Summary of Research Activities by Disease Categories

Infectious Diseases and Biodefense

By 1986, there were 5,833 reported AIDS cases in the United States and the 1-year mortality was 51 percent. Efforts were being made to find something—anything—that would slow disease progression. A seminal discovery, made in 1970, was that an enzyme called reverse transcriptase was necessary for retroviruses like HIV to replicate. Based on this understanding, scientists began to screen existing agents to find candidate drugs that inhibited the enzyme. Drs. Robert Yarchoan, Hiroaki Mitsuya, and Samuel Broder found that zidovudine (AZT) had this property. AZT was then quickly placed in a placebo-controlled clinical trial in patients with late-stage disease. The first review of data in September 1986 showed 19 deaths in the placebo group compared with 1 death in the AZT treatment group. The study was stopped and the FDA approved the drug in record time. It was 21 months from trial initiation to drug approval—an FDA record that has never been surpassed.

Introduction

The goals of NIH-supported research on infectious diseases and biodefense rest on two core components. NIH builds and maintains a base of fundamental knowledge about infectious and immune-related diseases and uses that knowledge to develop new and improved diagnostics, therapeutics, and preventive measures, including vaccines. At the same time, NIH continues to develop a flexible domestic and international infrastructure that allows it to respond to newly emerging and re-emerging threats wherever they occur, thereby protecting public health in the United States and abroad.

Infectious Diseases

Infectious diseases are caused by microbial pathogens—bacteria, viruses, fungi, protozoa, and helminths (worms)—that invade the body and multiply, causing physiological damage and illness. Pathogens cause a range of diseases from nonserious to life-threatening and can be transmitted in many ways. Influenza and TB can be transmitted from person to person via airborne inhalation; HIV, which causes AIDS, is transmitted through exposure to blood or other body fluids, during sexual intercourse, and from mother to child at birth or during breast-feeding; and malaria is caused by a microscopic parasite that is transmitted by an insect “vector,” in this case a mosquito. Unlike chronic and degenerative illnesses, transmissible infectious diseases can rapidly devastate large human populations and easily cross international borders.

Biodefense and Emerging and Reemerging Infectious Diseases

Public health threats that could cause large-scale disruption and devastation include the deliberate or accidental release of pathogenic agents such as anthrax or smallpox, biological toxins, chemical weapons such as nerve gas, or radioactive substances. The NIH biodefense strategy is designed to protect all civilian populations and integrates basic, applied, and clinical research knowledge and capabilities into a flexible and adaptable “network.” Other threats to public health change continually as new pathogens emerge and as familiar microbes reemerge with new properties or in unusual settings. Examples of recent emerging and reemerging public health threats include naturally occurring infectious diseases such as Ebola hemorrhagic fever and severe acute respiratory syndrome (SARS). The overall goal of research on biodefense and emerging and reemerging infectious diseases is to develop the knowledge and tools to respond quickly and effectively as public health threats emerge, whether they occur naturally, accidentally, or deliberately.

Although NIAID has primary responsibility for infectious diseases and biodefense research, many other NIH ICs play
critical roles, including FIC, NICHD, NINDS, and the NIH Office of AIDS Research (OAR). Nearly every NIH IC supports AIDS-related research activities, consistent with their individual missions. The ICs that conduct most of the research on AIDS and related co-infections, malignancies, cardiovascular and metabolic complications, and behavioral and social science issues are NIAID, NIDA, NCI, NIMH, the National Center for Research Resources (NCRR), NICHD, and NHLBI. All NIH AIDS research is coordinated by OAR.

In addition, the NIH Office of Science Policy manages and supports the National Science Advisory Board for Biosecurity (NSABB). The NSABB provides advice on strategies for the efficient and effective oversight of dual-use biological research—research that has a legitimate scientific purpose but could be misused to pose a threat to public health or national security—taking into consideration both national security concerns and the needs of the research community.

NIH-wide research on infectious diseases and biodefense includes basic research to understand fundamental mechanisms by which microorganisms cause disease, the host response to pathogens, and mechanisms by which insects and other vectors transmit infectious diseases. Translational research builds on basic research findings with the aim of developing new and improved diagnostics, therapeutics, vaccines, and other preventive measures. NIH conducts and supports clinical research to assess the efficacy and safety of new drugs, vaccines, and other products. As NIH pursues these goals, an overarching priority is to reduce health disparities and improve health for all people.

Infectious diseases and biodefense are inherently global concerns. NIH engages in international partnerships to improve means for detecting and controlling the spread of infectious diseases and supports international programs to foster research and research capacity in low- and middle-income countries. Within the United States, NIH seeks strategic partnerships with other governmental and nongovernmental organizations.

NIH supports research on HIV/AIDS, TB, malaria, emerging and reemerging infectious diseases (such as hemorrhagic fevers caused by Ebola and other viruses, West Nile virus, SARS, Lyme disease, prion diseases, and H5N1, a virus that causes avian influenza), sexually transmitted infections, and influenza and other respiratory infections. In addition, NIH funds research on many less familiar but still important diseases that exact an enormous global toll.24

NIH research on biodefense and emerging and reemerging infectious diseases is necessarily intertwined and includes the development of infrastructure and capacity-building, that is, facilities and human resources needed to conduct research on dangerous pathogens safely and effectively; basic research on microbes and host immune defenses; and the targeted development of medical countermeasures, including vaccines, therapeutics, and diagnostics that would be needed in the event of a biological, chemical, or radiological weapons attack.

**Burden of Illness and Related Health Statistics**

Infectious diseases cause approximately 26 percent of all deaths worldwide. Each year, more than 11 million people die from infectious diseases, the vast majority of deaths occurring in low- and middle-income countries. The top infectious disease killers in those countries for people ages 15 to 59 are HIV/AIDS, TB, and lower respiratory infections. HIV causes nearly 2.1 million total deaths each year,25 TB kills 1.6 million each year, and

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24 For more information, see [http://www3.niaid.nih.gov/Biodefense](http://www3.niaid.nih.gov/Biodefense)

lower respiratory infections in 2005 caused an estimated 3.7 million deaths\textsuperscript{26}. Malaria is a serious problem, especially in Africa, where one in every five childhood deaths is due to the effects of the disease\textsuperscript{27}. The infectious diseases that today cause the greatest number of human deaths worldwide are (in order) lower respiratory infections, HIV/AIDS, diarrheal diseases, malaria, and TB\textsuperscript{28}.

Each year infectious diseases kill approximately 6.5 million children, most of whom live in developing countries. For children younger than age 14, infectious diseases account for 7 of the top 10 causes of death. In this age group, the leading infectious diseases are lower respiratory infections, diarrheal diseases, and malaria. Among children younger than age 5, infectious diseases cause about two-thirds of all deaths\textsuperscript{29}.

The burden of infectious diseases is not evenly shared, even among developing nations. People who live in sub-Saharan Africa are most affected, particularly by HIV/AIDS, which accounts for one in five deaths in that region. Africa and the most populous countries of Asia harbor the largest number of TB cases. Together, Bangladesh, China, India, Indonesia, and Pakistan account for half of new TB cases each year\textsuperscript{30}.

In the United States, infectious diseases add significantly to the overall burden of illness. Together, influenza and pneumonia account for more than 60,000 deaths annually\textsuperscript{31}. More than a million cases of sexually transmitted diseases occur each year, and more than 42,000 new cases of AIDS were reported in 2004\textsuperscript{32}.

Also, many infectious diseases are increasingly difficult to treat because pathogens are developing resistance to antimicrobial drugs. For example, in recent years there have been dramatic increases in antiretroviral drug resistance in HIV, chloroquine resistance in malaria, the emergence of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB), and methicillin-resistant \textit{Staphylococcus aureus} (MRSA) infection.

\section*{NIH Funding for Infectious Disease and Biodefense Research}

FYs 2006 and 2007, NIH funding for infectious diseases research was $3.132 billion and $3.059 billion respectively. Funding for biodefense research was $1.766 billion and $1.735 billion. There is substantial overlap in these funding figures. The table at the end of this chapter indicates some of the research areas involved in this investment (see “Estimates of Funding for Various Diseases, Conditions, and Research Areas”).

\section*{Summary of NIH Activities}

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\begin{itemize}
\item \textsuperscript{26} For more information, see \url{http://www.dcp2.org/main/Home.html}; \url{http://www.who.int/entity/mediacentre/factsheets/fs310.pdf}
\item \textsuperscript{27} For more information, see \url{http://www.who.int/features/factfiles/malaria/en/index.html}
\item \textsuperscript{28} For more information, see \url{http://www.dcp2.org/pubs/GBD/3/Table/3.14}
\item \textsuperscript{29} For more information, see \url{http://www.dcp2.org/main/Home.html}
\item \textsuperscript{30} For more information, see \url{http://www.dcp2.org/main/Home.html}
\item \textsuperscript{31} For more information, see \url{http://www.cdc.gov/nchs/fastats/deaths.htm}
\item \textsuperscript{32} For more information, see \url{http://www.cdc.gov/nchs/fastats/infectis.htm}
\end{itemize}
NIH programs on infectious diseases and biodefense encompass a broad range of basic, translational, preclinical, and clinical research. These activities include developing critical research resources and infrastructure domestically and abroad that allow NIH to respond effectively to existing and emerging infectious diseases wherever they occur.

**Basic Research**

Basic research on infectious diseases and biodefense seeks to increase understanding of how pathogens cause disease and how hosts respond to infection; it provides the foundation for improvements in the prevention, diagnosis, and treatment of infectious diseases. For example, NIH researchers recently discovered how a surface protein of the virus that causes chicken pox and shingles attaches to a host cellular protein. That finding, in turn, has opened the door to designing and developing new treatments that block the virus-attachment process.

Many challenges remain in basic research on infectious diseases. These include further definition of the mechanisms by which the immune system protects against infection and of the intricate interactions that occur between pathogens and their hosts; more precise identification of the driving forces behind changing global patterns of infectious diseases; uncovering additional links between infectious diseases (and the immune responses to them) and the development of some cancers, as well as some autoimmune, cardiovascular, and neurological disorders; and discovering how and why genetic changes arise that make pathogens more dangerous. For example, HIV, H5N1 influenza, and Ebola virus originated in animals but mutated and acquired the ability to infect humans. Also, microbes that cause TB, AIDS, and influenza are mutating and acquiring resistance to antimicrobial drugs, which has prompted NIH to develop research initiatives and programs to expand investigations of the basis of antimicrobial resistance, including how bacteria develop and share resistance genes.

Many advances in understanding infectious diseases are the result of the revolution in genomic sequencing that has occurred in the past decade. In FYs 2006 and 2007, NIH-funded researchers and their collaborators completed a range of genome-sequencing projects that help reveal how microbes evolve, infect host cells, cause disease, develop drug resistance, and spread. The studies include sequencing the complete or partial genomes of 54 different samples of the malaria parasite, *Plasmodium falciparum*; a common sexually transmitted parasite, *Trichomonas vaginalis*; an oral bacterium; and more than 2,800 samples of avian and human influenza viruses.

Several of the genome-wide association studies funded by NIH examine genetic variations and explore susceptibility to infection or responses to smallpox, anthrax, typhoid, and cholera vaccinations (see also the section “Genomics” in Chapter 3).

**Major Infectious Diseases**

NIH conducts research on hundreds of infectious diseases, placing special emphasis on those that claim large numbers of lives each year and cause widespread suffering. NIH also explores how human behaviors as well as social, cultural, economic, and geographic factors affect disease transmission. Additionally, NIH conducts studies to evaluate and ensure the health of special populations, including minorities, individuals who are immunocompromised, the elderly, adolescents, young children, and infants. The ultimate goal is to translate knowledge gained through basic research into interventions that improve public health.

**Tuberculosis**

TB is an old disease but still ranks high among the foremost microbial killers of the 21st century and is particularly common among people with HIV. NIH supports a large portfolio of research to develop new drugs, vaccines, and diagnostics for TB and to evaluate improved treatment and prevention regimens. New drugs currently in clinical

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33 For more information, see [http://www.niaid.nih.gov/dmid/genomes/mscs/influenza.htm](http://www.niaid.nih.gov/dmid/genomes/mscs/influenza.htm)
trials include SQ-109, a promising candidate therapy being developed in a private-public partnership. After a hiatus of 60 years in which no new TB vaccines were clinically tested, at least 9 candidates are now in human trials and at least 10 more are in preclinical development.

The rapid emergence of drug-resistant forms of TB poses an increasing and dangerous public health threat. Both MDR-TB and XDR-TB are classified as emerging infectious diseases and are increasingly difficult to treat. NIH supports the development of new and improved diagnostic tools to more accurately diagnose early TB disease, help optimize therapy by identifying drug-resistant strains, and track the spread of TB in communities. To ensure that research continues to contribute effectively to the global response to the increasing TB threat, in 2007 NIH developed a comprehensive TB research agenda. The plan incorporates NIH collaborations with other U.S. Government agencies and multilateral organizations worldwide and supports public-private partnerships to benefit people who have TB, including individuals who are co-infected with HIV.

**Malaria**

The age-old scourge of malaria claims millions of lives every year, mostly among children. The broad NIH malaria research portfolio and the malaria research agenda currently under development are designed to improve understanding of malaria parasites, host responses, and vector biology, thereby accelerating the development of new and improved public health interventions, including vaccines, therapeutics, and vector management. NIH is collaborating with strategic partners to develop vaccines for malaria and is currently testing several candidate vaccines in malaria-endemic areas. In 2007, NIAID began a new initiative entitled “NIAID Partnerships with Public-Private Partnerships.” This initiative seeks to support the role of public-private partnerships in the development of new drugs, vaccines, and diagnostics for diseases such as malaria, trypanosomiasis, leishmaniasis, and other neglected tropical diseases.

**HIV/AIDS**

In the countries hardest hit by HIV/AIDS, the disease has lowered life expectancy, orphaned millions of children, lowered family income, reduced worker productivity, and diminished the supply of teachers and health care workers. NIH plays many critical roles in the global effort to conquer HIV. Antiretroviral therapies made possible by NIH-supported research have resulted in improved quality of life and life expectancy for people who have access to these drugs. A recent study concluded that, since 1996, these antiretroviral medications have saved at least 3 million years of life in the United States alone. Worldwide, more than 2 million people receive antiretroviral therapy, more than half of them with support from the President’s Emergency Plan for AIDS Relief (PEPFAR). However, the use of these antiretroviral therapies is associated with a range of side effects and long-term complications that may have a negative impact on mortality rates. The appearance of multidrug-resistant strains of HIV presents an additional serious public health concern. NIH AIDS research programs are addressing these and other complications.

The broad effort to extend the availability and use of anti-HIV drugs to regions most affected by HIV/AIDS continues. NIH is funding research to develop therapeutic regimens that are easier to use in resource-limited settings, as well as new antiretroviral drugs that target HIV in novel ways. In one of the largest HIV/AIDS treatment trials ever conducted, NIH-funded scientists participating in an international collaboration involving 318 clinical sites in 33 countries showed that HIV-positive individuals who receive episodic treatment with anti-HIV drugs have twice the risk of disease progression, including death from AIDS, than do those who receive continuous therapy with antiretroviral drugs. In addition, the recently Children with HIV Early Antiretroviral Therapy study in South Africa showed that treating HIV-infected children early with antiretroviral drugs helps them live longer.

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34 For more information, see [http://www.kff.org/hivaids/7661.cfm](http://www.kff.org/hivaids/7661.cfm)
Another key research priority is prevention and treatment of HIV-associated co-infections, such as TB and hepatitis C, and comorbidities, such as HIV-associated malignancies, cardiovascular disease, and neurological complications. Studies are evaluating the incidence and treatment of metabolic and cardiovascular disease in people who receive long-term antiretroviral therapy. In addition, the AIDS Malignancy Consortium has launched several clinical studies to identify appropriate treatment regimens for HIV-infected individuals with cancer.

Successful efforts to prevent the spread of HIV and improve adherence and access to treatment are also driven by research in behavioral and social sciences that extends understanding of decision-making, drug abuse, and sexual behavior. As people changed risky behaviors, new AIDS cases in the United States were nearly halved from a peak of over 80,000/year in 1993, to 42,000/year in 2005. Previously 1,650 babies were born infected with HIV each year but today that number is less than 50. Whether preventing transmission, engendering trust to encourage testing and early treatment, or increasing adherence and access to the latest medications and health services, slowing the spread of HIV/AIDS involves understanding (basic behavioral and social science) and changing human behavior at individual, group and community levels.

NIH continues to place a high priority on HIV prevention research, including research to develop vaccines, microbicides, strategies to prevent mother-to-child transmission, antiretroviral therapy as a pre-exposure prophylaxis strategy, treatment for drug addiction, and behavioral interventions. NIH-sponsored studies recently demonstrated that the use of antiretroviral prophylaxis can reduce the rate of mother-to-child transmission of HIV from approximately 25 percent to less than 2 percent. NIH also supports research to develop and test other prevention strategies, such as circumcision. For example, NIH-supported clinical trials in Kenya and Uganda showed that medically supervised circumcision of adult males can significantly lower their risk of contracting HIV through heterosexual intercourse by approximately 50 percent. In countries hit hard by HIV, adult male circumcision serves as another prevention strategy that could result in fewer HIV infections.

Topically applied microbicides for women and men are another promising avenue for preventing HIV transmission. Several microbicides have entered large-scale efficacy trials, the results of which are expected in the next few years. In 2006, NIH established the Microbicide Trials Network to develop safe and effective microbicides to prevent HIV transmission. In addition to basic and clinical research, studies of cultural and behavioral factors related to acceptability and adherence of prevention interventions are under way.

The ultimate prevention tool, and what is considered the best hope to end the HIV/AIDS pandemic, is a safe and effective vaccine that could prevent HIV infection. NIH-supported researchers around the world have developed candidate vaccines against HIV, some of which are now being tested in various phases of clinical trials. One example is the large-efficacy HIV vaccine trial in Thailand that is being conducted with support from NIH. The NIH Vaccine Research Center, as well as the NIH-supported HIV Vaccine Trials Network, is also dedicated to developing and testing new HIV vaccine candidates, including some that target different HIV types (called clades). To overcome key scientific roadblocks to HIV vaccine development and facilitate the design and testing of HIV vaccine candidates, NIH established the Center for HIV/AIDS Vaccine Immunology, an international consortium of


36 For more information, see http://www.cdc.gov/hiv/topics/surveillance/resources/reports/2005report/

37 For more information, see http://www.cdc.gov/hiv/topics/perinatal/resources/factsheets/perinatal.htm
Emerging Infectious Diseases and Biodefense

NIH has mounted a comprehensive and vigorous research program to address critical challenges posed by naturally emerging and reemerging infectious diseases, as well as to mitigate the threats of biological, chemical, or nuclear/radiological terrorism. The goals of these overlapping programs are to develop the capacity to respond rapidly to public health threats; better understand the patterns and means by which pathogens spread and how they cause disease; decipher the mechanisms by which pathogens that infect animals mutate and acquire the ability to infect humans; and develop safe and effective medical countermeasures against naturally occurring, accidental, and deliberately introduced public health threats.

Influenza is a classic example of a reemerging infectious disease. The influenza viruses that caused the pandemic World War I-era Spanish flu and the current avian flu (caused by the H5N1 influenza virus) began in birds, mutated and spread to mammals (pigs, cats, etc.), and then mutated further and acquired the ability to infect humans. Thus, the spread of H5N1 from birds to humans underscores the urgent need to develop better vaccines and drugs to protect against pandemic influenza, as well as the seasonal epidemics that claim an average of 36,000 lives per year in the United States alone.

In 2006, NIH undertook a comprehensive examination of its influenza portfolio and convened a Blue Ribbon Panel on Influenza Research to identify areas of influenza research in which progress is needed. To help implement the panel's recommendations and facilitate a broad spectrum of influenza research, NIH has adopted several strategies. In 2007, NIH made multiple awards to support innovative influenza research to advance the development of promising vaccines, adjuvants, therapeutics, immunotherapeutics, and diagnostics. NIH also established six Centers of Excellence for Influenza Research and Surveillance to expand its ability to conduct research on different strains of animal and human influenza viruses collected in other countries or the United States. NIH researchers are collaborating extensively with other Department of Health and Human Services (HHS) agencies, across other Federal agencies, with private industry, and internationally and are working with strategic partners to develop DNA-, recombinant virus-, and recombinant protein-based candidate influenza vaccines. NIH also leads an international collaborative effort to analyze national and global epidemiological patterns associated with influenza virus circulation.

To date, NIH research has laid the foundation for improved influenza vaccine manufacturing methods, new categories of vaccines that may work against multiple influenza strains, and the next generation of anti-influenza drugs. The inactivated-virus H5N1 vaccine currently stockpiled by HHS has been shown in NIH-sponsored clinical trials to be safe and capable of inducing an immune response predictive of being protective against the H5N1 virus in healthy adults, children, and seniors.

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Biological Countermeasures Research
NIH supports research on a range of emerging and reemerging pathogens that are also considered potential agents of bioterrorism, including Marburg and Ebola hemorrhagic fever viruses, smallpox, and anthrax. NIH-supported researchers are probing the ecology of how these infections arise, identifying the natural hosts and modes of natural transmission of pathogens and developing safe and effective vaccines and treatments. For example, NIH-funded scientists recently developed promising candidate vaccines for Ebola and Marburg hemorrhagic fever viruses. The Marburg vaccine has been tested in rhesus monkeys and helped all of them survive a later challenge with live virus. An experimental Ebola vaccine has entered human clinical trials.

**Chemical Countermeasures**

Within HHS, NIH is leading the development of new and improved medical countermeasures designed to prevent, diagnose, and treat the conditions caused by chemical agents that could be released either accidentally or deliberately. To guide this research, NIH has prepared the “Strategic Plan and Research Agenda on Medical Countermeasures Against Chemical Threats.” Under this plan and in collaboration with DoD, NIH has established the trans-agency [CounterACT Research Network](https://www.ncbrm.org/). The network has established four Centers of Excellence in Medical Chemical Research; funded more than two dozen research projects focusing on nerve agents, sulfur mustard and other blister-causing agents, cyanide and other metabolic poisons, and pulmonary agents; and awarded several Small Business Innovation Research grants for therapeutics and diagnostics development.

**Nuclear/Radiological Countermeasures**

To enhance readiness in the event of a radiological or nuclear threat, NIH has developed a [strategic plan and research agenda](https://nih.gov/). To help implement the plan, NIH has issued an RFA to conduct research to validate existing biodosimetry tools that evaluate radiation doses to which individuals have been exposed and to develop new [biodosimetry assays and tools](https://nih.gov/). NIH also issued RFAs to support the research and development of [medical countermeasures to enhance survival after radiation exposure](https://nih.gov/).

NIH works closely with HHS to periodically update and prioritize the research development activities of its strategic plan and ensure its integration as a key component of the larger national biodefense research agenda. The [Radiation Event Medical Management Program](https://nih.gov/) (REMM) provides online guidance to health care providers about diagnosis and treatment for radiation-induced injuries. Further, in collaboration with the HHS Office of the Assistant Secretary for Preparedness and Response, NIH has prepared a downloadable, online diagnostic and treatment tool kit to guide health care providers during a mass casualty radiation event.

**Infrastructure and Research Resources**

NIH continues to develop the infrastructure necessary to carry out pioneering research on infectious diseases. As research capabilities (e.g., genomics, proteomics, microarray technology) have evolved and research needs have changed, new facilities and research resources have been designed, implemented, and enhanced. However, since the U.S. anthrax attacks of 2001, the emergence of severe acute respiratory syndrome (SARS) in southeast Asia, repeated outbreaks of hemorrhagic fever viruses in Africa, the threat of pandemic influenza, and other actual and potential public health emergencies, there is an increased need to develop the ability to respond rapidly to public health threats. To this end, NIH has established or expanded reagent and tissue repositories, data centers, and centralized analytical laboratories and is expanding the number of extramural research facilities nationwide. The latter include the 6 Centers of Excellence for Influenza Research and Surveillance mentioned above, 10 Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research, 2 National Biocontainment Laboratories (with BSL-4 capacity, the highest level of containment), 13 Regional Biocontainment Laboratories with BSL-3 capacity, 8 Human Immunology Centers, 10 centers to study host immunity in special populations (children, pregnant women, elderly, immunosuppressed individuals), clinical trials networks at domestic and international sites, and nonhuman primate research centers. In addition, three intramural biocontainment laboratories—on the
NIH campus in Bethesda, Maryland (BLS-3); on the National Interagency Biodefense Campus at Fort Detrick in Frederick, Maryland (BSL-4); and at the NIAID Rocky Mountain Laboratories in Hamilton, Montana (BSL-4)—are operational or nearing completion.

**International Collaboration**

Much of NIH infectious disease and biodefense research is collaborative, interdisciplinary, and—increasingly—international. NIH supports research and training programs to develop and test safe and effective interventions for preventing and treating infectious diseases, exchanging scientific information, and building research capacity in other countries (see also the section “Research Training and Career Development” in Chapter 3). These efforts include programs to establish research resources and infrastructure, for example, to help train scientists from developing countries to engage in infectious disease research, including clinical, operational, and health services research, and to help establish sustainable research capacity in those countries. Because HIV/AIDS and TB take such an enormous global toll, NIH is strengthening the capacity for clinical, operational, and health services research in low- and middle-income countries where HIV/AIDS, TB, or both are significant problems. NIH has established critical global partnerships with the World Health Organization and other United Nations agencies, governmental and nongovernmental organizations, international foundations, and private-sector organizations. Additionally, NIH is establishing international collaborations to develop a safe, effective vaccine against malaria and to gather and analyze national and global epidemiological patterns associated with influenza virus circulation, including data on mortality, virus surveillance, genomics, and control strategies.

### Notable Examples of NIH Activity

**Key for Bulleted Items:**

- E = Supported through Extramural research
- I = Supported through Intramural research
- O = Other (e.g., policy, planning, and communication)
- COE = Supported through a congressionally mandated Center of Excellence program
- GPRA Goal = Concerns progress tracked under the Government Performance and Results Act

#### Basic Research

**Microbial Genomics:** NIH has made significant investments in large-scale, whole-genome sequencing of pathogens over the last decade. Sequenced pathogens include hundreds of bacteria, fungi, parasites, invertebrate vectors of diseases, and viruses (including the pathogens that cause anthrax, influenza, aspergillosis, TB, gonorrhea, chlamydia, and cholera and many that are potential agents of bioterrorism). NIH also provides comprehensive genomic, bioinformatic, and proteomic resources and reagents to the scientific community. These include the (1) Microbial Genome Sequencing Centers, which rapidly produce high-quality genome sequences of human pathogens and invertebrate vectors of diseases; (2) Pathogen Functional Genomics Resource Center, which provides functional genomic resources; (3) Bioinformatics Resource Centers, which provide access to genomic and related data in a user-friendly format; and (4) Proteomics Research Centers, which support research on the full set of proteins encoded in a microbial genome. The NIH Influenza Genome Sequencing Project has sequenced more than 2,800 human and avian isolates (as of November 28, 2007); NIH scientists recently exploited these data to explain the global spread of resistance to adamantanes, a first-generation class of anti-influenza drug.
Scientists Complete Full Sequence of Opportunistic Oral Bacterium: Over the last decade, scientists have assembled the complete DNA sequences of several important oral bacteria. Now NIH-funded investigators have decoded and added another important bacterium, *Streptococcus sanguinis*, a key player in the formation of the oral biofilm, to the list. Although not regarded as a pathogen in the mouth, *S. sanguinis* is known to enter the bloodstream, where it can colonize heart valves and contribute to bacterial endocarditis, a condition that kills an estimated 2,000 Americans each year. With the bacterium’s genetic blueprint now publicly available online, scientists can better study the dynamics of biofilm formation and possibly tease out new leads to prevent tooth decay and periodontal disease. They can also now systematically identify and target sequences within the DNA of *S. sanguinis* that are critical to the infectious process, invaluable information in designing more effective treatments for endocarditis.

- This example also appears in Chapter 3: Genomics.
- (E/I) (NIAID) (GPRA Goal)

Major Infectious Diseases

Malaria Vaccine Research: Malaria continues to be one of the most devastating diseases throughout the world today. The number of cases of the disease ranges from 350 million to 500 million each year, resulting in more than 1.1 million deaths, primarily among young children in Africa (World Health Organization [WHO]). To address this important public health issue, the WHO Initiative for Vaccine Research reports that, as of August 2005, there are at least 45 candidate vaccines in preclinical development and 26 in clinical trials. NIH plays a valuable role in funding a number of these activities, supporting 15 of the candidates in preclinical development and 5 of the candidates in clinical trials. Examples of NIH-supported activities include the following:

- NIH researchers have applied an innovative technology, tested in mice, that may prompt an individual’s immune system to eliminate the malaria parasite from the mosquito. Because the vaccine targets the parasite instead of conferring protection to the individual, it has the potential to eradicate malaria from large geographic regions.

- NIAID, in collaboration with the Walter Reed Army Institute of Research, GlaxoSmithKline Biologicals, the U.S. Agency for International Development, and others, has completed a Phase I adult trial in Mali of a novel candidate vaccine that works by blocking the replication of malaria parasites in the blood. Additional studies in children (who have the highest death toll among malaria cases) are under way.

- For more information, see http://www.who.int/vaccine_research/diseases/soa_parasitic/en/index4.html
- (I) (NIAID, NICHD, NIDDK)

Value of Early HIV Screening, Testing, and Counseling: HIV/AIDS disproportionately affects several minority groups, particularly African Americans. Although adult and adolescent African Americans make up approximately 13 percent of the population, they accounted for half of the new HIV/AIDS diagnoses in 2001-2005. This disparity is particularly striking because African Americans do not have higher rates of addiction or intravenous drug use than Whites. One contributing factor is that African Americans are often diagnosed with HIV infection at a later point in
the illness, increasing their likelihood of progressing to AIDS and of transmitting the disease. As part of efforts to prevent late diagnosis and HIV spread, NIH is working to identify and address the cultural barriers to making HIV screening more acceptable and to strengthen the links among education, testing and counseling, and treatment within all ethnic groups. Indeed, NIH-supported modeling research has shown that routine HIV screening, even among populations with prevalence rates as low as 1 percent, is as cost-effective as screening for other conditions such as breast cancer and high blood pressure. The CDC has recognized that these findings have important public health implications and has called for increased HIV screening as part of its recommended guidelines. NIH is eager to advance new HIV rapid-screen technologies and counseling in community drug treatment programs and in criminal justice settings.

- For more information, see [http://www.drugabuse.gov/ResearchReports/hiv/hiv.html](http://www.drugabuse.gov/ResearchReports/hiv/hiv.html)
- For more information, see [http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm).
- This example also appears in Chapter 2: *Minority Health and Health Disparities* and Chapter 3: *Clinical and Translational Research*.
- (E) (NIDA)

**Special Journal Issue: “Cultural Dynamics in HIV Prevention Among Young People”**: Twenty-five years of behavioral and biomedical research have led to breakthroughs in the prevention and treatment of HIV disease; however, young people have not fully benefited from these advances. In September 2005, NIH held a workshop, “Cultural Dynamics in HIV/AIDS Biobehavioral Research Among Young People.” In March 2007, a special issue of the *Journal of the Association of Nurses in AIDS Care* presented a series of papers developed from this workshop. These papers are focused on current research into preventing the spread of HIV infection among youths from many cultures across the United States and around the world.

- [Hare ML, Villarruel AM. J Assoc Nurses AIDS Care 2007;18:1-4, PMID: 17403490](http://www.ninr.nih.gov/NewsAndInformation/JANAC/)
- For more information, see [http://www.ninr.nih.gov/NewsAndInformation/JANAC/](http://www.ninr.nih.gov/NewsAndInformation/JANAC/).
- (E) (NINR)

**Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN)**: Although one-third to one-half of new HIV infections occur among adolescents and young adults, researchers know little about how the complex physiological changes associated with adolescence impact the transmission dynamics and course of HIV infection. NIH is supporting a national clinical research network to address the unique challenges and clinical management needs of HIV-positive youth and those at risk of infection. Researchers in this network are building the capacity to develop and conduct selected biomedical, behavioral, and community-based studies, including vaccine and microbicide trials to ensure that the needs of high-risk teens (e.g., alcohol- or drug-abusing adolescents) have access to the most promising treatment and prevention interventions as they are being developed.

- For more information, see [http://www.atnonline.org](http://www.atnonline.org)
- This example also appears in Chapter 2: *Life Stages, Human Development, and Rehabilitation*.
- (E) (NICHD, NIDA, NIMH)

**Diagnosis of Malaria by Microscopy**: Virtually all clinical decisions, epidemiological surveys, field trials of drugs and vaccines, and evaluations of intervention programs in malaria depend on diagnoses made by microscopy. NIH has undertaken the first systematic analysis of errors and sources of error in malaria microscopy. This multiyear study includes the best malaria clinics in the tropical world and found 13 percent false-negative and 24 percent false-positive rates. Follow-up work is analyzing the accuracy and effect of different microscopy techniques, using different blood samples from the same patient, different microscope slides from the same blood sample, aspects
of parasite and patient biology, microscopist training, and other factors.

- (O) (FIC)

**Microbicides:** With more than 19.2 million women worldwide living with HIV/AIDS and more than 80 percent of HIV infections spread through heterosexual activity, NIH collaborative research is developing new ways to help women protect themselves from the virus. This includes the development and testing of agents that, if applied topically to genital areas, inactivate the virus or otherwise prevent susceptible cells from being infected with HIV. Scientists are working to develop, standardize, and validate innovative ways to rapidly screen large numbers of potential antimicrobial agents for irritation and safety. In addition, work is under way to examine the behavioral and social factors influencing whether individuals or couples would adopt and use new antimicrobial products consistently and effectively.

- (E) (NICHD, NIAID)

**Culturally Appropriate Research to Prevent HIV Infection:** Great strides have been made in the past 25 years in treatment and prevention strategies to combat the spread of HIV/AIDS in the United States. However, many populations in the United States and around the world have not benefited from these developments, and this is especially true for young people. One possible reason for such disparities is the influence of cultural differences on the effectiveness of prevention and treatment strategies. In fall 2006, NIH solicited proposals for innovative research to design and test interventions to prevent HIV transmission among young people. Areas of research interest include developing prevention/treatment interventions for young people with HIV/AIDS that take into account the cultural differences of those infected, determining the influence of cultural differences on how young people view living with HIV/AIDS and how these differences affect their views on preventing the spread of the disease, and examining challenges in transferring successful interventions across cultures, especially to other parts of the world.

- (E) (NINR)

**The Program in HIV/AIDS < Cancer Virology:** The mission of this program is to facilitate and rapidly communicate advances in the discovery, development, and delivery of antiviral and immunologic approaches for the prevention and treatment of HIV infection, AIDS-related malignancies, and cancer-associated viral diseases. This includes basic laboratory, translational, and clinical studies of disease pathogenesis and the development of novel targeted treatment approaches for cancers in HIV-infected individuals, as well as HIV infection itself, and drug resistance. Recent advances include a new prophylactic vaccine for HPV and promising candidates for prophylactic and therapeutic vaccines for HIV.

- For more information, see [http://ccr.nci.nih.gov](http://ccr.nci.nih.gov)
- This example also appears in Chapter 2: *Cancer.*
- (E/I) (NCI)

**The NCI Vaccine Program:** NCI’s vaccine program develops novel vaccines for cancer immunotherapy and prevention and HIV. The program encourages collaborations, identifies organizational and reagent needs for the community, and develops the optimal infrastructure for vaccine development and novel clinical trial approaches. Gardasil®, the first vaccine to prevent cervical cancer induced by HPV, is now available and can potentially save
more than 5,000 U.S. women's lives each year. This FDA-approved vaccine resulted from the basic research performed at NIH that produced a prototype vaccine and the observation that linked HPV and cervical cancer.

- This example also appears in Chapter 2: Cancer and Chapter 3: Clinical and Translational Research
- (E/I) (NCI)

**Retrovirus Epidemiology Donor Study (REDS):** REDS was begun by NIH in 1989 to determine the prevalence and incidence of HIV infection among blood donors and the risks of transmitting HIV and other viruses via transfusions. In 2004, NIH launched REDS-II to monitor the appearance of newly discovered infectious agents in the blood supply, evaluate the characteristics and behaviors of voluntary blood donors, determine the causes of transfusion reactions of unknown etiology, assess the results of new donor screening methods, assess the effects of new blood-banking technologies, and evaluate the donation process. In 2005, an international component was added to REDS-II to conduct research on blood donors in selected countries seriously affected by the AIDS epidemic to ensure the safety and availability of blood for transfusion.

- For more information, see [http://clinicaltrials.gov/ct/show/NCT00097006;jsessionid=7A9763F65A8C734DA771CDB5210D4877?order=7](http://clinicaltrials.gov/ct/show/NCT00097006;jsessionid=7A9763F65A8C734DA771CDB5210D4877?order=7)
- This example also appears in Chapter 3: Epidemiological and Longitudinal Studies.
- (E) (NHLBI)

**Improved Management of Antiretroviral Therapy for Adults and Children:** Two recent NIH studies transformed the management of antiretroviral therapy by extending the survival of adults and children with HIV/AIDS. Results from the Strategies for Management of Antiretroviral Therapy (SMART) study, one of the largest HIV/AIDS treatment trials ever conducted, showed that episodic use of antiretroviral therapy based on CD4+ cell levels is inferior to the use of continuous therapy for treatment-experienced patients and that deliberately interrupting antiretroviral therapy more than doubles the risk of developing AIDS or dying from any cause. The Children with HIV Early Antiretroviral Therapy (CHER) Study examined early antiretroviral therapy in South African children. Interim data showed a 96 percent increase in survival among infants who received immediate antiretroviral therapy compared with infants who received therapy later.

- This example also appears in Chapter 3: Clinical and Translational Research.
- (E) (NIAID)

**New Approaches to Diagnostics:** Recognizing the urgent need for rapid, highly sensitive, and specific clinical diagnostics that can diagnose individuals exposed to or infected by human pathogens, NIH has developed a comprehensive research program that is taking advantage of genomic information and emerging technologies, such as nanotechnology, to develop new and improved diagnostic tools. The program covers a broad range of activities, including the development of improved sample preparation and processing, platform development, enhanced detection methods, and clinical validation. Program priorities include development of tools that can distinguish between a variety of pathogens or that can determine pathogen subtypes and their sensitivity to drug treatments.

- (E) (NIAID)

**NIAID HIV Vaccine Research Education Initiative (NHVREI):** This new national initiative is designed to educate the
public about HIV vaccine research, especially at-risk populations such as African Americans, Hispanics, men who have sex with men, and women at high risk of HIV infection. The goal is to increase awareness about the urgent need for an HIV vaccine within the communities that are most affected by HIV/AIDS, create a supportive environment for current and future volunteers in HIV vaccine trials, and improve the public's perceptions and attitudes toward HIV vaccine research. The NHVREI Local Partnership Program provides support to partner organizations in targeted communities to help achieve the initiative’s goals.

- For more information, see http://www3.niaid.nih.gov/news/newsreleases/2006/bethegeneration.htm
- This example also appears in Chapter 3: Health Communication and Information Campaigns and Clearinghouses.
- (E) (NIAID)

Research Agenda for MDR-TB/XDR-TB: Diagnosing, treating, and controlling the spread of TB has become increasingly complicated by the HIV/AIDS co-epidemic and the emergence of MDR-TB and XDR-TB, which together threaten to set TB control efforts back to the pre-antibiotic era. In response to this urgent situation, in June 2007, NIH released its research agenda, Multidrug-Resistant and Extensively Drug-Resistant Tuberculosis. The research priorities identified in the agenda build on a foundation of ongoing NIH-supported TB research, which currently comprises more than 300 research projects worldwide. This Web-based “living document,” identified as such because of NIH’s ability to modify, amend, or update it as scientific and public health needs and opportunities evolve, was prepared in close collaboration with other Government and non-Government organizations and reviewed by TB specialists in academia, advocacy groups, international organizations, and other Government agencies. It identifies six critical areas for additional investigation: (1) new TB diagnostic tools, (2) improved therapies for all forms of TB, (3) basic biology and immunology of TB, (4) MDR-TB and XDR-TB epidemiology, (5) clinical management of MDR-TB and XDR-TB in people with and without HIV infection, and (6) TB prevention, including vaccines.

- For more information, see http://www3.niaid.nih.gov/topics/tuberculosis
- (E/I) (NIAID)

The Evolving HIV Epidemic: Beyond Intravenous Drug Use: The nature of the HIV epidemic in this country is changing. Effective medications and HIV risk reduction interventions in intravenous drug abusers have helped to curb the spread of HIV though injection drug use to a point where it now accounts for a smaller percentage of new infections. However, drug abuse continues to play a major role in the spread of HIV through other mechanisms: drug abusers proffer sexual behaviors to obtain drugs or money to support their addiction, and drugs of abuse can worsen the course of the illness and produce intoxication, which can alter judgment and decision-making and lead to impulsive and risky sexual behaviors. Recognition of this link is critical for developing more integrated and effective prevention strategies. A critical aspect of this message is that treatment of drug abuse is HIV prevention, an idea being furthered by NIH in concert with other Federal agencies, such as CDC.

- For more information, see http://www.drugabuse.gov/ResearchReports/HIV/HIV.html
- (E) (NIDA)

Understanding Factors Affecting the Use of Microbicides: NIH is planning an initiative on research directed toward understanding the complex interplay among individual, dyadic, social, and other contextual factors that may influence the initiation and sustained use of microbicides that are proven to be efficacious in reducing the risk of acquiring or transmitting HIV. In addition, the initiative will address research on prevention strategies that incorporate the use of microbicides and on the development of behavioral and social tools to assess product acceptability, initiation, and sustained use in a manner that will directly inform microbicide product development
and improvement.

- (E) (NIH)

**OAR-Sponsored Initiatives Targeting Scientific Needs in AIDS Research:** OAR, through its planning process, identifies scientific areas that require focused attention and facilitates innovative, cross-institute, multi-institute, multidisciplinary activities to address those needs. OAR fosters these efforts by designating resources to jump-start program areas through funds for grant supplements to the ICs, establishing working groups or committees, sponsoring workshops or conferences to highlight a particular research topic, and sponsoring reviews or evaluations of research program areas. Examples include a Microbicide Innovation Program to accelerate the discovery of single and/or combination microbicides against HIV and STDs and a Prevention Science Initiative to foster innovative research in HIV prevention. OAR also supports initiatives to enhance dissemination of research findings, including sponsorship of a group of scientific panels that develop AIDS treatment and prevention guidelines, and the distribution of those guidelines through AIDSinfo, a Web-based service to provide up-to-date information for caregivers and patients about AIDS treatment and prevention.

- For more information, see [http://www.oar.nih.gov](http://www.oar.nih.gov)
- (O) (OAR)

**Trans-NIH Management and Coordination of HIV/AIDS Research:** NIH is the world's leader in AIDS research, representing the largest and most significant public investment in AIDS research in the world. Our response to the pandemic requires a unique and complex multi-institute, multidisciplinary, global research program. NIH supports a comprehensive program of basic, clinical, and behavioral research on HIV infection and its associated co-infections, opportunistic infections, malignancies, and other complications. Perhaps no other disease so thoroughly transcends every area of clinical medicine and basic scientific investigation, crossing the boundaries of nearly every NIH IC. This diverse research portfolio demands an unprecedented level of scientific coordination and management of research funds. OAR, located within the NIH Office of the Director, coordinates the scientific, budgetary, and policy elements of NIH AIDS research. Through its unique, trans-NIH planning, budgeting, and portfolio assessment processes, OAR ensures that AIDS research dollars are invested in the highest priority areas of scientific opportunity, allowing NIH to pursue a united research front against the pandemic.

- For more information, see [http://www.oar.nih.gov](http://www.oar.nih.gov)
- (O) (OAR)

**Development of New TB Diagnostic Tool:** By detecting TB as early as possible, health providers can more effectively treat and control the disease in a population. An NIH-funded investigator working in Lima, Peru, has developed a new assay for TB. This simple and relatively inexpensive diagnostic test offers faster, more sensitive detection of TB and drug-resistant TB than the currently used method and cuts diagnostic time from an average of 28 days to 7 days. The new, inexpensive method is appropriate for countries with limited resources, and several countries are in the process of incorporating it into TB control protocols.

- (E) (FIC, NIAID)

**Adult Male Circumcision Significantly Reduces Risk of Acquiring HIV:** NIH-supported scientists announced an early end to two clinical trials of adult male circumcision because an interim review of trial data revealed that medically performed circumcision, with appropriate care in the postoperative period, significantly reduces a man's risk of
acquiring HIV through heterosexual intercourse. The trials, which enrolled 2,784 men in Kisumu, Kenya, and 4,996 men in Rakai, Uganda, showed that HIV acquisition in circumcised men relative to uncircumcised men was reduced by roughly half. Although the initial benefit will be fewer HIV infections in men, ultimately adult male circumcision could lead to fewer infections in women in those areas of the world where HIV is spread primarily through heterosexual intercourse. Circumcision remains only part of a broader HIV prevention research agenda that includes development of vaccines, microbicides, behavioral interventions, and prevention of mother-to-child transmission.

- (E) (NIAID)

**Emerging Infectious Diseases and Biodefense**

**Biodefense Vaccines:** NIH is the lead Federal agency within HHS for conducting research on potential agents of bioterrorism that directly affect human health. The terrorist attacks of September 11, 2001, and the deliberate exposure of civilians to anthrax spores prompted HHS to emphasize the importance of advancing vaccines for specific pathogens that could be used in bioterrorist attacks. In response, in February 2002, NIH convened the Blue Ribbon Panel on Bioterrorism and Its Implications for Biomedical Research. This panel was brought together to provide objective expertise on NIH’s future biodefense research agenda in both the short and the long term. As expected, one of the identified areas of research emphasis was the development of new and improved vaccines against agents of bioterrorism, with the initial focus on smallpox and anthrax. Since that time, substantial progress has been made in biodefense vaccine research and development, which has resulted in the following advances:

- Modified Vaccinia Ankara, a new, safer smallpox vaccine that is the outcome of several years of NIH-sponsored research and development, has been purchased for the Strategic National Stockpile.
- An Ebola vaccine has been developed and is currently being tested in humans at NIH.
- A promising new anthrax vaccine candidate made with a purified protein has been developed and will enable researchers to determine the minimum level of protein needed to confer protection and minimize side effects.

- (E/I) (NIAID, NICHD)

**Microneedle-Based Immunization Against Pandemic Influenza:** NIH is supporting a team of investigators under the Bioengineering Research Partnership grant mechanism to develop a low-cost, room temperature-stable, microneedle-based transdermal vaccine patch against pandemic influenza that could be rapidly distributed through pharmacies, fire stations, or the U.S. mail and painlessly self-administered. This dose-sparing delivery system will not produce any sharp, biohazardous waste and would avoid the expensive and time-consuming hypodermic vaccination process administered by medical personnel, thus allowing for a rapid response to pandemic influenza. This innovative application impacts the “HHS Pandemic Influenza Plan” and NIH's directives on high-priority influenza research areas.

- For more information, see [http://www.hhs.gov/pandemicflu/plan](http://www.hhs.gov/pandemicflu/plan)
- This example also appears in Chapter 3: Technology Development.
- (E) (NIBIB)

**Probes and Cell Arrays for Detection of Bacterial Toxins:** Microarray technology offers an opportunity for
simultaneous monitoring the behavior of multiple markers within a mammalian cell and ultimately could be used for detection and elucidation of mechanisms of action of different biologically active agents, including those that are considered a threat in the biodefense area. The ultimate goal of this research project is to provide a general and robust approach for the detection of biologically active agents, especially when these agents have been engineered to elude currently available immunoassays. Cell arrays offer a new opportunity for sensitive and precise monitoring of biologically active substances. The goal of this project is to develop a system for the identification of regulatory elements that will allow a substantial extension of the discriminative abilities of cell arrays and the creation of cell arrays that are capable of detection and identification of potential biowarfare agents.

- (E) (NIEHS)

**Antimicrobial Resistance Research:** Antimicrobial resistance, which is caused by factors such as overuse of antibiotics, is severely jeopardizing the utility of many “first-line” antimicrobial agents and has emerged as a major public health threat. NIH supports a robust basic research portfolio on antimicrobial resistance, including studies of how bacteria develop and share resistance genes. NIH is also pursuing translational and clinical research in this area, including clinical studies to test interventions for community-acquired MRSA infection, and to evaluate the efficacy of off-patent antimicrobial agents. NIH will continue to address high-priority research questions regarding resistance to help public health officials hold the line against drug-resistant microbes.

- For more information, see [http://www.niaid.nih.gov/factsheets/antimicro.htm](http://www.niaid.nih.gov/factsheets/antimicro.htm)
- This example also appears in Chapter 3: *Clinical and Translational Research.*
- (E) (NIAID) (GPRA Goal)

**Ecology of Infectious Diseases (EID):** Jointly administered by NIH and the National Science Foundation (NSF), the EID program uniquely fills a critical gap in our national effort to protect public health against the threat of emerging infectious diseases. Most emerging diseases are initially transmitted from animals to humans, and some are capable of becoming pandemics. This program supports the discovery of the principles that govern the relationships between ecological disturbances and transmission of infectious agents, and the use of those principles to develop predictive models of epidemics. Potential benefits of the program include an increased capacity to forecast outbreaks and to improve understanding of how diseases emerge and reemerge.

- (E) (IFIC, NIAID, NIEHS)

**Biodefense Therapeutics Development:** Treatments against NIAID Category A-C priority pathogens, microbes, and toxins, which are considered to be the most significant threats to the Nation’s well-being, are either nonexistent, of limited utility, or threatened by the emergence of antimicrobial resistance or intentional engineering to increase virulence or decrease drug susceptibility. Given the absence of a substantial commercial market, regulatory hurdles, and extensive clinical trial requirements, the private sector has little incentive to invest in antimicrobial countermeasures. To remedy this situation, NIH supports unique partnerships among Government, industry, small businesses, and academia to facilitate the movement of promising products through all stages of the drug research and development pipeline, with the goal of developing therapeutics against diseases such as smallpox, botulism, and Ebola and West Nile virus infection. These projects range from preclinical services (such as performing medicinal and analytical chemistry, custom drug synthesis, formulation, clinical manufacturing, microbiology and virology screening, pharmacokinetics, and safety testing) to the development and testing of DAS 181 (Fludase),
which is potentially a broad-spectrum therapeutic agent for use against all annual and pandemic variations of influenza.

- For more information, see http://www3.niaid.nih.gov/topics/BiodefenseRelated/Biodefense/research/funding/FY2006+Awards/therapeutic_awards.htm
- (E/I) (NIAID)

**Developing New Adjuvants to Boost Vaccine Effectiveness:** The NIH Innate Immune Receptors and Adjuvant Discovery initiative encourages the discovery of novel adjuvants to meet the growing need to boost the effectiveness of vaccines against potential agents of bioterrorism and emerging infectious diseases. Adjuvants activate the body’s innate immune system—microbe-engulfing phagocytes and soluble immune stimulators—leading to effective adaptive immune responses by B cells, which make antibodies, and T cells, which can directly kill infected cells. Using high-throughput screening, several groups of researchers have identified, optimized, and developed adjuvants that are now in preclinical development.

- This example also appears in Chapter 3: *Molecular Biology and Basic Sciences.*
- (E) (NIAID)

**Medical Countermeasures Against Nuclear and Radiological Threats:** NIH is leading the HHS effort to sponsor and coordinate research to develop a means to counter the detrimental effects of a range of radiological threats. Most medical countermeasures to treat radiation injury are still in the early stages of development but are progressing. NIH-funded researchers recently (1) screened more than 40,000 candidate compounds and identified 52 candidates for evaluation as protective agents against the toxic effects of ionizing radiation, (2) developed improved forms of the chelating agent diethylenetriaminepentaacetic acid (DTPA), which animal testing data suggest can effectively clear the radionuclide americium-241 from the blood, and (3) studied 29 candidate drugs that are active against a broad range of radionuclides and might be useful in treating victims of radiological dispersion devices (“dirty bombs”).

- For more information, see http://www3.niaid.nih.gov/research/topics/radnuc
- This example also appears in Chapter 3: *Clinical and Translational Research.*
- (E) (NIAID)

**Pandemic and Seasonal Influenza Vaccine Research:** In FYS 2006 and 2007, NIH made significant progress toward the development of new and more effective vaccines for the control of both seasonal and pandemic influenza. For example, an NIH-supported clinical trial provided the scientific data on which the FDA based its recent licensure of the first pandemic influenza vaccine against H5N1 virus (“bird flu”) in the United States. NIH also developed and conducted clinical trials of whole-inactivated and live-attenuated vaccines against H5N1 influenza and developed DNA, recombinant virus, and recombinant protein-based influenza vaccines. NIH also supports activities to expand and accelerate the development of additional manufacturing methods; evaluate various strategies to optimize a limited vaccine supply, including intradermal vaccines and the use of adjuvants; and explore the concept of developing a vaccine that raises immunity to parts of the influenza virus that vary little from season to season and from strain to strain, thereby potentially reducing or eliminating the need for annual immunization against seasonal influenza. Such a vaccine might also strengthen protective immunity against an emerging pandemic strain of influenza virus.

- For more information, see http://www3.niaid.nih.gov/topics/flu/understandingflu/Prevention.htm
For more information, see http://www3.niaid.nih.gov/topics/Flu/PDF/InfluenzaBlueRibbonPanel2006.pdf

(E/I) (NIAID)

**Radiation Event Medical Management (REMM):** As a part of an effort to improve public health emergency preparedness and response, NIH and the HHS Office of the Assistant Secretary for Preparedness and Response announced in 2007 a new downloadable online diagnostic and treatment toolkit to guide health care providers during a mass casualty radiation event. The REMM toolkit includes easy-to-follow procedures for diagnosis and management of radiation contamination and exposure, guidance for the use of radiation medical countermeasures, and a variety of other features to facilitate medical responses to radiation emergencies.

For more information, see http://remm.nlm.gov

This example also appears in Chapter 3: Disease Registries, Databases, and Biomedical Information Systems.

(E/I) (NLM)

**Infrastructure and Research Resources**

**Biodefense Research Infrastructure:** NIH has invested substantially in the intellectual and physical infrastructure needed to build the Nation’s capacity for research on biodefense and emerging infectious diseases. This effort draws scientists from many disciplines to conduct research and development activities and to train future researchers. It also provides facilities that will greatly enhance the safe and efficient conduct of research on infectious agents. The NIH-funded infrastructure includes (1) 10 Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research, which use a multidisciplinary approach to research and development, (2) two National Biocontainment Laboratories (with BSL-4 capacity, the highest level of containment) and (3) 13 Regional Biocontainment Laboratories with BSL-3 capacity.

For more information, see http://www3.niaid.nih.gov/topics/BiodefenseRelated/Biodefense/PublicMedia/BioLabs.htm

(E/I) (NIAID) (GPRA Goal)

**The National Science Advisory Board for Biosecurity (NSABB):** NSABB was established to advise the U.S. Government on strategies for the efficient and effective oversight of dual-use biological research, taking into consideration both national security concerns and the needs of the research community. The term “dual use” in conjunction with life sciences research is an acknowledgment that some of the information and technologies used to advance human, animal, and plant health can also be used to threaten public health and safety. NSABB brings together 25 voting non-Federal members who represent the scientific, biosafety, security, legal, ethics, scientific publishing, and intelligence communities. In addition, there is active participation by 14 major Federal departments, agencies, and offices across the Government. NSABB has issued two sets of reports and recommendations. The first is focused on the biosecurity issues raised by the rapidly increasing ability to synthesize select agents and other dangerous pathogens. The report identifies a number of biosecurity considerations; assesses whether the current Federal regulations, policies, and guidelines afford adequate oversight in this arena; and provides recommendations for addressing the issues. The second report is a proposed framework for local and Federal oversight of dual-use research. It is intended as a springboard for the development of Federal guidelines and procedures for oversight of dual-use research and includes guidance for identifying dual-use research of concern, considerations for developing codes of conduct for life scientists, and considerations and tools for the responsible communication of dual-use research. NSABB is currently developing strategies for fostering international engagement of dual-use life sciences issues and for education and outreach regarding these issues.

For more information, see http://www.biosecurityboard.gov
HIV/AIDS Research Network Restructuring: To better address the evolving scientific challenges of the HIV/AIDS epidemic, in FY 2006 NIH restructured its HIV/AIDS clinical research infrastructure into six research networks: the AIDS Clinical Trials Group (ACTG), the HIV Prevention Trials Network (HPTN), the HIV Vaccine Trials Network (HVTN), the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Group, the International Network for Strategic Initiatives in Global HIV Trials (INSIGHT), and the Microbicide Trials Network (MTN). Each network consists of a leadership group that provides administrative and technical support, as well as a number of the 73 HIV/AIDS Clinical Trials Units NIH funds in the United States and abroad (some Clinical Trials Units belong to more than one network). The reorganization will improve the efficiency, flexibility, and coordination of HIV/AIDS clinical research.

- This example also appears in Chapter 3: Clinical and Translational Research.
- (E) (NIAID) (GPRA Goal)

Translational Research at Primate Research Centers: Nonhuman primates are critical components for translational research because of their close physiological similarities to humans. Nonhuman primates are widely used for both hypothesis-based and applied research directly related to human health, such as the development and testing of vaccines and therapies. The NIH-supported National Primate Research Centers and other primate resources provide investigators with the animals, facilities, specialized assays, and expertise to perform translational research using nonhuman primates. In FY 2007, more than 1,000 research projects used nonhuman primates from these resources. Highlights of research activities include:

- Use of the simian immunodeficiency virus for AIDS-related research, including development of novel microbicides to prevent infection by the AIDS virus and testing of AIDS vaccines
- Identification of the central role of specific genes and molecules in drug addiction and neurological conditions and diseases, studies of the biochemistry and physiology of drug and alcohol addiction, and development of stem cell-based therapies for neurodegenerative diseases
- Sponsored scientific workshops in FYs 2006 and 2007 that further defined the genetic tools necessary for translational research using nonhuman primates

- For more information, see [ncrr.nih.gov/comparative%5Fmedicine/resource_directory/primates.asp](http://ncrr.nih.gov/comparative%5Fmedicine/resource_directory/primates.asp)
- This example also appears in Chapter 3: Clinical and Translational Research.
- (E) (NCRR)

Centers of Excellence for Influenza Research and Surveillance: Six Centers of Excellence for Influenza Research and Surveillance, established in 2007, significantly expand the ability of NIH to conduct research on different strains of animal and human influenza viruses collected internationally or in the United States. The centers will lay the groundwork for the development of new and improved control measures for emerging and reemerging influenza viruses, help determine the prevalence of avian influenza viruses in animals in close contact with humans, and extend understanding of how influenza viruses evolve, adapt, and are transmitted. The centers will also bolster research on questions such as how influenza viruses cause disease and how the human immune system responds to infection and will inform public health strategies to control and minimize the impact of seasonal and pandemic influenza.

- For more information, see [http://www3.niaid.nih.gov/research/resources/ceirs](http://www3.niaid.nih.gov/research/resources/ceirs)
• This example also appears in Chapter 3: Molecular Biology and Basic Sciences.
• (E) (NIAID)

**Urinary Tract Infections:** NIH supports a Specialized Center of Research on Sex and Gender Factors Affecting Women's Health. This program advances new understanding of host-pathogen interactions that occur throughout the infectious cycle, including host defense response in the bladder and the virulence mechanisms by which bacterial pathogens subvert the defenses.

- For more information, see [http://clinicaltrials.gov/ct/show/NCT00068120](http://clinicaltrials.gov/ct/show/NCT00068120)
- This example also appears in Chapter 2: Chronic Diseases and Organ Systems.
• (E) (NIDDK)

**NIH Countermeasures Against Chemical Threats (CounterACT) Research Network:** CounterACT, as reflected in an NIH GPRA goal, develops medical countermeasures to prevent, diagnose, and treat conditions caused by chemical agents that might be used in a terrorist attack or released by industrial accidents or natural disaster. The network, which has collaborated with DoD from its inception in 2006, includes Research Centers of Excellence, individual research projects, small business research grants, contracts, and other programs that conduct basic, translational, and clinical research. One promising countermeasure, midazolam, which DoD researchers identified as a potential countermeasure against chemical agent-induced seizures, is entering clinical trials in epilepsy patients through the NINDS Neurological Emergency Clinical Trials Network, and NIH is collaborating with DoD to complete animal studies necessary for its FDA approval as a nerve agent treatment.

- For more information, see [http://www.ninds.nih.gov/funding/research/counterterrorism/index.htm](http://www.ninds.nih.gov/funding/research/counterterrorism/index.htm)
- This example also appears in Chapter 2: Neuroscience and Disorders of the Nervous System.
• (E) (NINDS, NEI, NIAID, NIAMS, NIEHS, NIGMS)

**Influenza Virus Resource:** This database of more than 40,000 influenza virus sequences allows researchers around the world to compare different virus strains, identify genetic factors that determine the virulence of virus strains, and look for new therapeutic, diagnostic and vaccine targets. The resource was developed by NCBI using data obtained from NCB|’s Influenza Virus Sequence Database and from NIAID|’s Influenza Genome Sequencing Project, which has contributed sequences of the complete genomes from more than 2,500 influenza samples. In FY 2006 more than 11,000 influenza virus sequences were entered into the database, and new search and annotation tools were added to assist researchers in their analyses.

- For more information, see [http://www.niaid.nih.gov/dmid/genomes/mscs/influenza.htm](http://www.niaid.nih.gov/dmid/genomes/mscs/influenza.htm)
- This example also appears in Chapter 3: Disease Registries, Databases, and Biomedical Information Systems, Chapter 3: Genomics, and Chapter 3: Molecular Biology And Basic Sciences
• (I) (NLM)

**Wireless Information System for Emergency Responders (WISER®):** WISER is a system designed to assist first responders in hazardous material incidents by providing a wide range of information on hazardous substances, including substance identification support, physical characteristics, human health information, and containment and suppression advice. In 2007, several important features were added to WISER, including radiological support

- For more information, see http://wiser.nlm.nih.gov
- This example also appears in Chapter 3: Technology Development.
- (I) (NLM)

**HIV/AIDS Epidemiological and Long-Term Cohort Studies:** NIH supports epidemiological HIV research through a wide range of cohort studies that contribute to our understanding of risk factors that lead to HIV transmission and disease progression. Established in 2005, the International Epidemiologic Databases to Evaluate AIDS (IeDEA) compiles data from NIH-funded international HIV research to answer population-level questions about HIV variants and resistance, HIV pathogenesis in different settings, success of antiretroviral therapy, treatment history of HIV in different populations, success of prevention strategies, and vaccines. The Pediatric HIV/AIDS Cohort Study (PHACS), established in 2005, addresses two critical pediatric HIV research questions: the long-term safety of fetal and infant exposure to prophylactic antiretroviral chemotherapy and the effects of perinatally acquired HIV infection in adolescents. The Women's Interagency HIV Study (WIHS) and the Multicenter AIDS Cohort Study (MACS) are the two largest observational studies of HIV/AIDS in women and homosexual or bisexual men, respectively, in the United States. These studies exceed standard clinical care diagnostics and laboratory analysis on both HIV-infected, and, importantly, HIV-negative controls, which allows for novel research on how HIV spreads, how the disease progresses, and how it can best be treated. The studies focus on contemporary questions such as the interactions among HIV infection, aging, and long-term treatment; cardiovascular disease; and host genetics and their influence on susceptibility to infection, disease progression, and response to therapy.

- For more information, see http://www3.niaid.nih.gov/about/organization/daids/daidsepi.htm
- This example also appears in Chapter 2: Life Stages, Human Development, and Rehabilitation and Chapter 3: Epidemiological and Longitudinal Studies.
- (E) (NIAID, NICHD)

**National NeuroAIDS Tissue Consortium (NNCT):** The NNCT is a repository of brain tissue and fluids from highly characterized HIV-positive individuals. Established as a resource for the research community, NNCT includes information from more than 2,000 individuals, including approximately 641 brains, thousands of plasma and cerebrospinal fluid samples, and additional organs and nerves of interest.

- For more information, see http://grants1.nih.gov/grants/guide/rfa-files/RFA-MH-08-021.html
- This example also appears in Chapter 2: Neuroscience and Disorders of the Nervous System and Chapter 3: Disease Registries, Databases, and Biomedical Information Systems.
- (E/I) (NIMH, NINDS)

**International Collaboration**

**Success in Treating Drug Addiction Internationally:** International efforts to disseminate effective drug abuse treatments have seen success in countries with epidemic opiate addiction/HIV problems. Because of NIH research demonstrating that addiction is a chronic, relapsing disease that can be effectively treated, a culture change is starting to occur in these countries. For example, despite experiencing severe drug problems, Malaysia lagged behind in the treatment of drug addiction and related disorders, even as it coped with having the second-highest
HIV prevalence rate among adult populations and the highest proportion of HIV cases from injection drug use. Historically, drug abusers were “rehabilitated” involuntarily in correctional facilities. Although 60 percent of prisoners had drug-related offenses, no or minimal treatment was available in prison, and no medications were permitted. This primarily criminal treatment approach had limited effectiveness, which led to widespread public dissatisfaction and the recent introduction of medications for addiction. These include naltrexone (1999), buprenorphine (2001), and methadone (2003). These drug treatment programs, which were rapidly embraced by the country’s medical community, have resulted in tens of thousands of opiate-dependent patients receiving medical treatment. Now, the Ministry of Health rather than the Ministry of Security has authority for providing medical treatment for heroin addiction. This shift signals a remarkable change in Malaysian policies and approaches to addiction and an important opportunity to develop, implement, and disseminate effective treatments. A similar success story is starting to unfold in China as well.

- This example also appears in Chapter 2: Chronic Diseases and Organ Systems and Chapter 3: Clinical and Translational Research.
- (E) (NIDA, NIAID)

**Multinational Influenza Seasonal Mortality Study:** NIH is leading an international collaborative effort to analyze national and global epidemiological patterns associated with influenza virus circulation. Twenty countries have contributed data on mortality, virus surveillance, genomics, and control strategies. The goals of this large-scale collaboration are to evaluate and compare public health strategies to alleviate the impact of seasonal influenza in different countries and to understand the global circulation patterns of influenza and their impact on populations. A better understanding of influenza epidemiology worldwide can inform vaccine strain selection and strategies to mitigate future influenza pandemics.

- For more information, see [http://origem.info/misms](http://origem.info/misms)
- This example also appears in Chapter 3: Epidemiological and Longitudinal Studies.
- (O) (FIC)

**HIV Vaccine Development:** NIH supports research around the world to find a safe and effective vaccine against HIV. Since the first HIV vaccine trial in 1987, NIH has worked with its partners in academia, Government, the private sector, and non-Government organizations to conduct more than 100 HIV vaccine clinical trials that have enrolled more than 26,000 volunteers. In 2005, NIH formed the Center for HIV/AIDS Vaccine Immunology (CHAVI), a consortium of scientists committed to overcoming key scientific roadblocks to HIV vaccine development and to designing and testing HIV vaccine candidates. NIH is also involved in the Global HIV Vaccine Enterprise and the Partnership for AIDS Vaccine Evaluation (PAVE). Several clinical trials are testing vaccine candidates around the globe. Recently, however, two large vaccine trials stopped immunizations upon recommendation of a Data Safety Monitoring Board review. However, the new large-scale trial, called PAVE 100, is still under discussion and may begin in 2008. This trial will test whether an NIH-developed candidate vaccine can prevent acquisition of infection or progression of disease (using viral load as a surrogate marker) in those who become infected.

- For more information, see [http://www3.niaid.nih.gov/topics/HIVAIDS/Research/vaccines/default.htm](http://www3.niaid.nih.gov/topics/HIVAIDS/Research/vaccines/default.htm)
- (E/I) (NIAID) (GPRA Goal)

**Global Infectious Disease Research Training:** A major barrier to improved treatment and control of infectious diseases is the scarcity in endemic countries of scientists with expertise in infectious disease research. This program supports institutions in the United States and developing countries to train scientists from developing
countries to engage in research on infectious disease other than HIV/AIDS. The program is contributing to the long-term goal of building sustainable research capacity in endemic infectious diseases in institutions in developing countries to enhance prevention, treatment, and control of infectious diseases that cause major morbidity and mortality in the developing world.

- For more information, see [http://www.fic.nih.gov/programs/training_grants/gid.htm](http://www.fic.nih.gov/programs/training_grants/gid.htm)
- This example also appears in Chapter 3: Research Training and Career Development.
- (E) (FIC, NIAID)

**HIV Research Training Programs:** The AIDS International Training and Research Program (AITRP) builds institutional, national, and regional HIV research capacity in low- and middle-income countries. Over the past 19 years, this program has been responsible for many of the first generation of research scientists from these countries, with many more in the pipeline. The program offers multidisciplinary biomedical, behavioral, and social science research training to a wide range of professionals. Building on the AITRP, the Clinical, Operational and Health Services Research Training Program for HIV/AIDS and TB (ICOHRTA AIDS/TB) began in 2002 to strengthen the capacity for clinical, operational, and health services research in low- and middle-income countries where AIDS, TB, or both are significant problems. Through training health professionals that reach across the spectrum of clinical and public health research, this program is strengthening the capacity of scientists, program managers, and policymakers to evaluate and better implement large-scale prevention, treatment, and care interventions that are locally relevant and effective. Many local leaders of programs supported by the President’s Emergency Plan for AIDS Relief have received or are receiving their research training through the AITRP and the ICOHRTA AIDS/TB programs.

- For more information, see [http://www.fic.nih.gov/programs/training_grants/aitrp/index.htm](http://www.fic.nih.gov/programs/training_grants/aitrp/index.htm)
- For more information, see [http://www.fic.nih.gov/programs/training_grants/icohrtas/aids_tb.htm](http://www.fic.nih.gov/programs/training_grants/icohrtas/aids_tb.htm)
- This example also appears in Chapter 3: Clinical and Translational Research and Chapter 3: Research Training and Career Development.
- (E) (FIC, NCI, NIAID, NHLBI, NIDA, NIDCR, NIMH, NINDS, NINR, OAR, ORWH)

**Mechanisms of HIV Neuropathogenesis: Domestic and Global Issues:** Neurological manifestations, including HIV dementia and opportunistic infections and tumors, are among the most threatening complications of HIV infection. Emerging data indicate that the prevalence of HIV-related neurological disease differs across regions of the world, suggesting that different subtypes of HIV may be more or less capable of causing neuropathology or that genetic variance among people in various regions of the world could affect susceptibility to HIV’s neuropathological effects. NIH sponsored a meeting in the spring of 2007 to address these issues, resulting in the release of a funding announcement.

- For more information, see [http://synapse.neurology.unc.edu/venice/](http://synapse.neurology.unc.edu/venice/)
- This example also appears in Chapter 2: Neuroscience and Disorders of the Nervous System.
- (E) (NIMH, NINDS, OAR)

**HIV Virus Transmission From Primates to Humans:** Through the International Research Scientist Development Award (IRSDA), FIC provides career development and research support to U.S. postdoctoral scientists in the formative stages of their careers to solidify their commitment to global health research. For example, under this program, FIC supported the career development of Dr. Nathan Wolfe, whose work in Cameroon advanced our understanding of how retroviruses enter into human populations and determined that the likely point of
transmission of the HIV occurred between primates and bushmeat hunters. Dr. Wolfe has now received the NIH Director's Pioneer Award. Co-funded by FIC and NIAID, this award builds on Dr. Wolfe's IRSDA-supported research and is enabling the establishment of the first global network to monitor the transmission of new viruses, including those causing pandemic disease threats such as Ebola, anthrax, and monkeypox, from animals into human populations. This hunter cohort distributed throughout key habitats will provide a framework for a range of research projects aimed at predicting and preventing disease emergence, including studies of risk factors associated with primary and secondary infections with zoonotic microorganisms, anthropological studies of hunting and meat processing practices that lead to exposure, and ecological studies of the animal and human populations that influence transmission among and between groups.

- For more information, see http://www.fic.nih.gov/programs/training_grants/irsd.htm
- This example also appears in Chapter 3: Research Training and Career Development.
- (E) (FIC)

NIH Strategic Plans Pertaining to Infectious Diseases and Biodefense Research

National Institute of Allergy and Infectious Diseases (NIAID)


HIV/AIDS

- Vaccine Research Center Strategic Plan: Research Toward Development of an Effective AIDS Vaccine (2001)

Infectious Diseases (non-biodefense, non-AIDS)

- Blueprint for Tuberculosis Vaccine Development (1997)

Biodefense and Emerging Infectious Diseases

- NIAID Strategic Plan for Biodefense Research (2007 update)
- NIAID Strategic Plan for Biodefense Research (2002)
- NIAID Biodefense Research Agenda for CDC Category A Agents (2002)
Special Populations

- *Women's Health in the U.S.: Research on Health Issues Affecting Women (2004)*

National Institute of Dental and Craniofacial Research (NIDCR)

- *NIDCR Strategic Plan*
- *NIDCR Implementation Plan*

Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)

Branch Reports to Council with Future Scientific Directions

- *Pediatric, Adolescent, and Maternal AIDS Branch (PAMAB), NICHD, Report to the NACHHD Council, June 2007*

National Institute on Drug Abuse (NIDA)

- *Bringing the Power of Science to Bear on Drug Abuse and Addiction* (under revision)

National Institute on Alcohol Abuse and Alcoholism (NIAAA)

- *National Institute on Alcohol Abuse and Alcoholism Five-Year Strategic Plan, FY08-13*
- Recommendations of the NIAAA Extramural Advisory Board (EAB)
- *Developing an NIAAA Plan for HIV-Related Biomedical Research*

National Center for Complementary and Alternative Medicine (NCCAM)

- *Expanding Horizons of Health Care: Strategic Plan 2005-2009*

John E. Fogarty International Center (FIC)

- *Pathways to Global Health Research* (Draft)

Office of AIDS Research (OAR)

- *FY 2008 Trans-NIH Plan for HIV-Related Research*
  CC, CSR, FIC, NCCAM, NCI, NCMBD, NCRR, NEI, NHGRI, NHLBI, NIA, NIAAA, NIAID, NIAMS, NIBIB, NICH, NIDA, NIDCD, NIDCR, NIDDK, NIEHS, NIGMS, NIMH, NINDS, NINR, NLM, OAR, OBSSR, OIR, ORD, ORWH

Other Trans-NIH Strategic Plans

- *NIH Strategic Plan and Research Agenda for Medical Countermeasures Against Radiological and Nuclear Threats*
  NCI, NHLBI, NIAID, NIEHS