

Biomedical Research — An Integral Component of National Security

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The attacks on the World Trade Center and the Pentagon on September 11, 2001, and the deliberate release of anthrax spores that occurred soon thereafter starkly revealed our vulnerability to the threat and reality of multiple categories of terrorism, including biologic, chemical, nuclear, and radiologic assaults. As a result of the events of late 2001, the focus on national security in the United States has intensified greatly, and extensive efforts to prepare for and prevent future attacks have been undertaken, particularly by the newly established Department of Homeland Security. In the arena of biologic terrorism against the civilian population, the Department of Health and Human Services has taken a lead role; efforts have focused on surveillance and activities to promote public health preparedness, led by the Centers for Disease Control and Prevention (CDC), and biomedical research, led by the National Institutes of Health (NIH), particularly the National Institute of Allergy and Infectious Diseases (NIAID).

The NIAID supports a broad-based program of basic and applied research to prevent, diagnose, and treat infectious and immune-mediated diseases. Integral to this mission is the responsibility to conduct biomedical research aimed at addressing the constant threat of naturally occurring, newly emerging, and reemerging or resurging infectious diseases. The specific mandate of the NIAID in the post-September 11 national security effort is to support research that will ultimately lead to the development of medical countermeasures in the form of therapies, vaccines, and diagnostic tools to protect the country from deliberate attacks with biologic agents.^{1,2} This role is consistent with the NIAID's long-established mandate with regard to infectious diseases, including emerging diseases such as AIDS and the severe acute respiratory syndrome (SARS) and resurging infectious diseases such as malaria, West Nile virus, and tuberculosis.³ Although the factors that precipitate the appearance of emerging, resurging, and deliberately propagated infectious diseases are quite distinct, the devel-

opment of countermeasures for all three may be addressed with very similar scientific approaches.

Many members of the research communities in microbiology, infectious diseases, and immunology responded to the events of 2001 by expressing their willingness to contribute their skills and insights to the evolving biodefense efforts. The NIAID harnessed this spirit through a series of blue-ribbon panel meetings that were designed to enlist the best and the brightest in the development of a research agenda and strategic plan for biodefense research. The outcome of these discussions and deliberations is found in the *NIAID Strategic Plan for Biodefense Research* and the more detailed research agendas for agents in CDC categories A, B, and C, which are those pathogens most likely to be used and to cause harm in a bioterrorist attack.^{4,5} These documents provide the framework for addressing the research and training needs posed by this challenge to national security.

These plans are living documents that are regularly updated as progress is made. In August 2003, a progress report for category A agents was published and made available online.⁴ As detailed in the report, 50 new and expanded initiatives have been implemented, and substantial scientific accomplishments have been achieved in a relatively short period. Specifically, important progress has been made in the development of new or improved vaccines against anthrax, smallpox, and Ebola virus; the capacity for testing drugs and vaccines in animals, particularly nonhuman primates, has been markedly expanded; promising new drugs for the treatment of smallpox are being pursued; the genomes of all category A agents have been sequenced; and our understanding of the basic properties of the agents that pose threats has improved markedly. Despite these accomplishments, we are only in the early stages of a long-term process.

Our biodefense research agenda consists of a variety of programs designed to balance basic, translational, and applied research, with the objective of

developing new and improved vaccines, drugs, and diagnostic tests (see Table). These programs involve collaboration with the academic community, as well as with the biotechnology sector, large pharmaceutical companies, and government partners.

Among a variety of new and expanded programs,⁴ the Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research (RCEs) and the National and Regional Biocontainment Laboratories deserve particular mention. The RCE program has established regional consortia of investigators who operate within a synergistic and coordinated framework. The goals of the program are to develop and conduct programs of investigator-directed research, particularly in the area of agents in CDC categories A, B, and C⁵; train people to conduct research related to biodefense and emerging infectious diseases; develop and maintain comprehensive core facilities that support the research and training activities of the RCE; make these core facilities available to qualified investigators from academia, biotechnology companies, the pharmaceutical industry, and other appropriate entities in the geographic region of the center; develop translational research capacity for the testing and validation of concepts for vaccines, therapies, and diagnostic tools for biodefense and emerging infectious diseases; and provide facilities and scientific support to first-line responders in the event of a national biodefense emergency. The NIAID funded eight RCEs in the fall of 2003.⁴

The program for constructing biocontainment laboratories is essential to the success of the biodefense research agenda and includes funding for the design, construction, and certification of biosafety level 4 and biosafety level 3 facilities. The national laboratories will include capacity for research at biosafety levels 4, 3, and 2; facilities for the conduct of research in nonhuman primates and other animals; and facilities and resources for small-scale phase 1 clinical trials in humans. The regional laboratories will provide capacity for research at biosafety levels 3 and 2, as well as facilities for research in animals. The laboratories will provide additional infrastructure for the RCEs and other NIAID-funded biodefense research. They will also be available to assist public health efforts in the event of a bioterrorism emergency. These will be state-of-the-art facilities, designed and built to the highest standards of safety and security, where 21st century research can be conducted.⁴ Together with the RCEs, these laboratories will provide a network for link-

Table. NIH Biodefense Research Agenda.

Area	Estimated Fiscal Year 2005 Funding (President's Budget)
	Millions of U.S. \$
Basic research, including genomics	550.2
Diagnostic tools	66.8
Therapies	274.5
Vaccines	652.7
Construction of extramural biosafety laboratories	150.0
Total	1,694.2

ing basic science and discovery to the product-development pathway, creating the capacity to address important scientific problems in a safe and expeditious manner. The NIAID funded two national laboratories and nine regional laboratories in the fall of 2003.⁴

Successful research requires not only access to appropriate technology and facilities, but also a robust corps of talented and committed scientists. Training and other efforts to increase the number of investigators engaged in this effort are essential, and to this end, several training programs in biodefense research have been initiated or expanded.⁴

Although we all hope that events such as the anthrax attacks of 2001 will never occur again and that our efforts to prepare and protect ourselves will be successful, the challenge of bioterrorism will be with us indefinitely. It is difficult to assess the probability of future deliberate releases of microbes or their products, but the potential consequences of such attacks are enormous. Furthermore, we will certainly face naturally occurring emerging and resurging infectious diseases, and the potential for devastation associated with such diseases as pandemic influenza or SARS may surpass that associated with bioterrorism.³ The research agenda of the NIAID and the NIH is designed to prepare for and provide protection against both types of threats. Given the nature of these threats, it is imperative that we move ahead with the biodefense research agenda as rapidly as possible. To do otherwise would be extremely risky and, in many respects, unconscionable.

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Buying Biosafety — Is the Price Right?

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On September 30, 2003, Boston University and the University of Texas at Galveston were each awarded \$120 million by the National Institute of Allergy and Infectious Diseases to build a biosafety level 4 laboratory. Nine regional biocontainment laboratories were funded along with these two national biocontainment laboratories. In announcing the awards, Secretary of Health and Human Services Tommy Thompson described them as “a major step towards being able to provide Americans with effective therapies, vaccines and diagnostics for diseases caused by agents of bioterror as well as for naturally occurring emerging infections.”¹

The funding was provided by the Department of Homeland Security. Of the department’s \$37.7 billion budget for 2003, \$5.9 billion, or 16 percent, was devoted to defending the United States against bioterrorism. Of this amount, \$2.4 billion was allocated to support scientific research and development to “provide America with the medical tools necessary to effectively respond to a biological attack.”²

The University of Texas and Boston University, which won a competitive bidding process to receive the awards, have promised \$50 million in matching funds. In Boston, estimates are that the laboratory will generate up to \$1.7 billion in research grants during the next 20 years. The university anticipates the creation of 1960 new jobs, of which about 600 will be permanent research positions and the rest will be in construction work.

Economic benefits notwithstanding, there has been considerable popular opposition to such projects. Citing U.S. environmental law, community groups in California and New Mexico are suing to

stop the expansion of biodefense facilities. The University of California at Davis competed for funding but was unsuccessful, at least in part because of community opposition: activists sent more than 1200 pages to the National Institutes of Health documenting their opposition, and the Davis City Council voted unanimously against the project. The University of Texas, which has been actively engaged in discussions with the community since 1997, has nevertheless faced public concern about building the facility in an area that is prone to hurricanes; the university has also been fighting freedom-of-information requests for details of its biodefense research.

In Boston, in spite of the support of the mayor, the governor of Massachusetts, and most state and local politicians, the project has met with vocal opposition from some community groups. The opponents argue that the facility would pose a health threat because of the possible release of deadly pathogens and the risks associated with transporting dangerous materials through busy city streets. They argue, moreover, that the presence of the facility would make Boston a target for terrorists. They also maintain that those who live in the community would not be qualified for the highly skilled jobs that would become available. Others oppose the facility on the grounds that much of the proposed research would be prohibited under Boston’s 1994 public health regulations. Still others fear that the research in biocontainment laboratories undermines the international nonproliferation regime and particularly the 1975 Biological and Toxin Weapons Convention (BWC), which prohibits research on offensive biologic weapons.