

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2009 Budget Request

Witness appearing before the
Senate Subcommittee on Labor-HHS-Education Appropriations

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National Institute of Allergy and Infectious Diseases

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Richard J. Turman, Deputy Assistant Secretary, Budget

Mr. Chairman and Members of the Committee:

I am pleased to present the President's budget request for the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH). The Fiscal Year (FY) 2009 budget of \$4,568,778,000 includes an increase of \$8,123,000 over the FY 2008 appropriated level of \$4,560,655,000.

The mission of NIAID is to conduct and support research to understand, treat, and prevent infectious and immune-mediated diseases. The biomedical research that NIAID supports to combat diseases of worldwide concern, such as HIV/AIDS, tuberculosis, malaria, neglected tropical diseases, emerging and re-emerging infectious diseases, has taken on added importance in today's globalized society. As we address these problems in a global context, we naturally contribute to our country's preparedness against the threat of bioterrorism as well as naturally occurring disease outbreaks. In addition, we are advancing efforts to address other domestic health problems, such as HIV/AIDS, influenza, and asthma, allergy, and other immune-mediated diseases. Using a multidisciplinary approach that engages industrial, academic, governmental, and non-governmental partners, NIAID remains committed both to basic infectious and immune-mediated disease research and the application of this knowledge to the development of strategies to detect, prevent, and treat these diseases. This approach is emphasized in the recently updated NIAID strategic plan, *NIAID: Planning for the 21st Century—2008 Update*.

Looking forward, it is clear that the research activities of NIAID will become more important than ever, as current and as-yet unrecognized health threats will require new diagnostic, preventive, and therapeutic interventions. These new tools promise to have a great impact on public health over the next two decades.

EMERGING INFECTIOUS DISEASES AND GLOBAL HEALTH

Threats posed by infectious microbes do not remain static, but change over time as new microbes emerge and familiar ones re-emerge with new properties, such as drug resistance, or in new settings. Since 2006, we have witnessed numerous examples of newly emerging and reemerging infectious diseases outbreaks, including extensively drug resistant tuberculosis (XDR-TB), methicillin-resistant *Staphylococcus aureus*

(MRSA), H5N1 avian influenza, Chikungunya fever, and dengue. We must anticipate that we will see more and more of these outbreaks in the coming decades. As economies and societies around the world have become increasingly interdependent, responding to emerging infectious diseases, as well as to long-established global health challenges such as neglected tropical diseases, has taken on a new urgency.

Tuberculosis is an example of a re-emerging threat. The World Health Organization (WHO) estimates that in 2006, new cases of active tuberculosis (TB) worldwide exceeded 9 million and 1.7 million people died from TB. Antiquated and insensitive techniques for accurately diagnosing TB, complex and lengthy drug regimens and an increase in the prevalence of multi-drug resistant (MDR-) and XDR-TB continue to present major challenges to effective TB control. In 2007, the Institute released the *NIAID Research Agenda: Multidrug-Resistant and Extensively Drug-Resistant Tuberculosis*, which identifies research needs and priorities in several critical TB-related areas. The agenda also highlights the importance of fostering partnerships with public and private organizations to fuel the pipeline of available drugs, diagnostics, and preventive measures for TB.

Malaria is an established infectious disease that continues to pose a significant global health burden. Malaria is becoming even more problematic with the emergence of drug-resistant malaria parasites and insecticide-resistant mosquito vectors. NIAID collaborations with public and private partners, including the Bill & Melinda Gates Foundation, build on the foundation of NIAID's robust malaria basic research program to foster the development of promising drug and vaccine candidates. Over the next two decades, we hope to have a major impact on the global TB and malaria burden through the development of vaccines that protect against these infectious killers. Our aim is excellent control of both TB and malaria through the use of vaccines and other interventions with the ultimate goal of eliminating malaria as a global disease threat.

TB and malaria are not the only diseases emerging in drug-resistant forms. The Centers for Disease Control and Prevention estimated that in 2005, more than 90,000 individuals in the United States developed invasive infections with methicillin-resistant *Staphylococcus aureus* (MRSA) and nearly 19,000 of these patients died. NIAID supports an extensive basic research portfolio on antimicrobial resistance, including

studies of how bacteria develop and share resistance genes and the identification of new therapeutic targets. The Institute is partnering with industry, other federal agencies, academia and other organizations such as the Infectious Diseases Society of America, to identify research priorities, including clinical trials, to address this growing problem, and recently published a detailed research agenda on antimicrobial resistance in *The Journal of Infectious Diseases*.

Seasonal influenza, which changes slightly every year, is the classic example of a re-emerging infectious disease. Influenza viruses also can undergo more drastic genetic changes that periodically enable them to evade pre-existing immunity and cause a pandemic, such as the deadly influenza pandemic in 1918 that killed more than 50 million people worldwide. NIAID supports a broad portfolio of research on influenza, including basic and applied research on the development of vaccines, diagnostics, and therapeutics against both seasonal and pandemic influenza. This foundation of research has underpinned the significant progress made in the development of new influenza interventions. For example, in 2007, based on clinical data from NIAID-supported research, the FDA approved the first vaccine for humans against the H5N1 avian influenza virus. Further, NIAID-supported studies performed in collaboration with various industrial partners have demonstrated the extraordinary potential for a variety of other vaccine formulations and adjuvants to not only expand the number of doses of vaccine but also to broaden the vaccine's reactivity against various strains of influenza.

As we look to how we might respond to unknown emerging and reemerging infectious disease threats in the future, it is apparent that the most practical approach may not always be the development of interventions such as diagnostics, vaccines, and therapeutics against just one microbe. Rather, the future of diagnostics will be rapid, accurate tools that can be used at the bedside or in the field in "real time" to detect a wide variety of pathogens. We are working to develop vaccine platforms that can be easily adapted to different microbes by shuttling the genes for different antigens in and out and that can provide protection against a broader group of pathogens. Similarly, we are developing antimicrobial therapeutics that truly are "broad spectrum" in their activity, both within and between classes of pathogens. Such antimicrobials could prove effective against drug-resistant bacteria, including MRSA.

HIV/AIDS RESEARCH

HIV/AIDS continues to exact a staggering toll. Although the Joint United Nations Programme on HIV/AIDS (UNAIDS) recently revised estimates to indicate a stabilization or decline in HIV infections and deaths in some parts of the world, the HIV/AIDS pandemic remains an enormous global health challenge. An estimated 33.2 million people worldwide are infected with HIV. In 2007, approximately 2.5 million people were newly infected with HIV, and 2.1 million died of AIDS.

Despite the grim numbers, the federal investment in HIV research has generated promising new results in the prevention and treatment of HIV/AIDS and in advancing our understanding of the virus and disease. An important example is the demonstration by NIAID-supported researchers that medically supervised adult male circumcision reduced by more than 50 percent the risk of heterosexual African men becoming infected with HIV. Our hope is that this and other advances in HIV prevention research will become part of a comprehensive HIV prevention “toolkit” that will markedly decrease new infections over the next two decades.

Perhaps the greatest success story in NIAID-funded AIDS research is that of therapeutics. NIAID-supported research helped make possible antiretroviral therapies that have transformed HIV from an almost uniformly fatal infection into a manageable chronic condition. Still, existing drugs are no longer sufficient for some HIV-infected patients because of the ability of the virus to develop resistance or because of the toxicities that can be associated with the therapies. Among the fruits of NIAID fundamental HIV research is the recent approval of three new potent and highly effective antiretroviral drugs: etravirine, maraviroc, and raltegravir. NIAID will continue to support the fundamental research that will be the foundation for future therapeutics that will be even more user-friendly and inexpensive, making universal access to therapy more feasible over the next two decades.

Prevention efforts continue to be a major component of the HIV research program of NIAID, and the most powerful prevention tool would be a safe and effective HIV vaccine. The development of an HIV vaccine remains one of our greatest scientific priorities, but also one of our greatest scientific challenges. The pathway to a vaccine is being elucidated through the fundamental basic research that remains the foundation

of NIAID. For example, researchers at the NIAID Vaccine Research Center and their collaborators determined the atomic structures of a neutralizing antibody and the conserved area of the HIV surface protein (gp120) to which the neutralizing antibody binds. This binding site is the same site that the virus uses to bind to cells of the immune system. Such studies are helping us to identify components of HIV that may serve as targets for future vaccine candidates and may bring us closer to a safe and effective HIV vaccine.

BIODEFENSE RESEARCH

Since the beginning of the acceleration of our biodefense research program in FY 2003, NIAID has achieved a number of successes in the development of countermeasures against significant bioterrorism threats; these countermeasures are either in the Strategic National Stockpile or available for use in an emergency. Promising candidate countermeasures in development include ST-246, a smallpox drug candidate that has protected both rodents and nonhuman primates from an otherwise lethal exposure to live poxviruses. The FDA has granted orphan drug status to ST-246 and awarded the compound fast-track status which will expedite its regulatory review. The vaccine platforms, rapid diagnostics, and broad spectrum antimicrobial therapeutics that we aim to develop for emerging infectious diseases over the next two decades will also be directly applicable to our biodefense research program.

In addition, and as important, NIAID has developed a physical and intellectual research infrastructure that has been critical to our ability to respond to new and re-emerging infectious diseases. Without this expanded infrastructure, the biomedical research response to the emergence of infectious disease threats such as H5N1 avian influenza, MRSA, and XDR-TB would not have been as rapid.

RESEARCH ON IMMUNE-MEDIATED DISEASES

Autoimmune diseases, allergic diseases, asthma, rejection of transplanted organs, and other immune-mediated disorders are significant causes of chronic disease and disability in the United States and throughout the world. NIAID-supported research in immune-mediated diseases has led to significant advances in our understanding of the

mechanisms underlying these diseases and in the development of strategies to detect, prevent, and treat them.

Food allergies continue to be a growing concern and an emerging focus of public attention. NIAID remains committed to basic research to advance the understanding of food allergy and food allergy-associated anaphylaxis. To bring new investigators and novel ideas into food allergy research, NIAID is supporting a new initiative, *Exploratory Investigations in Food Allergy*, in collaboration with public and private partners. NIAID also is expanding support for clinical trials in food allergy, with ongoing trials to prevent the development of allergies to particular foods, such as peanut, and to reverse established allergy to milk, eggs, and peanut.

The Institute also supports research to improve outcomes for transplant recipients, with establishment of immune tolerance as a major priority in this area. The NIAID Immune Tolerance Network is making steady progress towards the long-term goal of reducing the need for costly and potentially risky immunosuppressive drugs that are the current standard treatment to prevent transplant rejection. A total of 11 kidney and liver transplant recipients are no longer on immunosuppressive drugs, some for as long as four years. We hope that eventually a substantial proportion of organ transplant recipients will not require immunosuppressive drugs.

The establishment of immune tolerance is a goal not only for transplantation, but also for other immune-mediated disorders, such as allergies. We look forward to the use of tolerance to have a major impact on allergies, including food allergies, and other immune-mediated disorders in the coming decades.

CONCLUSION

For more than six decades, NIAID has conducted and supported basic research on infectious and immune-mediated diseases that has underpinned the development of vaccines, therapeutics, and diagnostics. These, in turn, have improved health and saved millions of lives in the United States and around the world. Through partnerships with industrial, academic, governmental, and non-governmental partners, the Institute will continue to leverage these fundamental discoveries into the tools needed to achieve a healthy world.

ANTHONY S. FAUCI, M.D.
Director, National Institute of Allergy and Infectious Diseases
National Institutes of Health

Dr. Anthony S. Fauci, a native of Brooklyn, New York, received his M.D. degree from Cornell University Medical College in 1966. He then completed an internship and residency at The New York Hospital-Cornell Medical Center. In 1968, Dr. Fauci came to the National Institutes of Health (NIH) as a clinical associate in the Laboratory of Clinical Investigation (LCI) at the National Institute of Allergy and Infectious Diseases (NIAID). In 1980, he was appointed Chief of the NIAID Laboratory of Immunoregulation, a position he still holds. In 1984, Dr. Fauci became Director of NIAID, where he oversees an extensive research portfolio of basic and applied research to prevent, diagnose, and treat infectious diseases such as HIV/AIDS and other sexually transmitted infections, influenza, tuberculosis, malaria and illness from potential agents of bioterrorism. NIAID also supports research on transplantation and immune-related illnesses, including autoimmune disorders, asthma and allergies. The NIAID budget for fiscal year 2008 is approximately \$4.4 billion. Dr. Fauci serves as one of the key advisors to the White House and Department of Health and Human Services on global AIDS issues, and on initiatives to bolster medical and public health preparedness against emerging infectious disease threats such as pandemic influenza.

Dr. Fauci has made many contributions to basic and clinical research on the pathogenesis and treatment of immune-mediated and infectious diseases. He has pioneered the field of human immunoregulation by making a number of basic scientific observations that serve as the basis for current understanding of the regulation of the human immune response. In addition, Dr. Fauci is widely recognized for delineating the precise mechanisms whereby immunosuppressive agents modulate the human immune response. He has developed effective therapies for formerly fatal inflammatory and immune-mediated diseases such as polyarteritis nodosa, Wegener's granulomatosis, and lymphomatoid granulomatosis. A 1985 Stanford University Arthritis Center Survey of the American Rheumatism Association membership ranked the work of Dr. Fauci on the treatment of polyarteritis nodosa and Wegener's granulomatosis as one of the most important advances in patient management in rheumatology over the previous 20 years.

Dr. Fauci has made seminal contributions to the understanding of how the AIDS virus destroys the body's defenses leading to its susceptibility to deadly infections. He also has delineated the mechanisms of induction of HIV expression by endogenous cytokines. Furthermore, he has been instrumental in developing highly effective strategies for the therapy of patients with this serious disease, as well as for a vaccine to prevent HIV infection. He continues to devote much of his research time to identifying the nature of the immunopathogenic mechanisms of HIV infection and the scope of the body's immune responses to the AIDS retrovirus.

In 2003, an Institute for Scientific Information study indicated that in the twenty year period from 1983 to 2002, Dr. Fauci was the 13th most-cited scientist among the 2.5 to 3 million authors in all disciplines throughout the world who published articles in

scientific journals during that time frame. Dr. Fauci was the world's 10th most-cited HIV/AIDS researcher in the period 1996-2006.

Through the years, Dr. Fauci has served as Visiting Professor at major medical centers throughout the country. He has delivered many major lectureships all over the world and is the recipient of numerous prestigious awards for his scientific accomplishments, including the Presidential Medal of Freedom, the National Medal of Science, the George M. Kober Medal of the Association of American Physicians, the Mary Woodard Lasker Award for Public Service, the Albany Medical Center Prize in Medicine and Biomedical Research, and 33 honorary doctorate degrees from universities in the United States and abroad.

Dr. Fauci is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, the Institute of Medicine (Council Member), the American Philosophical Society, and the Royal Danish Academy of Science and Letters, as well as a number of other professional societies including the American College of Physicians, the American Society for Clinical Investigation, the Association of American Physicians, the Infectious Diseases Society of America, the American Association of Immunologists, and the American Academy of Allergy Asthma and Immunology. He serves on the editorial boards of many scientific journals; as an editor of Harrison's Principles of Internal Medicine; and as author, coauthor, or editor of more than 1,100 scientific publications, including several textbooks.

Department of Health and Human Services
Office of Budget
Richard J. Turman

Mr. Turman is the Deputy Assistant Secretary for Budget, HHS. He joined federal service as a Presidential Management Intern in 1987 at the Office of Management and Budget, where he worked as a Budget Examiner and later as a Branch Chief. He has worked as a Legislative Assistant in the Senate, as the Director of Federal Relations for an association of research universities, and as the Associate Director for Budget of the National Institutes of Health. He received a Bachelor's Degree from the University of California, Santa Cruz, and a Masters in Public Policy from the University of California, Berkeley