



Testimony
Before the Committee on Government Reform
Subcommittee on National Security, Emerging
Threats, and International Relations
United States House of Representatives

**The Role of NIH Biomedical
Research in Responding to the
Threats of Chemical, Biological,
Radiological and Nuclear (CBRN)
Terrorism**

Statement of

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**For Release on Delivery
Expected at 2:00PM
Tuesday, June 14, 2005**



Introduction

Mr. Chairman and Members of the Subcommittee, thank you for the opportunity to speak with you today concerning the role of the National Institutes of Health (NIH) in conducting research to further the development of medical countermeasures to protect civilians against attacks using biological, chemical and radiological or nuclear weapons.

I will briefly outline the status of NIH's research and development program in each of these three areas, including a sketch of the strategic planning process that guides the program and a few examples of recent accomplishments. I will then summarize how NIH research in these three areas is coordinated with research conducted by other Federal agencies.

The events of September and October of 2001 clearly exposed the vulnerability of the United States to acts of terrorism that employ unconventional weapons or tactics. In particular, the anthrax attacks made it clear that the potential for terrorist use of deadly pathogens or biological toxins such as those that cause anthrax, smallpox or botulism represents a serious threat. The Administration and Congress immediately responded to this threat by a number of initiatives including significantly increasing funding for research to develop medical countermeasures against a wide variety of biological agents.

Because the National Institute of Allergy and Infectious Diseases (NIAID), a component of the NIH, has for decades played a central role in the conduct of research on emerging and re-emerging infectious diseases, the Institute was chosen to take the lead in Federal research to develop new and improved vaccines, drugs, and diagnostic tools to counter deliberate attacks with biological agents.

We also face other unconventional threats in addition to those from biological agents. These include threats from chemical weapons or toxic industrial compounds; ionizing radiation from the deliberate release of radioactive materials; or, in a worst case scenario, a nuclear explosion of a stolen or improvised nuclear device. NIH has recently been tasked with developing medical countermeasures appropriate for the civilian population for chemical, radiological and nuclear threats, in addition to biological threats. Because NIAID has extensive experience and expertise in developing medical countermeasures against biological agents, it was assigned the role of guiding and coordinating these NIH efforts.

The development of medical countermeasures against non-infectious disease threats presents a different set of scientific challenges that require additional technical expertise and institutional experience. To maintain these distinctions, in my testimony today I will use the terms “biological countermeasures research,” “chemical countermeasures research,” and “radiological and nuclear

countermeasures research,” to refer to research for medical countermeasures to infectious agents or toxins, chemical agents, and ionizing radiation, respectively.

NIH Biological Countermeasures Research

The NIH research agenda for defense against threats from infectious agents or biological toxins was developed through a comprehensive strategic planning process initiated in late 2001. In February 2002, NIAID convened a meeting of the *Blue Ribbon Panel on Bioterrorism and Its Implications for Biomedical Research*, whose members were distinguished experts from academic centers, private industry, civilian government agencies, and the military. Three key documents were developed based on this Panel's advice and on extensive discussions with other Federal agencies: the *NIAID Strategic Plan for Biodefense Research*, the *NIAID Research Agenda for CDC Category A Agents* (for those agents that pose the gravest threat), and the *NIAID Research Agenda for CDC Category B and C Priority Pathogens* (agents whose biological properties make them more difficult to deploy or less likely to cause widespread harm). These documents are available on the NIAID biodefense research program website at http://www2.niaid.nih.gov/biodefense/research/strat_plan.htm.

The *Strategic Plan* provides a blueprint for the conduct of basic research on microbes and host immune defenses, as well as targeted, milestone-driven development of drugs, vaccines, diagnostics and other interventions and resources that would be needed in the event of a bioterror attack. The two

biodefense research agendas describe short-term, intermediate, and long-term goals for research on the wide variety of agents that could be used to conduct such an attack. Two recent progress reports describe the significant progress made toward the goals set forth in these research agendas.

The NIH biodefense research agenda encompasses expansion of biodefense infrastructure, basic research, and medical countermeasures development.

Overall, the effort to develop new countermeasures rests on a foundation of basic research needed to better understand how pathogens interact with human hosts. For example, one major NIAID basic biodefense research initiative is focused on the human innate immune system, which is comprised of broadly active "first responder" cells and other non-specific mechanisms that are the first line of defense against infection. The development of methods to boost innate immune responses could lead to the development of a relatively small set of fast-acting countermeasures that would be effective against a wide variety of pathogens or toxins that could be used in an attack.

NIH biodefense research is ultimately directed toward the creation of new and effective medical countermeasures, including vaccines, therapeutics, and diagnostics against potential bioterror agents. Substantial progress toward these goals has already been achieved. In the area of therapeutics, for example, NIAID-supported scientists recently discovered that smallpox virus may be halted by aiming a drug not at the virus, but at the cellular machinery the virus needs to

spread from cell to cell; this approach might completely circumvent the problem of antiviral drug resistance, and might also be applicable to other viruses.

Researchers supported by NIAID also are investigating the use of antibodies that can bind to and block the action of toxins produced by the anthrax bacterium, as well as botulinum toxin.

New and improved strategies for the development of vaccines against potential bioterror agents are being vigorously pursued, with the objective of adding them to the Strategic National Stockpile (SNS) as quickly as possible. For example, NIAID played a major role in the rapid development of the next-generation anthrax vaccine known as recombinant protective antigen, or rPA. Clinical trials to evaluate rPA are currently underway. To date, the immune responses elicited in humans are similar to those elicited in animal studies, which have demonstrated that the rPA vaccine protected animals against aerosol challenge with anthrax spores. Last November, the Department of Health and Human Services (DHHS) awarded a contract for the acquisition of 75 million doses of rPA vaccine to be held in the Strategic National Stockpile (SNS). NIAID's rPA product development initiatives were instrumental in making the SNS initiative possible.

Our preparedness to respond to an attack using smallpox virus has improved enormously since 2001, when only 90,000 doses of smallpox vaccine were readily available for domestic use. Today, because of clinical research on the

dose required to produce immunity and an aggressive acquisition program, more than 300 million doses are held in the SNS. Moreover, NIAID-supported researchers also are testing next-generation smallpox vaccines that may prove to be effective for smallpox and safer than the current smallpox vaccines, thus potentially allowing them to be used by populations that have contraindications for currently available smallpox vaccines, including people with weakened immune systems. One of these, modified vaccinia Ankara (MVA), is based on a strain of the vaccinia virus that causes fewer side effects than the traditional Dryvax vaccinia virus strain because it does not replicate effectively in human cells. Human trials of MVA vaccines are under way at NIH and elsewhere. Encouragingly, vaccine manufacturers Bavarian Nordic and Acambis announced this year that Phase I and Phase II trials demonstrated MVA vaccine to be safe and immunogenic in human volunteers, confirming earlier studies by NIAID intramural scientists and their colleagues showing that MVA protects monkeys and mice from smallpox-like viruses.

NIH also has expanded national biodefense research capabilities by investing in several research infrastructure expansion programs. NIAID has established a nationwide network of Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research (RCE). These Centers are now conducting fundamental research on infectious diseases that could be used in bioterrorism, developing diagnostics, therapeutics and vaccines needed for biodefense, and providing training for future biodefense researchers. Two new

RCE awards were announced on June 1, 2005, bringing to ten the total number of RCEs nationwide. In addition, NIAID supports the construction of two National Biocontainment Laboratories, built to Biosafety Level 4 standards and therefore capable of safely containing any pathogen, and nine Regional Biocontainment Laboratories (RBLs) with Biosafety Level 3 facilities. NIAID will also support the construction of another four to five RBLs this year. These high-level research laboratories, some of which are already under construction, will provide the facilities needed to carry out the Nation's expanded biodefense research program with the highest degree of safety and security.

NIH-Supported Radiological/Nuclear Countermeasures Research

Threat scenarios that could result in exposure of civilians to ionizing radiation include contamination of food or water with radioactive material, placement of radiation sources in public locations, detonation of a radiological dispersal device (often referred to as an RDD or a “dirty bomb”) that scatters radioactive material over a populated area, and attacks on nuclear power plants or high-level nuclear waste storage facilities. The most dangerous scenario would be the detonation of a nuclear explosive device which, in addition to causing enormous destruction from blast and heat, would produce an intense burst of radiation and large quantities of radioactive “fallout.”

In 2004, DHHS tasked NIAID with developing a research program to accelerate the development and deployment of new medical countermeasures against

ionizing radiation for the civilian population. Through a organized series of structured meetings and other contacts, NIAID worked to build upon prior experience and ongoing research efforts, including those of NCI, as it gathered input from across the Federal government—including the Centers for Disease Control and Prevention (CDC), the Armed Forces Radiobiology Research Institute (AFRRI), and the Department of Energy (DoE)-affiliated National Laboratories—as well as from experts in industry and academia. These activities contributed to the development of an overarching strategic plan and draft research agenda. NIAID next convened a Blue Ribbon Panel in October 2004 to review the draft strategic plan and refine the research agenda for this program. NIAID then assembled the final planning document, entitled *The NIH Strategic Plan and Research Agenda for Medical Countermeasures against Radiological and Nuclear Threats*. This document is in the final stages of production and will be made available shortly.

This *Strategic Research Plan and Agenda* is organized into four sections: (1) basic and translational research on the mechanisms of radiation injury, repair, and restoration that can lead to the identification and characterization of new therapeutics; (2) bioassays and tools for biodosimetry, which will aid in diagnosis; (3) immediate product development of promising therapies; and (4) infrastructure to support the necessary research. The document is intended to unify and strengthen the research community focused on these areas, promote increased collaboration, and facilitate transition from research to product development. NIH

will work closely with DHHS to prioritize the research and development activities in this ambitious agenda within the resources available and as one component of the larger National medical countermeasures research agenda.

Even before the *Plan* and *Agenda* were complete, NIH recognized the need to collaborate and work in partnership with other Federal agencies involved with radiological research. For example, through an Interagency Agreement signed in 2003, NIAID assisted AFRRRI in the restoration of a Cobalt-60 source of gamma irradiation critical for ongoing animal studies to evaluate the effectiveness of anti-radiation drugs. NIAID continues to work closely with AFRRRI on collaborative projects involving biodosimetry and promising therapeutics.

NIAID also works closely with our sister Institute at NIH, the National Cancer Institute (NCI), on medical issues involving radiation. Since NCI is involved with therapeutic applications of radiation in the treatment of cancer and has similar concerns about the hazardous effects of ionizing radiation on normal cells and tissues, a partnership effort has evolved that brings together the scientific strengths of NIAID in immunology with those of NCI in therapeutic radiation oncology.

Funding for NIH radiation countermeasures research in fiscal year (FY) 2005 is \$47 million; these funds are provided through an appropriation to the Public Health and Social Services Emergency Fund in the Office of the Secretary and

are not part of the annual NIH budget. A proposal for specific project commitments for FY 2005 funds has recently been discussed within the Department. The *Strategic Plan* will be reviewed periodically and modified as necessary, subject to progress toward specific milestones.

NIH-Supported Chemical Countermeasures Research

A wide variety of chemicals, with a broad range of toxicities and harmful effects, could be employed in an attack on the civilian population. Threat scenarios include the release of illegally obtained or manufactured chemical warfare agents, the release of purchased or stolen industrial chemicals, and attacks on chemical manufacturing plants, storage sites, or transport vehicles. Some of the many challenges that require medical countermeasures include:

- neurotoxic chemicals, such as organophosphates, that have a direct and deadly effect on the central nervous system;
- vesicating agents, such as mustard gas, that cause skin blisters, blindness, and airway injury;
- metabolic poisons, such as cyanide, that can be inhaled or ingested and lead to death within a matter of minutes or days; and
- lung-damaging liquids and gases, such as chlorine and phosgene, two commonly used industrial chemicals.

The FY 2006 President's Budget requests \$50 million for this research. DHHS recently tasked NIAID with drafting a strategic plan and research agenda to guide

development of medical countermeasures against chemical threats, in an effort similar in scope and purpose to that for radiological/nuclear countermeasures. Building on an NIAID expert panel convened in 2003 to review the current state of medical chemical defense research, NIAID recently held two focused expert workshops on countermeasure development, one to examine countermeasures for cyanide poisoning and another to assess anticonvulsant drugs that could be used in nerve agent poisoning to prevent and treat seizures. A third workshop on therapies for pulmonary edema is scheduled for August of this year. Ideas developed at these meetings will be incorporated into a Strategic Plan and Research Agenda, which is expected to be complete by the end of this calendar year.

Throughout this process, NIAID has collaborated closely with other Federal agencies. The United States Army Medical Research Institute for Chemical Defense (USAMRICD), headquartered at the Aberdeen Proving Ground in Maryland, is the primary Department of Defense (DoD) research organization for chemical countermeasures and one of our most important institutional partners in this effort. USAMRICD is part of the U.S. Army Medical Research and Materiel Command headquartered at Fort Detrick, Maryland. It is our intent to continue to work closely with the Army on medical products that could benefit both the civilian and military communities. NIAID also is partnering with several NIH laboratories and exploring collaboration with other NIH Institutes, such as the National Institute of Neurological Disorders and Stroke (NINDS).

Coordination of NIH-Supported Medical Countermeasures Research

Although NIH is a leading agency in government-sponsored research to develop medical countermeasures against biological, chemical, or radiological terrorist threats, it is by no means the only agency involved; the CDC, the Food and Drug Administration (FDA), the DoD, the Department of Homeland Security (DHS), the Department of Agriculture (USDA), the DoE, and other governmental organizations also play important roles. Coordination among the various agencies involved is, therefore, extremely important. In broad terms, NIH-supported medical countermeasures research activities in all three areas are coordinated using similar mechanisms, at three distinct levels: within NIH, within DHHS, and across the government as a whole.

Within NIH. NIAID is responsible for the majority of NIH-sponsored medical countermeasures research for infectious agents and toxins, although other NIH Institutes and Centers make significant contributions. Because the immune system is highly susceptible to damage from radiation, NIAID also is directly involved in both the planning and conduct of radiological/nuclear countermeasures research in collaboration with NCI. NIAID's direct role in the development of chemical countermeasures is more limited, and consists mainly of planning and coordination of activities. This may change as the civilian chemical and toxin threats are further defined. The focal point for trans-NIH coordination and planning of all medical countermeasure research activities in all

these areas is the NIH Biodefense Research Coordinating Committee. I am Chairman of this committee, which meets at least quarterly. It is administered by the NIAID Office of Biodefense Research, which also serves as liaison office for NIH contacts with other Federal agencies such as DoD and DHS regarding biodefense research and response.

Within DHHS. At the level of DHHS, coordination of medical countermeasures research between the CDC, NIH, FDA, and other agencies within DHHS is the responsibility of the DHHS Office of the Assistant Secretary for Public Health Emergency Preparedness (ASPHEP). The ASPHEP Office of Research and Development Coordination holds periodic meetings with all governmental stakeholders in the development of medical countermeasures.

Across Federal Agencies. 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. The focal point for USG interagency efforts to prioritize and coordinate medical countermeasures acquisition programs under Project BioShield is the Weapons of Mass Destruction Medical Countermeasures (WMDMC) Subcommittee (“WMDMC Subcommittee”). Assistant Secretary Simonson of HHS, along with representatives from the Department of Homeland Security (DHS) and the Department of Defense (DoD), co-chairs the WMDMC Subcommittee and stakeholders from throughout the USG are represented on it. Since it is the

primary federal agency responsible for the development and acquisition of priority medical countermeasures, HHS has a major leadership role in the WMDMC Subcommittee.

Although these three levels describe the basic structure through which the Nation's biodefense research programs are formally 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. For example, members of my staff meet regularly with the research community at Fort Detrick and the United States Army Medical Research and Materiel Command, and with the staff of AFRRRI. Through such meetings, synergy in research and mutual support leading to the development of new drugs, vaccines, and diagnostic tests for the nation are achieved. My staff also holds meetings periodically with the Defense Threat Reduction Agency and the Defense Advanced Research Projects Agency, two important entities within the research infrastructure in the DoD.

In order to monitor and understand new threats that may arise, we work closely with DHS and intelligence agencies, which provide threat assessments concerning issues germane to our research. Because new infectious disease challenges emerge naturally on a regular basis, NIH has considerable

experience in rapidly mobilizing research resources to confront new infectious disease threats. This experience serves us well when called upon to adjust our research priorities in response to new information.

In closing, although we are concerned and take very seriously the threats of biological, chemical, and nuclear/radiological terrorism, we are confident that our current and planned efforts will lead to new and improved medical countermeasures against these threats. I am also pleased with the degree of coordination and cooperation between NIH and other Federal agencies involved in carrying out these various research programs. Having said that, we will continue to try to improve these interactions.

I appreciate this opportunity to testify before you today, and I would be pleased to answer any questions that you may have.