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NIAID/NIH Biodefense Research Efforts and Biocontainment Laboratories

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Introduction

I express my thanks to the American Biological Safety Association for putting together such an outstanding conference. I also congratulate CDC for sponsoring another fine conference in Atlanta—meetings that promote sharing of information across agencies and the coordination of activities in biodefense and emerging diseases. I also express my appreciation to the organizing committee for the invitation to speak to you today. The focus today is on research infrastructure across the nation.

Events over the last 3 years have highlighted the challenges posed by bioterrorism and emerging infections and the need for focused and well-organized efforts. Today, I will address a variety of topics, including a general review of the biodefense research agenda at the NIH and plans related to laboratory biocontainment facilities and infrastructure development. I will discuss the extramural and intramural aspects of the program pertaining to biocontainment facilities, a main topic of interest in this conference.

Addressing the National Needs for Laboratories

Over 2 years ago, NIAID, with the assistance of CDC and several other Federal agencies, began a collaborative effort examining public health infectious disease threats requiring research. The result was a listing of pathogens that has since come to be known as the CDC Category A, B, and C List of Critical Biological Agents. The need for new and effective medical countermeasures was evident, since many of the diseases of concern had not received high priority in research funding. NIAID conducted a review of its programs and developed a parallel list that would be the focus of the biodefense research agenda. Several Blue Ribbon panels of experts were convened and recommendations were received as to the specifics of a research agenda for the Nation. These results are summarized in reports available on the NIAID web site (www.niaid.nih.gov/biodefense). One of the recommendations of the Category A Blue Ribbon Panel was to expand the extramural and intramural research and clinical infrastructure, which included the construction and renovation of much-needed BSL-3 and BSL-4 laboratories. The Category B and C Blue Ribbon Panel also emphasized the need for access to BSL3/4 facilities.

The final NIAID biodefense research budget for FY2003 was $1.162 billion. The funds were directed at expansion of the research capacity to include facilities, vaccines, basic research, genomics, therapeutics, and diagnostics.

Bioterrorism and Emerging Infections

Dr. Anthony S. Fauci, the Director of NIAID, recognized the need to consider the issues of biodefense and emerging infections together. From the standpoint of national defense, classic biowarfare agents were pathogens being addressed by the Department of Defense in its military research program, but these agents were now evolving into civilian public health issues with their potential availabil-

ity to transnational subversive groups. It was recognized that many naturally occurring emerging infections also had bioterror potential, and it would be difficult to distinguish initially between the two scenarios in an outbreak situation. From an infrastructure perspective, biocontainment laboratories are necessary to address both situations.

When one reviews what has transpired with SARS and avian influenza over the past year and examines the questions that needed to be answered through research and surveillance, it becomes clear that research resources were brought to bear on the problem. The result was a much clearer understanding of the epidemiology, biology, options for intervention, and medical countermeasures. Recognizing the political need to differentiate a malicious event from a natural outbreak of disease, the public health aspects required quick intervention and answers that could be obtained only through an aggressive research effort. It is likely that such scenarios will occur again in the future, and the Nation is much better prepared with the heavy investment that has now been made in biodefense.

The Biodefense Research Pathway

The research pathway leading from basic research through product development is complex. It is recognized that unexpected results in the research process could impact final decisions and delivery of product. The involvement of industry and academia is a necessary part of the product development process leading through preclinical and early clinical studies and through advanced development. But it is also important to recognize the need for resources to support research. These resources include having access to and using the most suitable animal models simulating human infection when the Animal Rule must be applied; having the specialized training programs for researchers and technicians to learn and familiarize themselves with methodologies in aerobiology and toxicology; being able to have access to "special immunizations" as a part of a biosafety occupational health program; and being familiar with all aspects of operating a biocontainment facility, to include security and contingency considerations. The "special immunizations" include certain vaccines that may be in Investigational New Drug (IND) status by the FDA and are not fully licensed, as well as products under the control of the CDC.

It is understood that all biodefense research must be conducted in compliance with all Federal and State laws and regulations pertaining to Select Agents. The need for standardization of animal models, research methodologies that will allow for valid comparisons of results, and the specific strains of pathogens or reagents is also recognized. This can be successfully accomplished through a program emphasizing interagency and academic cooperation.

Regional Centers of Excellence for Biodefense and Emerging Infectious Disease Research (RCEs)

The RCEs support extramural interdisciplinary research on Category A, B, and C agents. The RCEs develop and conduct programs of investigator-directed research, train researchers and other individuals involved in biodefense research, and develop translational research capacity for testing and validation of vaccines and drugs. The RCEs also maintain and make available core facilities and other support to approved investigators from academia and industry (to include the pharmaceutical companies and biotech firms), and also provide facilities and scientific support in the event of a national biodefense emergency. In their proposals, the RCEs were encouraged to develop partnerships with other institutions in certain geographical regions that would enable cross-utilization of laboratory resources and the sharing of information and expertise.

In FY 2003, the following eight institutions received RCE grants: Duke University, Harvard Medical School, New York State Department of Health, University of Chicago, University of Maryland, University of Texas Medical Branch (Galveston), University of Washington, and Washington University (St. Louis). The RCE program gives 5 years of funding at a total cost of approximately $350 million. An RFP to fund additional RCEs has just recently been released and is available at http://grants1.nih.gov/grants/guide/rfa-files/RFA-AI-04-018.html.

In FY2003, NIAID also funded two Planning

Grants for Regional Centers of Excellence, or "P-RCEs," to support planning, research program initiation, and resource acquisition that could potentially lead to the establishment of a regional center. The P-RCE recipients awarded in FY 2003 were University of Iowa and University of Minnesota. It has not been decided if the P-RCE effort will be renewed.

More information about the RCE program is available on the NIAID web site at http://www.niaid.nih.gov/Biodefense/Research/rce.htm.

National Biocontainment (NBLs) and Regional Biocontainment Laboratories (RBLs)

"NBLs" are the National Biocontainment Laboratories, or those laboratories having BSL-3/4 capabilities. The "RBLs" are the Regional Biocontainment Laboratories with capability up to the BSL-3 level. In FY 2003, NIAID initiated a construction program providing funding for the design and construction of state-of-the-art BSL-2-4 facilities with additional administrative support space. It was recognized at the start that special engineering and design standards would be needed to ensure that specialized research with hazardous agents could be conducted safely. These facilities would be in accordance with the established guidelines in the publication "CDC Biosafety in Microbiological and Biomedical Guidelines." The BSL-2-4 facilities would also have an insectary for vector-borne research. It was and continues to be the intent of these biocontainment facilities to complement and support the research activities of the RCEs and be available in the event of a national emergency.

The decision to limit construction of NBLs at this time to a maximum of two facilities was deliberate. It was recognized that it would take 3-5 years for completion of construction, but the costs associated with maintenance of such facilities were a consideration. The NIAID intramural efforts with biocontainment and the plans of other agencies, including the Department of Defense, the Department of Homeland Security, and the Department of Justice, were also considerations in the assessment of the number of biocontainment facilities needed at this time.

In FY 2003, NIAID funded two NBLs at Boston University and the University of Texas Medical Branch at Galveston (UTMB). NIAID funded nine RBLs at the following locations: Colorado State University, Duke University, Tulane University, University of Alabama at Birmingham, University of Chicago, University of Medicine and Denistry of New Jersey, University of Missouri, University of Pittsburgh, and University of Tennessee.

It is recognized that the greatest need for biocontainment laboratories to address both bioterrorism and emerging infections will be at the BSL-3 level.

NIAID's Intramural Facilities

NIAID's intramural effort involves offices and laboratories at several locations, including the main Bethesda NIH campus. One effort centers on Building 33 on the main NIH campus that will provide BSL-3 laboratory space to researchers. The total space will be 65,000 square feet and its planned occupancy is November 2005. The NIAID Vaccine Research Center (VRC), a vital part of the ongoing NIAID biodefense effort, is a five-story facility that opened in the fall of 2000 and supports HIV and biodefense vaccine work. Linked with the VRC is a Pilot Vaccine Production Laboratory that will be built in Frederick, Maryland with a scheduled completion date at the end of FY 2005.

At the Rocky Mountain Laboratories in Hamilton, Minnesota, plans are under development for a 15,000 square feet BSL-3/4 facility to support ongoing research with tularemia, plague, Q fever, and rickettsial pathogens. Plans are to have this facility completed and operational by the fall of 2007.

At Fort Detrick in Frederick, Maryland, NIAID is planning construction of a 120,000 square feet biocontainment BSL3/4 facility that would support clinical research with bioterrorist agents. Working closely with the Department of Defense and the Department of Homeland Security, NIAID is building this facility in close proximity to the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) to promote collaboration. The focus of the NIAID laboratory will be on the clinical aspects of disease, a mission that differs from the other

partners in establishing a biodefense research campus at Fort Detrick.

Finally, pertaining to overall security, a perimeter fence encircling the entire Bethesda campus is almost completed, and controlled access to the campus is a reality. A new parking garage that can be better secured is being constructed and will be ready by mid-summer. Building security has been enhanced in all buildings owned or operated by NIH.

Summary

In summary, NIAID has been fully engaged in biodefense research for several years. The design and construction of biocontainment facilities are a part of the commitment to improving our research infrastructure. These facilities support research in both biodefense and emerging infections and are a part of the national capability in responding to new threats and situations.

Once again, I thank CDC for sponsoring such an outstanding and critically important conference. I also acknowledge the presence of my fellow NIAID representatives at this meeting, including individuals from the Office of Biodefense Research (OBRA) at NIAID, who will be willing to discuss in more detail any of the ongoing NIAID initiatives.