBL guidelines for BSL-3 and BSL-4 research is voluntary; however, the select agents regulations require regulated entities to comply with the BMBL guidelines or equivalent standards.

The NIH is deeply concerned about recent reports of accidents occurring in BSL-3 facilities. When these events involve recombinant DNA, they are reported to the OBA, and a root cause analysis is done so that NIH can assess the adequacy of the institution's response and work with the institution to put mechanisms in place to mitigate the chance of a reoccurrence. To enhance all of the functions of the IBCs, the NIH has worked intensively with the IBC community. These efforts have included an extensive program of outreach and education, involving frequent day-long training sessions, exhibits at major scientific conferences, policy guidances, educational resources for institutions to use in local training, and other means. Furthermore, each of the institutions receiving one of the new facilities construction grants from NIAID has an IBC appropriately registered with NIH and each has willingly accepted responsibility for adhering to BMBL standards.

The NIH is examining ways to strengthen local and federal oversight of facilities that conduct NIH-funded research. The issues associated with oversight of

research in BSL-3 and BSL-4 facilities transcend the NIH, or even the HHS. Biodefense research involving BSL-3 and BSL-4 facilities is conducted by many government agencies, including the Department of Defense (DoD), the Department of Homeland Security (DHS), and the USDA, as well as by universities and biotechnology companies. As I noted earlier, BSL-3 facilities exist in hospitals for routine handling of clinical samples. It is important to devise a framework that improves oversight, training, and reporting to enhance safety without causing unintended negative consequences for either patient care or the biodefense research program. For that reason, HHS, USDA, DHS, and DoD have already agreed to establish a Trans-Federal Task Force to undertake, in consultation with other relevant agencies, an intensive analysis of the current biosafety framework and to develop a set of recommendations for improvement. Given the critical importance of biosafety to protecting public health and the concerns that the high containment facilities engender among local communities, active participation in this process from the public at large will be essential.

Conclusion

Support for infrastructure for biodefense research is essential if we are to fulfill our biodefense research agenda and protect the Nation from disease threats, be they deliberate or acts of nature. We have already made substantial progress with the facilities now available. For example, NIH-funded scientists have developed a safer second-generation smallpox vaccine called ACAM2000 and a very promising new smallpox drug named ST-246. Investigators have developed

and tested a new anthrax vaccine called rPA and have achieved promising results with antibodies capable of neutralizing anthrax toxins. They have developed first- and second-generation vaccines against Ebola virus, and investigated a promising Ebola therapy based on RNA interference. These and many other advances required the use of containment facilities of the type that are now under construction. Progress should occur more rapidly as the new facilities become available.

NIH-funded biodefense researchers are acutely aware of the threat posed by the pathogens they study. These experts understand the need to handle them with utmost care, the need for rigorous training and state-of-the-art equipment, and the need to scrupulously follow all required procedures. Their awareness also includes a deep understanding that the Nation's biosecurity depends on their work, which is the conduct of research that will lead to new tools essential to meet emerging and re-emerging threats to public health.

Thank you for this opportunity to discuss this very important issue with you. I will be happy to answer questions.