

DEPARTMENT OF HEALTH AND HUMAN SERVICES

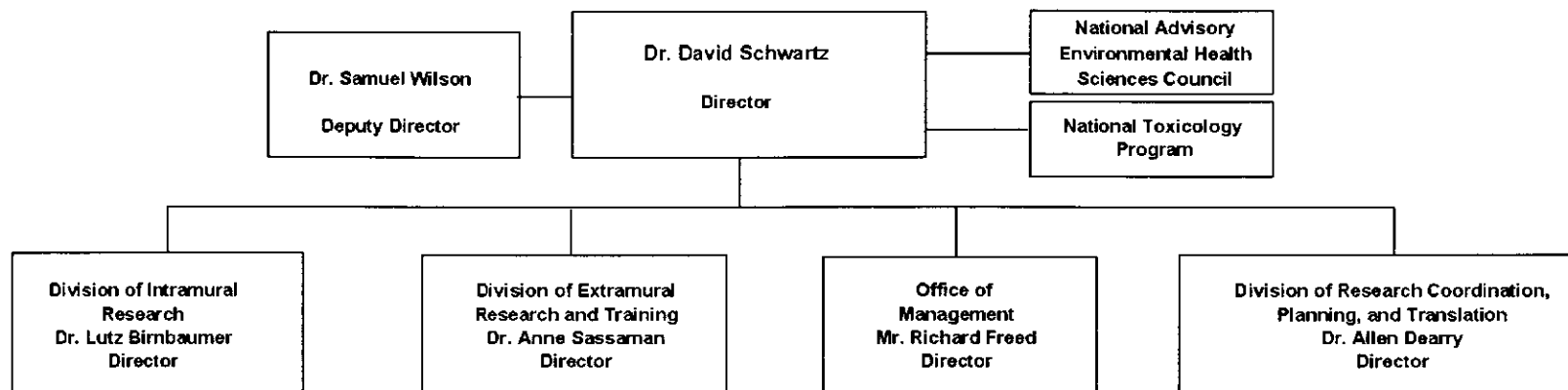
NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

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**NATIONAL INSTITUTES OF HEALTH**  
**National Institute of Environmental Health Sciences**

Organization Structure



## **NATIONAL INSTITUTES OF HEALTH**

### **National Institute of Environmental Health Sciences**

For carrying out sections 301 and 311 of title IV of the Public Health Service Act with respect to environmental health sciences, [\$647,608,000] *\$637,323,000*.

[Departments of Labor, Health and Human Services, Education and Related Agencies Appropriations Act, 2006, as enacted by Public Law (109-149)]

**National Institutes of Health  
National Institute of Environmental Health Sciences**

**Amounts Available for Obligation 1/**

Source of Funding	FY 2005 Actual	FY 2006 Appropriation	FY 2007 Estimate
Appropriation	\$650,027,000	\$647,608,000	\$637,323,000
Enacted Rescissions	(5,522,000)	(6,476,000)	---
Subtotal, Adjusted Appropriation	644,505,000	641,132,000	637,323,000
Real transfer under NIH Director's one-percent transfer authority for Roadmap	(4,075,000)	(5,729,000)	
Comparative transfer from OD for NIH Roadmap	4,075,000	5,729,000	
Subtotal, adjusted budget authority	644,505,000	641,132,000	637,323,000
Unobligated Balance, start of year	0	0	0
Unobligated Balance, end of year	0	0	0
Subtotal, adjusted budget authority	644,505,000	641,132,000	637,323,000
Unobligated balance lapsing	(25,000)	---	---
Total obligations	644,480,000	641,132,000	637,323,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:

FY 2005 - \$5,342,000 FY 2006 - \$5,000,000 FY 2007 - \$5,000,000

Excludes \$132,412 in FY 2006 and \$194,068 in FY 2007 for royalties.

## Justification

### National Institute of Environmental Health Sciences

Authorizing Legislation: Section 301 of the Public Health Service Act, as amended.

Budget Authority:

FY 2005 Actual		FY 2006 Appropriation		FY 2007 Estimate		Increase or Decrease	
<u>FTEs</u>	<u>BA</u>	<u>FTEs</u>	<u>BA</u>	<u>FTEs</u>	<u>BA</u>	<u>FTEs</u>	<u>BA</u>
651	\$644,505,000	652	\$641,132,000	655	\$637,323,000	3	-\$3,809,000

This document provides justification for the Fiscal Year 2007 activities of the National Institute of Environmental Health Sciences, including HIV/AIDS activities. A more detailed description of NIH-wide Fiscal Year 2007 HIV/AIDS activities can be found in the NIH section entitled "Office of AIDS Research (OAR)." Detailed information on the NIH Roadmap for Medical Research may be found in the Overview section.

## INTRODUCTION

Environmental exposures may adversely affect those who are vulnerable temporally (age, developmental stage), spatially (geographic location), or by unique circumstance (comorbid disease, nutritional status, socioeconomic status, genetics). Understanding the complex relationship between endogenous and exogenous risks within populations and affected individuals, how environmental exposures affect human biology, and how this knowledge can be used to reduce morbidity and extend longevity is precisely the opportunity and challenge that faces the National Institute of Environmental Health Sciences (NIEHS). The NIEHS mission is to improve human health by increasing this understanding through support of research and professional development in the environmental sciences (toxicology, relevant basic science), environmental medicine, and environmental public health. In addition to understanding how environmental exposures affect human biology, the NIEHS aims to understand how this knowledge can be used to reduce morbidity and extend longevity.

Because environmental exposures contribute substantially to the etiology of many common and complex human diseases, the NIEHS is in a unique position to focus on the interface between environmental exposures, vulnerable populations, human biology and genetics, and the common diseases that limit our longevity. In the postgenomic era of biomedical research, the NIEHS can take a leadership role in improving human health by using environmental exposures to understand how genes work in biological systems, how genetic variants contribute to the development of disease, and why individuals with the same disease have very different clinical

outcomes. Moreover, because of its focus and concentrated expertise, the NIEHS is uniquely poised to:

- develop sensitive preclinical markers of exposure and biological response,
- develop strategies to prevent disease in exposed and biologically responsive individuals and populations,
- establish population-based cohorts to understand the impact of environmental exposures on human health,
- understand how environmental exposures affect the course and prognosis of a medical condition, and
- stimulate dialogue to advance our understanding of environmental health policy and ethical issues of environmental concern.

To achieve this vision, NIEHS has developed individual and programmatic efforts to understand the role of environmental exposures on human health and disease. These goals will be achieved through the following broad strategies:

- development of interdisciplinary research opportunities that will focus on common, complex diseases with a substantial environmental component;
- efforts to define the epidemiological and clinical significance of environmental exposures in high-risk populations, including those in the international community;
- efforts to understand how genes and genetic variants interact with environmental stimuli to either preserve health or cause disease;
- programmatic integration of basic findings in the environmental health sciences with populations of diseased patients, communities at the extremes of exposure and vulnerability, other academic medical centers, and industry;
- study of environmental toxicants to understand basic mechanisms in human biology;
- use of eukaryotic model systems (yeast, worms, zebrafish, fruitflies, rodents) to accelerate understanding of how environmental exposures affect human health;
- support of the development of high-throughput *in vitro* and *in vivo* bioassays to establish reliable toxicity screens for potential toxicants;
- efforts to strengthen and expand the next generation of environmental health scientists by creating research incentives to encourage basic scientists, epidemiologists, and physician-scientists to develop research careers in the environmental health sciences;

- fostering of an integrated scientific approach that supports partnerships between the NIEHS and other NIH institutes, national and international research agencies, academia, industry, and community organizations to improve human health; and
- support of programs for environmental scientists to work with ethicists and policy makers to fully consider the regulatory implications of our scientific advances in environmental health.

The NIEHS is a complex institute with a distinguished history, a clear purpose, and a dedicated constituency. To develop a plan for fulfilling its mission of improving human health, the Institute recently engaged the scientific and public community in a process of strategic planning that will culminate in a formal Strategic Plan published in February, 2006. A number of initiatives have been developed in response to specific strategic needs, including: 1) interdisciplinary research centers that will more efficiently use environmental sciences to understand complex human diseases; 2) an Exposure Biology Initiative to develop biomarkers of exposure and biologic effect that are critically needed to move the field forward; 3) programs designed to develop physician-scientists and support young investigators; and 4) a Global Health Initiative that will better coordinate our international research efforts that examine unique exposures that occur throughout the world and substantially impair human health.

Environmental health sciences is like no other field of biomedical research. It is not limited by a biological system, a disease process, or an organ system. In fact, this scientific discipline represents the critical link between exposure and disease for many other fields of biomedical research. Through the efforts of NIEHS, the field of environmental health science will be shaped so as to fulfill its critical role in understanding human disease, reducing morbidity, and extending longevity. The Institute's success will be measured in the disease and suffering that is prevented.

## STORY OF DISCOVERY

### Story of Discovery - Asthma

With annual costs of \$12.7 billion<sup>a</sup>, asthma is a major public health problem in the U.S. It is the most common chronic disease of childhood and a leading cause of disability in children. Since 1980, asthma prevalence has increased dramatically in children. In addition to being a significant public health problem, asthma is an important health disparity problem because it is more common in poor, inner-city households. Over the past years, NIEHS has contributed to the following major findings:

#### *Indoor Exposures*

- Discovered that cockroach allergens worsen asthma symptoms more than other common allergens. Interestingly, cat exposure, once thought to increase a child's asthma risk, appears to protect a child from developing asthma if the exposure to cat allergens occurred during infancy. If, however, a child's mother had asthma, the opposite effect was observed – exposure to a cat actually increased risk of asthma in these children.<sup>b</sup>
- Identified simple interventions that, targeted to a child's individual sensitivities, noticeably reduced the severity and frequency of asthma attacks. Children were assessed for their sensitivity to six major irritants – dust mites, cockroaches, pet dander, rodents, passive smoking, and mold. Environmental interventions were tailored to reduce exposures for the sources for which the individual child was sensitive. Interventions included allergen-impermeable mattress and pillow covers, air purifiers with high efficiency particulate air (HEPA) filters, vacuum cleaners with HEPA filters, and professional pest control. Children who received the intervention had 19% fewer unscheduled clinic visits and a 13% reduction in use of asthma medication.<sup>b</sup>

- In a nationwide assessment of allergen levels in U.S. homes<sup>c</sup>, discovered that:
  - 100% of U.S. homes had detectable levels of cat and dog allergens, even though only 24% of homes had a resident cat and only 32% had a dog. Most homes had allergen levels that exceeded thresholds for allergic sensitization and one-third exceeded thresholds for asthma symptoms.
  - 82% of U.S. homes had mouse allergens, with the highest level appearing in kitchens.
  - 63% of homes had cockroach allergens.
  - Fungal allergens were found in 95% - 99% of homes.
  - Childcare facilities were also examined; seven allergens were assayed in 89 NC childcare facilities with each allergen being found in the majority of these facilities.

#### *Outdoor Exposures*

- Beginning in 1974, NIEHS funded several long-term studies that established a relationship between polluted air and increases in the number of hospital admissions, asthma attacks, and deaths from all causes. The elderly, asthmatics, and children were identified as particularly susceptible subpopulations. Newer studies have validated these earlier findings.
- Found that even levels of ozone below the federal standards posed risks to asthmatic children on maintenance medication. A 50-ppb (parts per billion) increase in 1-hour ozone was associated with increased likelihood of wheeze (by 35%) and chest tightness (by 47%) [Gent et al., JAMA 290:1859-1867, 2003].
- Identified ozone as a cause of asthma, not just an irritant to existing disease states. In a study of symptom-free children engaged in outdoor sports, those who were athletically active in high-ozone environments were three times more likely to develop asthma than children who did not play sports. Moreover, other NIEHS-supported investigators have found that short-term exposure to ozone is independently associated with excess mortality rate.
- Discovered that dietary supplements can reduce ozone-related asthma attacks, particularly in children with a particular genetic sensitivity. In this study asthmatic children living in high-ozone exposures of Mexico City were given vitamins C and E. These antioxidants were able to counteract the decreased lung function arising from ozone exposure, but the results were most significant in children who lacked an enzyme, glutathione S-transferase (GSTM1), that plays a major role in protecting cells against the oxidative damage caused by ozone. This genetic deficiency makes them more susceptible to the deleterious effects of ozone, so the antioxidant supplementation is of particular benefit.

#### *Airway Sensitivities and Endotoxin Exposures*

Another important airway toxin is endotoxin, derived from fragments of the outer coat of common bacteria. Endotoxin is widespread and can be found in household and grain dusts. Curiously, although high-dose exposure to endotoxin causes airway symptoms (wheeze and shortness of breath), early life exposure to endotoxin appears to protect against development of allergies. What, then, is its relationship to asthma? Recent results<sup>c</sup> have now definitively linked household endotoxin exposures with asthma symptoms, use of asthma medications, and wheezing. The protective effect of endotoxin observed for allergy sensitization was not found for asthma.

The molecular basis of endotoxin-induced airway sensitivity was elegantly assessed in studies using healthy human volunteers. People were exposed to increasing levels of endotoxin that represented typical occupational exposures and a marked difference in airway constriction was experienced by different people. It was found that the difference in response to endotoxin was related to mutations in the gene that encodes a specific receptor for endotoxin – the toll-like receptor-4 (TLR4) gene. Those with a normal TLR4 gene were sensitive to endotoxin-induced airway reactivity; those with a common polymorphism in this gene were much less affected by endotoxin. Thus the TLR4 gene was identified as having an important role in endotoxin-induced asthma. Taking the study of this gene further, researchers constructed mice lacking the TLR4 gene and again found that this gene was critical in the development of endotoxin-induced asthma.



### References

- a. Weiss KB and Sullivan SD: The health economics of asthma and rhinitis. I. Assessing the economic impact. J Allergy Clin Immunol 107:3-8, 2001.
- b. This study was part of the Inner City Asthma Study, done in collaboration with the National Institute for Allergy and Infectious Diseases (NIAID).
- c. This study was done in collaboration with the Department of Housing and Urban Development (HUD).

## SCIENCE ADVANCES

### **Bone Marrow Suppression in Workers Exposed to Very Low Concentrations of Benzene**

*Background:* Benzene is known to have toxic effects on the blood and bone marrow, but its impact at levels below the U.S. occupational standard of 1 part per million (ppm) remains uncertain. Exposure to benzene occurs worldwide to workers in the oil, shipping, automobile repair, shoe manufacturing, and other industries.

*Advance:* Researchers found that white blood cell counts and platelet counts were significantly lower in benzene-exposed workers, even for exposures below 1 ppm. Cells that eventually become mature white blood cells (progenitor cells) also declined significantly with increasing benzene exposure. Because the enzymes involved in benzene metabolism are known, these investigators measured the influence of genetic variants of key detoxifying enzymes on the concentration of progenitor and mature white blood cells. Two genetic variants in key metabolizing enzymes, myeloperoxidase and NAD(P)H:quinine oxidoreductase, were found to influence susceptibility to benzene.

*Implications:* Toxicity of benzene in blood cells and bone marrow of exposed workers was evident even below the U.S. occupational standard of 1 ppm. Individuals with particular genetic variants in two key metabolizing enzymes may be especially susceptible to benzene toxicity.

### **Ozone Affects Mortality in U.S. Cities**

*Background:* Ozone pollution is widespread in urban areas in the U.S. and in many other countries. Ozone exposure has been associated with various adverse health effects, including increased rates of hospital admissions and exacerbation of respiratory illnesses. Although numerous studies have estimated associations between day-to-day variation in ozone levels and measures of mortality, results have been inconclusive.

*Advance:* Using analytical methods and databases developed for the National Morbidity, Mortality, and Air Pollution Study, these investigators found that the mortality rate was increased in relation to short-term exposure to ozone. Specific models were used to adjust for confounders such as particulate matter, weather, and seasonality. After accounting for these factors, a 10-part per billion increase in the previous week's ozone was associated with a 0.52%

increase in daily mortality and a 0.64% increase in cardiovascular and respiratory mortality (Bell et al., JAMA 292:2372-2378, 2004).

*Implications:* In addition to the other health effects that have been associated with ozone exposure, this report provides further evidence that ozone exposure in urban areas increases mortality.

### **Red Tide Toxin Research Yields Potential Therapies for Cystic Fibrosis**

*Background:* “Red tide” is an algal bloom that results in toxin formation that can kill fish, contaminate shellfish, and lead to severe lung irritation and breathing problems in people who are exposed to this toxin when it is dispersed in the air. Coughing, shortness of breath, and other lung problems occur in normal people exposed to red tide toxins during bloom episodes, but seem particularly enhanced in people with preexisting airway diseases. For these reasons, researchers were interested in finding ways to neutralize the toxin. Unexpectedly, these same therapies might benefit people suffering from cystic fibrosis and other lung disorders characterized by excessive mucus secretion.

*Advance:* Researchers developed two anti-toxins to treat breathing problems caused by red tide and tested them in sheep. They found that not only did these compounds block the effect of red tide toxin, but that they sped up the clearance of mucus from the lungs. In fact, this ability of the anti-toxins mimicked the action of drugs used to treat cystic fibrosis, only at much lower doses than required by conventional therapies.

Cystic fibrosis is a genetic disease that causes the body to produce abnormally thick mucus in the lung and leads to life-threatening lung infections. On average, people with cystic fibrosis live only 30 years (US Department of Health and Human Services, NIH, NHLBI, *NHLBI Listens and Responds*. pp.13-14, 2004). These individuals are very dependent on drugs that help thin and clear the mucus from their lungs. The anti-toxins developed by these researchers appear to operate the same way, but at very safe doses (1 million times lower than current medications).

*Implications:* The anti-toxin compounds developed against red tide toxin offer new models for development of drug therapies to help sensitive individuals affected during episodes of red tide algal blooms. Interestingly, these same drugs may be useful for patients with cystic fibrosis. The potential is that a long-term therapy with these drugs may have fewer side effects than treatments currently available treatment for this disease.

### **Naturally Occurring Bronchodilator Protects Against Asthma in Mice**

*Background:* The incidence of asthma has been steadily growing over the past 30 years. Approximately 15 million people in the United States have asthma, leading to more than 500,000 hospitalizations and over 5,000 deaths annually (Weiss and Sullivan, J Allergy Clin Immunol 107:3-8, 2001). A variety of theories have been postulated for this rise including increased

exposure to indoor allergens, air pollutants, and other inflammatory agents. Scientists and doctors have known about the effects of airway constriction on asthma exacerbation for some time, however, very little effort has been given to naturally occurring airway relaxants and the balance between constricting and relaxing agents.

*Advance:* Researchers at Duke University, supported by NIEHS and the Howard Hughes Medical Institute, have discovered a naturally occurring bronchodilator that relaxes the airway and helps keep it open. Asthmatic animals and humans are deficient in the compound, which is known as S-nitrosoglutathione (GSNO). In laboratory animal studies, mice exposed to allergens exhibited airway constriction and increased levels of GSNO reductase, an enzyme that breaks down GSNO and other S-nitrosothiols (SNOs). However, mice missing the gene for GSNO reductase, when exposed to allergens, showed increases in lung SNOs and didn't develop airway constriction.

*Implications:* This study shows that GSNO reductase is very important in the regulation of the size of the airway under normal conditions and in response to allergen challenge. A deficiency of SNOs may make fundamental contributions to the development of asthma and GSNO repletion may prove to be a novel treatment for asthma.

### **Lead Accumulation May Lead to Cataracts**

*Background:* Despite significant reduction of environmental lead in the U.S., exposure has not been completely eliminated and most adults continue to have substantial body burdens of lead. Much of the lead taken up by the body is incorporated into bone; however, lead constantly exchanges from the bone to other tissues. Recent studies have revealed that long-term lead exposure is associated with a number of chronic disorders, including hypertension and cognitive decline. There have also been reports that lead may accumulate in the lens of the eye. These observations led to the question: "Does lead exposure play a role in increasing risk of cataracts?"

*Advance:* Researchers showed that lifetime lead exposure may cause an increase in the risk of developing cataracts, the leading cause of blindness. This study included over 600 men and found that participants with high levels of lead in the long bone of the leg (tibia) were more than 2.5 times as likely to develop cataracts as men with low levels of lead in the tibia. Blood lead levels, which are more indicative of short-term lead exposure, were not significantly associated with increased risk of cataract development.

*Implications:* This study suggests that accumulated lead exposure, common in the United States and other parts of the industrialized world, may be an important, but as yet unrecognized risk factor for cataract development. Reducing lead exposure may not only preserve the vision of many Americans as they age, it may also reduce the financial burden for cataract surgery and its attendant costs which for Medicare alone are approximately \$4 billion/year (Steinberg, et al. Arch Ophthalmol 111:1041-1049, 1993).

## **Sperm Motility Study Identifies Unique Target for Male Contraception**

*Background:* The ability of sperm to move quickly is a primary determinant for successful fertilization of eggs. Several systems exist that could generate the energy needed for sperm motility. Researchers recently identified the energy system responsible for sperm motility and made a surprising discovery that could lead to a male contraceptive drug.

*Advance:* Two systems exist for energy production – oxidative phosphorylation and glycolysis. Glycolysis was of interest to these researchers because, although the enzymes that control this system are found throughout the body, a very specific version of an enzyme critical for glycolysis (glyceraldehydes 3-phosphate dehydrogenase-S or GAPDS) appears only in sperm.

Mice lacking this particular enzyme GAPDS were constructed and it was found that deficiency of this enzyme resulted in severely impaired sperm motility and infertility.

*Significance:* This study identifies an enzyme necessary for generating energy for sperm motility, an activity critical to successful fertilization of eggs. Although this study was done in mice, it is expected that the results may be applicable to humans which also have a sperm-specific form of this energy-producing enzyme that is found nowhere else in the body. Thus, it may be possible to develop a contraception scheme that would target this enzyme only, and leave all other similar energy-producing enzymes in the body unaffected.

## **Mouse Life-Span Increases 20% with Reduction of Oxidative Stress**

*Background:* The free radical theory of aging refers to the role reactive oxygen species play in aging processes. Reactive oxygen molecules damage biological molecules and cause decline in the function of cells, tissues, and organ systems that eventually lead to death. The cumulative effect of oxidative damage is thought to play an important role in the physiological declines associated with aging as well as in a diversity of diseases associated with aging including cataracts, neurological diseases, atherosclerosis, and cancer. To test whether life-span in higher organisms can be extended by reducing oxidation, these investigators developed three genetically engineered (transgenic) strains of mice that overexpress the antioxidant enzyme, catalase, specifically targeted to key organelles in the cell such as mitochondria.

*Advance:* In the transgenic animals that have catalase (antioxidant enzyme) targeted to their mitochondria, life-span was extended by about 5 months or about 20%, and antioxidant activities were increased in the heart, skeletal muscle, and brain tissue. In fact, cardiac levels of antioxidant activity were 50 times higher in the transgenic animals than wild-type mice. The life-span extension in these animals was accomplished without deleterious side effects such as those seen in other studies using caloric restriction and other models of delayed aging. Cardiac disease and cataract development were delayed in these animals, and oxidative damage and the production of reactive oxygen molecules were reduced.

*Implications:* These results support the theory that free radical and reactive oxygen molecules generated in the mitochondria are very important in aging processes. It is too early to say that

human lives could be extended by the administration of antioxidant compounds; however, this study has produced exciting results with implications for longevity, possible new treatments for aging related illnesses, and healthier aging.

### **Standardizing Gene Expression Analysis Between Laboratories: A Critical Step for Environmental Genomics**

*Background:* The first papers describing the technique of DNA microarrays appeared in the scientific literature in the mid-1990s. Since that time, over 15,000 papers have been published in the peer-reviewed literature. Despite the growing popularity of the technique, the reproducibility of results between laboratories and across microarray platforms has not been adequately studied. Differences in techniques, platforms, instrumentation, and analytical software raise questions about the accuracy and reproducibility of results and possibly delay the full benefit of the technique.

*Advance:* The Toxicogenomics Research Consortium, a group of seven research centers, began a study in 2001 to determine the sources of variability in gene expression profiling done on microarrays by analyzing results collected across multiple labs using multiple technology platforms and techniques. The study was conducted in seven laboratories, in which two standardized samples were analyzed using twelve microarray platforms. Either laboratory or commercial microarrays were used in each laboratory. Data reproducibility was generally good within a single platform used in any one laboratory, but was poor between labs. When standardized protocols were used across all labs, reproducibility between the labs improved. The study found that commercially manufactured microarrays produced the most reproducible results.

*Implications:* The results from these studies indicate that microarray experiments can be comparable across multiple laboratories, especially when a common platform and set of procedures are used. These advances in microarray technology demonstrate to the scientific community how to obtain more consistent and reliable results. Standardizing microarray techniques can accelerate the pace of scientific discovery about biological responses to environmental stressors. Ultimately this could improve our ability to detect very early indicators of a biological response to an environmental agent that could eventually be used to prevent the development of a specific disease.

### **NIH ROADMAP**

NIEHS participates in, and benefits from, a number of Roadmap initiatives. For example, since August 2005, the NIEHS, through the National Toxicology Program (NTP), has formally participated in the NIH Roadmap Molecular Libraries Initiative (MLI). This collaborative effort is aimed at assisting the MLI project leaders with development of their screening program by adding a toxicity testing capability to the MLI effort. In addition, this collaboration is allowing rapid implementation of the NTP's High Throughput Screening Assays program by providing the NTP access to established testing laboratories through inter-institute cooperation. This collaboration is useful for both the MLI and the NTP. Specifically, the NTP, through its

association with the MLI, has the opportunity to generate information that links data on the biological activity of environment substances generated from high throughput screening assays with toxicity endpoints identified in NTP's toxicology testing program. The NTP can then use this information to identify mechanisms of action for further investigation, develop predictive models for biological response, and help prioritize substances for further toxicological evaluation. The NTP hopes to use this technology in the future as a means for screening large numbers of environmental substances as part of its testing program. Through its interaction with the NTP, the MLI components -National Chemical Genome Center (NCGC) and other Molecular Libraries Screening Center Network (MLSCN) laboratories- will obtain information on biological activity for a wide range of compounds for which their potential toxicity in laboratory animals and standard *in vitro* assays is known and will gain input on additional assays for adding to their screening battery. The NTP has currently provided approximately 1,400 chemicals to the NCGC and is working to identify commercially available high throughput screening assays that the NCGC will adapt to their current testing battery and run routinely. Eventually, the chemicals will be distributed to each of the MLSCN laboratories for screening. Data collected on chemical activity from the high throughput assays will be stored in a mutually accessible database for future analysis. In addition, the NTP held a public workshop on high throughput screening assays in December 2005 in Washington with the goal of gaining input on the selection of targets for these assays, assay design and chemical selection, and data storage, analysis, and interpretation.

### **NIH BLUEPRINT**

NIEHS research investment in environmental neurosciences has increased dramatically in the past decade, mirroring the growing understanding of the far-reaching effects of environmental influences on neurological development and disease. Many, if not most, of the NIEHS's investments have occurred in partnership with one or more of our sister Institutes in order to leverage resources and share expertise. In recognition of the benefits of these partnerships, NIEHS joined the group of Neuroscience Blueprint Institutes in FY2005. Our Blueprint membership gives NIEHS a chance to influence the development of research tools and infrastructure that will benefit the work of our environmental neuroscientists and contribute substantially to the success of our mission in environmental health.

In 2007, the Blueprint will focus on neurodegeneration—the progressive death of nerve cells. Neurodegeneration occurs in classical neurodegenerative disorders such as Alzheimer's and Parkinson's disease, in macular degeneration and other disorders of sight and hearing, in drug and alcohol abuse, and perhaps in mental disorders and chronic pain. As our population ages, the already enormous impact of neurodegeneration on society will become even larger without better prevention and treatment. Developing strategies to prevent degeneration of neurons and to promote a healthy nervous system is thus critical to the missions of all Blueprint members.

Following the successful model of the NIH Roadmap, the Blueprint will convene scientific workshops with leaders in research on neurodegeneration to identify barriers to progress and exceptional opportunities. The Blueprint will address these barriers and opportunities through initiatives targeted to provide resources, create tools, and answer key questions in neurodegeneration.

## FY 2007 INITIATIVES

*Exposure Biology Initiative:* In order to be able to use environmental health sciences to understand human disease and improve human health, we need better tools to quantify both an individual's exposure and the characteristics that account for individualized responses to common exposures. This initiative will enhance exposure assessment tools so that researchers can, for certain exposures, have the same degree of individual-level precision in exposure measurement that is being achieved in genetics through the sequencing of the human genome. Technologies that could provide new exposure tools are medical imaging, nanotechnology, and sensor technology. They could potentially lead to development of research tools that quantitatively assess the temporal and biological response to multiple environmental exposures. Ideally, these new technologies will generate insight on exposures across the exposure–disease continuum, from the point of human contact to the internal dose to the early biological response. To the extent feasible, new technological developments should complement efforts that are ongoing in the public and private sectors, such as biodefense and national health surveillance. Our ability to develop and validate exposure-response indicators, and to correlate them with genetic variation, will be critical to our success in reducing the burden of human disease.

*Environmental Genomics Initiative:* In the postgenomic era of biomedical research, the NIEHS is moving to implement an Environmental Genomics Initiative using its leadership in investigating environmental toxicants to understand how genes work in biological systems, how genetic variants contribute to the development of disease, and why individuals with the same disease have very different clinical outcomes. This Initiative will feature new or redirected activities in multiple levels.

- **Epigenetics.** There are mechanisms outside of normal inheritable mechanisms that are particularly relevant to environmental health sciences. A number of environmental and nutritional factors can substantially alter gene expression and generate developmental abnormalities or functional changes via alterations in genetic programming or control of gene expression. These changes in gene expression can cause or affect the risk of developing cancer, immunologic diseases and other complex diseases. NIEHS is proposing to develop a comprehensive program in epigenetics to specifically identify how gene expression is altered under different forms of environmental stress and how this alters the risk of developing disease.
- **Comparative Biology of Environmental Disease.** The application of “omics” technologies and comparative biology approaches to the study of environmentally-responsive genes will allow the role of these genes in environmentally-relevant disease pathways to be further elucidated. These different sets of technologies and applications can be used to understand why people exposed to the same environmental stressors respond differently. The development of pathway analysis tools informed by comparative genomics will be instrumental to understanding toxicological mechanisms.

- **Training in Environmental Genomics.** The existing T32 training grants program at NIEHS will be broadened to include other training opportunities in genetics and genomics. These will complement the existing areas of environmental health sciences which will continue to be covered.
- **Cohort and Case-Control Studies in Environmental Genomics.** The initiatives described above will inform and complement ongoing epidemiology studies funded by NIEHS, both case-control and population-based, such as the Sister Study, which examines environmental factors in the risk of breast cancer, and the Carolina Lupus Study.

*Human Health and Disease Initiative:* Traditionally, NIEHS has focused on basic science and public health research. However, environmental sciences can be applied to research in human health and disease. In fact, we believe that environmental sciences are critical to understanding complex human diseases, like cancer, diabetes, heart disease, and lung disease. NIEHS is taking several approaches to integrate environmental health sciences with clinical and translational research that focuses on human health and disease.

- **DISCOVER.** NIEHS is developing a new program called DISCOVER (Disease Investigation for Specialized Clinically Oriented Ventures in Environmental Research). It will bring together basic, clinical, and population-based scientists to conduct integrative research programs on: (1) understanding the etiology and pathogenesis of human diseases influenced by environmental factors, (2) using exposure to understand the interplay between genetic and environmental factors, and (3) applying available state-of-the-art technologies and methods to improve human health.
- **Environmental Health Sciences Core Centers.** New guidelines have been developed for the NIEHS Environmental Health Sciences Centers (EHS) programs. The next generation of EHS Core Centers is expected to bring their efforts to bear to a greater degree on translating environmental health research and related basic science results to public health and clinical arenas.
- **ONES.** The Outstanding New Environmental Scientist Award, or ONES, is a first independent research grant designed to attract the most talented younger researchers into the field of environmental health sciences. NIEHS aims to identify a cadre of outstanding scientists in the early, formative stages of their careers who are interested in developing a career in environmental health sciences research and to provide a strong start for these individuals. These grants will assist young scientists in launching innovative research programs focusing on problems of environmental exposures and human biology, human pathophysiology, and human disease.
- **Physician Scientist Training.** NIEHS is planning to expand its pool of qualified physician scientists who are engaged in environmental health sciences research. Several approaches will be taken to meet this objective, including: expansion of NIEHS' MD/PhD training awards; increasing our awards for clinical training (K awards); and reaching out to



schools of medicine to let them know about the scientific opportunities for clinical research in environmental health and disease.

*Global Environmental Health Initiative:* NIEHS-supported scientists have long taken advantage of the fact that environmental exposures vary around the world and can offer fruitful avenues for defining the impact of the environment on human health. Other countries often have much higher levels of exposure to certain pollutants that can lead to insight into potential health effects from the lower levels of these pollutants found in the U.S. The combinations of environmental exposures around the globe can also offer unique “laboratories” for teasing apart different environmental contributors. Moreover, strategic interventions within these populations can have a profound effect on global health. One example is the discovery that liver cancer can arise from a dual combination of Hepatitis B infection and aflatoxin exposures arising from mold in food. Both these exposures are found in the U.S., but the levels of exposure are much greater in Africa and Asia. It was NIEHS-supported studies in these countries that led to significant milestones in aflatoxin research, culminating in preventive steps in the U.S. that greatly limit consumer exposure to aflatoxin. These research efforts continue as U.S. scientists investigate simple intervention techniques for reducing the risks of liver cancer arising from these environmental exposures.

As the nation’s premier environmental health research institute, NIEHS has an opportunity and an obligation to address environmental health issues globally in a way analogous to how NIAID has addressed health crises of an infectious nature that extend beyond U.S. borders, such as AIDS, malaria, and bird flu. To enhance its ability to fulfill this obligation, the Institute will target global environmental health sciences as an area for greater focus. NIEHS is investigating a number of mechanisms to give greater focus and emphasis to this important area of research and is in the process of developing partnerships to better leverage resources in pursuit of new and emerging opportunities in global environmental research.

## **OTHER HIGHLIGHTS**

*Public Health Response – Hurricane Katrina:* Hurricane Katrina served to highlight the dedication and creativity of NIEHS staff in responding to an unexpected crisis. The Institute played a major role in recruiting physicians, nurses, and other health care providers from NIEHS and Duke University to join the NIH team to deliver medical care to victims in the Gulf Region during the hurricane’s aftermath. This team was stationed at a 500-bed medical facility in Meridian, Mississippi that had a triage area, ambulatory care area, and acute care component. Medical attention was only one of the needs of those affected by this disaster. Recognizing that many of the health issues from Katrina would relate to environmental toxicants and clean-up, the NIEHS launched a new website (<http://www-apps.niehs.nih.gov/katrina/>) that used a Global Information System to assess environmental hazards caused by the storm. The website helps public health and safety workers identify contaminants in flood waters, provides infrastructure and industry maps, and gives demographic information on local populations. NIEHS is training workers in the Gulf Region and also helping its grantees to find new laboratory space where they can continue their research.

As the nation moves forward in repairing the damage from Katrina's flooding, it is expected that mold and microbial toxins will be significant environmental exposures. These exposures will be particularly devastating to people already at risk for airway disease. NIEHS is working with its federal partners, the Centers for Disease Control and Prevention (CDC) and the Environmental Protection Agency (EPA), to develop a coordinated response to monitor and ameliorate these anticipated adverse environmental effects in the aftermath of Hurricane Katrina. These efforts will complement the ongoing environmental sampling and prevention efforts already identified in the Environmental Health Needs and Habitability Assessment developed by EPA and CDC.

*Breast Cancer and Environment Research Centers (BCERC):* NIEHS and NCI are partnering to support a network of research centers in which multidisciplinary teams of scientists, clinicians, and breast cancer advocates work collaboratively on understanding the impact of early life exposures on breast cancer risk. The focus is on the interaction of chemical, physical, biological, and social factors in the environment with genetic factors on the process of mammary gland development. This period of time is a vulnerable one during which exposures may increase susceptibility to future breast cancer. The network is working towards integrating histological, pathological, cellular, and sub-cellular changes that occur in normal mammary gland tissue across the lifespan along with comparisons to exposure-induced changes.

The BCERC also has a working group of approximately ten scientists and advocates that provides input and advice on the progress of the program. Representatives from the National Environmental Health Advisory Council and the National Cancer Advisory Board are also included. Input and oversight of the working group have been used to monitor and improve many parts of the program. The BCERC program has other ways of interacting with breast cancer advocacy groups and the public, including interactions with these groups during the BCERC's annual meetings. At the most recent meeting, approximately 150 participants were updated with the latest data, plans, and potential applications of the BCERC. In addition, invited speakers provided thoughtful perspectives on other studies with respect to environmental health and breast cancer. A complete report on the meeting is being prepared for distribution to interested communities, organizations, and policy makers.

## **INNOVATION IN MANAGEMENT AND ADMINISTRATION**

*Strategic Plan:* To identify the emerging areas with greatest opportunities for understanding disease processes and contributing to public health, the NIEHS embarked on a strategic planning exercise in 2005. It was inaugurated with an initial outreach to the public to elicit input on what, in their opinion, the important issues are in environmental health sciences. Request for this input was advertised in the *Federal Register*, in *Environmental Health Perspectives*, in the *NIH Guide*, through the NIEHS website, and through outreach to environmental advocacy groups. People responding via mail or the internet included scientists, regulators, administrators, environmental advocates, public school teachers, and students.

Following web input and analysis, a Strategic Planning Forum was convened October 17 – 18, 2005. Ninety scientists and environmental advocates came to develop the best ideas in response to six broad issues that emerged from the public's input. These were:

- Using environmental sciences and environmental exposures to understand human biology;
- Using environmental sciences and environmental exposures to understand human diseases and improve human health;
- Needs, opportunities, and challenges in exposure sciences;
- Technological needs and applications for infrastructure investment;
- Environmental health priorities and opportunities in the global health arena;
- Training needs.

Participants selected for the Forum were well-respected representatives in their fields. Break-out groups were assigned to ensure that all fields were represented and that the participants were exposed to individuals and viewpoints outside of their own area or group. This dynamic approach was done in order to avoid the narrow vision that often occurs when people remain within the comfort zone of their own discipline. Participants were also repeatedly shuffled so that each topic had three separate working groups focused on it at various times. The format of the Forum greatly enhanced the synergy across disciplines, a synergy that is evident in the recently released 2006 Strategic Plan. This plan has already led to a number of significant new initiatives at the NIEHS and further change is expected as more of the ideas are integrated into the Institute's research and training portfolios. Outgrowths of this plan will be a greater initial focus on human disease, a more rapid transmission of environmental findings into clinical applications, improved exposure assessment methodologies, greater focus on insights from global environmental research, and development of a cadre of environmental health scientists with expertise in multiple, rather than single, disciplines. Ultimately, the 2006 NIEHS Strategic Plan is the Institute's blueprint for ensuring that environmental health sciences can fulfill its tremendous potential to improve public health across a wide spectrum of chronic complex diseases.

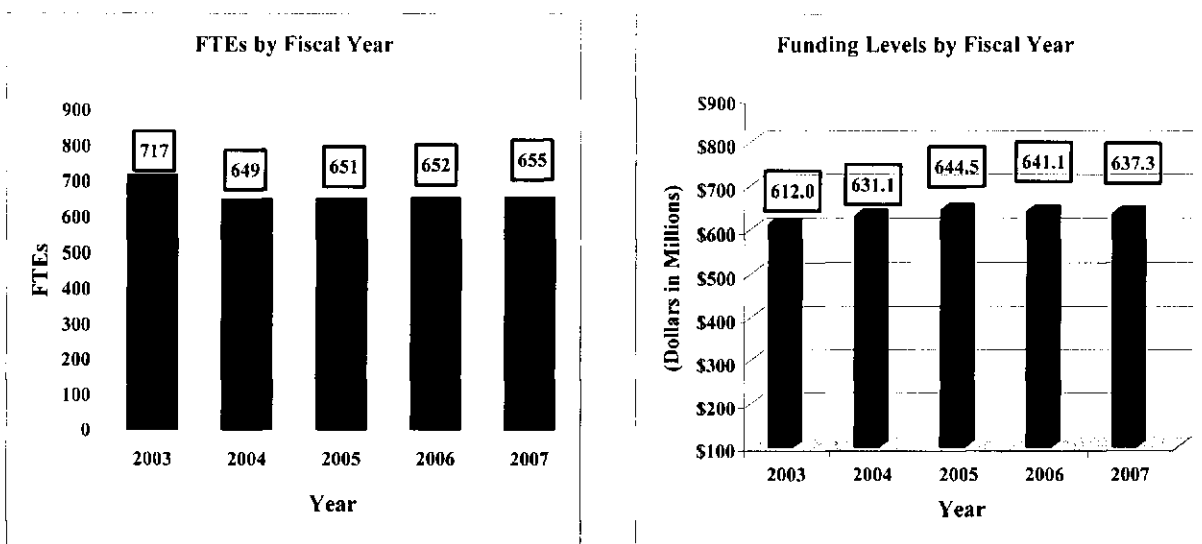
*Management Initiative in Integrative Research:* The NIEHS Division of Intramural Research (DIR) is planning to institute Centers for the Study of Complex Diseases (CSCD) which will integrate research efforts across the Institute's disciplines and use environmental sciences to understand disease and improve human health. These Centers will be virtual structures that will exist as an overlay to the existing Lab and Branch organization of the DIR.

*Evaluation of Ongoing Programs:* Environmental health sciences is a rapidly evolving field that requires regular assessments of current projects to ensure that the best science is pursued in the most efficient way possible. Two projects – the Mouse Genomics Research Centers and the Toxicogenomics Research Consortium – were discontinued in 2005.

## Budget Policy

The Fiscal Year 2007 budget request for the NIEHS is \$637,323,000, a decrease of \$3,809,000 and -0.9 percent from the FY 2006 Appropriation. Included in the FY 2007 request is NIEHS' support for the trans-NIH Roadmap initiatives, estimated at 1.2% of the FY 2007 budget request. A full description of this trans-NIH program may be found in the NIH Overview.

A five year history of FTEs and Funding Levels for NIEHS are shown in the graphs below. Note that as the result of several administrative restructurings in recent years, FTE data is non-comparable.



NIH's highest priority is the funding of medical research through research project grants (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while pursuing new research opportunities. We estimate that the average cost of competing RPGs will be \$331,000 in FY 2007. While no inflationary increases are provided for direct recurring costs in noncompeting RPGs, where NIEHS has committed to a programmatic increase for an award, such increases will be provided.

NIH must nurture a vibrant, creative research workforce, including sufficient numbers of new investigators with new ideas and new skills. In the FY 2007 budget request for NIEHS, \$900,000 will be used to support 10 awards for the new K/R "Bridges to Independence" program.

NIEHS will also support the Genes, Environment, and Health Initiative (GEHI) to: 1) accelerate discovery of the major genetic factors associated with diseases that have a substantial public health impact; and 2) accelerate the development of innovative technologies and tools to measure dietary intake, physical activity, and environmental exposures, and to determine an individual's

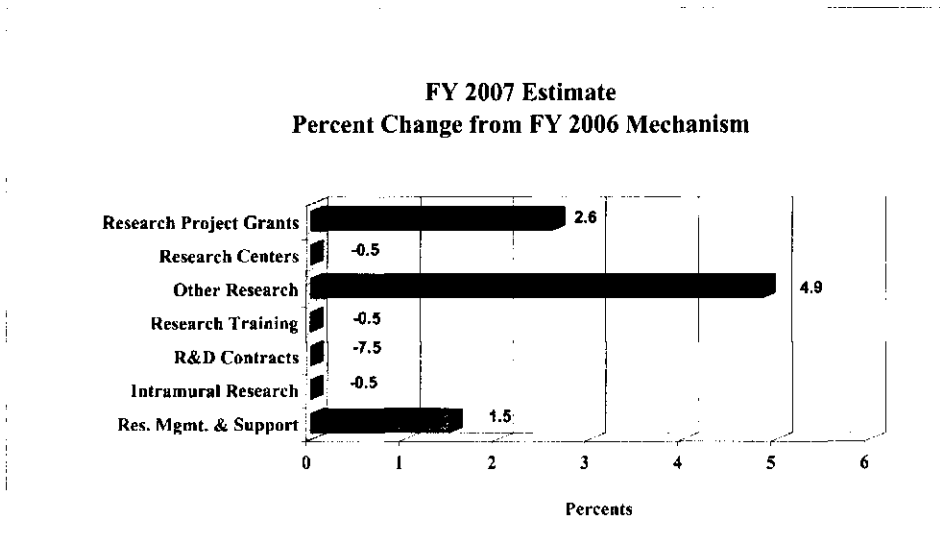
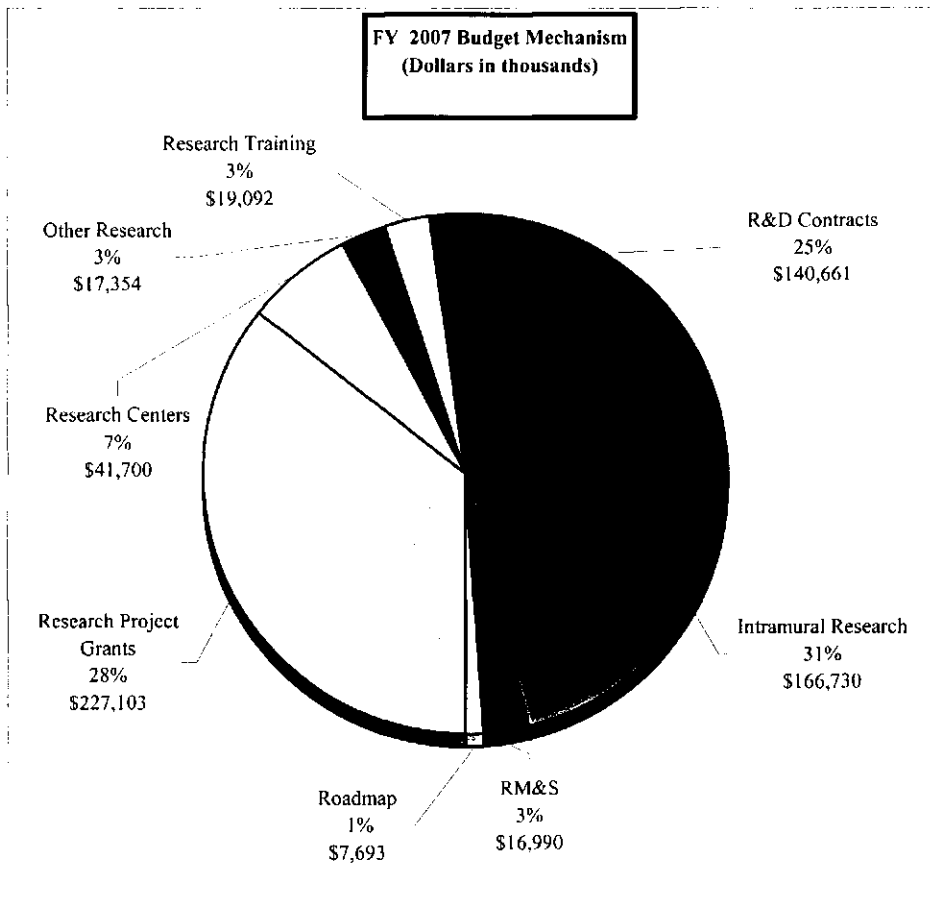
biological response to those influences. The FY 2007 request includes \$1,084,000 to support this project.

In the FY 2007 request, stipend levels for trainees supported through the Ruth L. Kirschstein National Research Service Awards will remain at the FY 2006 levels.

The FY 2007 request includes funding for 35 research centers, 107 other research grants, including 51 career awards, and 110 R&D contracts. Intramural Research decreases by 0.5 percent. Research Management and Support increases by 1.5 percent.

Innovative information technology (IT) is required to support scientific research, to increase staff productivity, and to streamline administrative processes. However, to be most effective, the IT investments must be well managed and closely aligned with the goals of the Institute. To ensure that NIEHS IT is meeting the Institute's needs efficiently and effectively, NIEHS plans to conduct an assessment of its IT. Outside experts from government and academia will be asked to review resource levels, organization, governance, service levels and most important, effectiveness in facilitating the Institute's research programs. Recommendations will address improvements to collection and management of requirements, setting priorities, choosing appropriate technologies and setting service levels. Changes as a result of this assessment are expected to target IT investment to those activities that produce the greatest return for the NIEHS research program and to produce savings by eliminating expenditures that are no longer effective.

The mechanism distribution by dollars and percent change tables are shown on the following page.



**NATIONAL INSTITUTES OF HEALTH**  
**National Institute of Environmental Health Sciences**

Budget Mechanism - Total

MECHANISM	FY 2005 Actual		FY 2006 Appropriation		FY 2007 Estimate	
	No.	Amount	No.	Amount	No.	Amount
Research Grants:						
Research Projects:						
Noncompeting	393	\$168,539,000	363	\$142,359,000	400	\$154,898,000
Administrative supplements	(33)	2,558,000	(39)	9,250,000	(32)	2,480,000
Competing:						
Renewal	35	16,510,000	62	20,624,000	62	20,624,000
New	109	31,160,000	114	37,712,000	114	37,712,000
Supplements			2	589,000	2	589,000
Subtotal, competing	144	47,670,000	178	58,925,000	178	58,925,000
Subtotal, RPGs	537	218,767,000	541	210,534,000	578	216,303,000
SBIR/STTR	35	10,928,000	35	10,800,000	35	10,800,000
Subtotal, RPGs	572	229,695,000	576	221,334,000	613	227,103,000
Research Centers:						
Specialized/comprehensive	35	41,892,000	35	41,892,000	35	41,700,000
Clinical research						
Biotechnology						
Comparative medicine						
Research Centers in Minority Institutions						
Subtotal, Centers	35	41,892,000	35	41,892,000	35	41,700,000
Other Research:						
Research careers	41	5,110,000	41	5,110,000	51	6,010,000
Cancer education						
Cooperative clinical research						
Biomedical research support						
Minority biomedical research support	3	2,000,000	3	2,000,000	3	2,000,000
Other	51	8,427,000	59	9,438,000	53	9,344,000
Subtotal, Other Research	95	15,537,000	103	16,548,000	107	17,354,000
Total Research Grants	702	287,124,000	714	279,774,000	755	286,157,000
Research Training:	<u>FTTPs</u>		<u>FTTPs</u>		<u>FTTPs</u>	
Individual awards	48	1,914,000	48	2,105,000	48	2,105,000
Institutional awards	450	17,274,000	442	17,083,000	440	16,987,000
Total, Training	498	19,188,000	490	19,188,000	488	19,092,000
Research & development contracts (SBIR/STTR)	117 (6)	152,524,000 (1,616,000)	116 (6)	152,119,000 (1,453,000)	110 (6)	140,661,000 (1,366,000)
Intramural research	<u>FTEs</u> 558	164,938,000	<u>FTEs</u> 559	167,583,000	<u>FTEs</u> 562	166,730,000
Research management and support	93	16,656,000	93	16,739,000	93	16,990,000
Cancer prevention & control						
Construction						
Buildings and Facilities						
NIH Roadmap for Medical Research		4,075,000		5,729,000		7,693,000
Total, NIEHS	651	644,505,000	652	641,132,000	655	637,323,000
(Clinical Trials)		(2,678,000)		(2,657,000)		(2,633,000)

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research

**NATIONAL INSTITUTES OF HEALTH**  
**National Institute of Environmental Health Sciences**

**Budget Authority by Activity**  
**(dollars in thousands)**

ACTIVITY	FY 2005 Actual		FY 2006 Appropriation		FY 2007 Estimate		Change	
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
<u>Extramural Research:</u>								
Environmental Health		\$458,836		\$451,081		\$445,910		(\$5,171) 0
Subtotal, Extramural research		458,836		451,081		445,910		(5,171)
Intramural research	558	164,938	559	167,583	562	166,730	3	(853)
Res. management & support	93	16,656	93	16,739	93	16,990		251
NIH Roadmap for Medical Research		4,075		5,729		7,693		1,964
Total	651	644,505	652	641,132	655	637,323	3	(3,809)

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research



**NATIONAL INSTITUTES OF HEALTH**  
**National Institute of Environmental Health Sciences**

**Summary of Changes**

FY 2006 Appropriation		\$641,132,000	
FY 2007 Estimated Budget Authority		637,323,000	
Net change		(3,809,000)	
CHANGES	FY 2006		Change from Base
	FTEs	Budget Authority	FTEs Budget Authority
A. Built-in:			
1. Intramural research:			
a. Within grade increase		\$68,471,000	\$978,000
b. Annualization of January 2006 pay increase		68,471,000	907,000
c. January 2007 pay increase		68,471,000	1,130,000
d. Payment for centrally furnished services		21,495,000	322,000
e. Increased cost of laboratory supplies, materials, and other expenses		77,617,000	1,513,000
Subtotal			4,850,000
2. Research Management and Support:			
a. Within grade increase		10,231,000	172,000
b. Annualization of January 2006 pay increase		10,231,000	136,000
c. January 2007 pay increase		10,231,000	169,000
d. Payment for centrally furnished services		2,276,000	34,000
e. Increased cost of laboratory supplies, materials, and other expenses		4,232,000	76,000
Subtotal			587,000
Subtotal, Built-in			5,437,000

**NATIONAL INSTITUTES OF HEALTH**  
**National Institute of Environmental Health Sciences**

**Summary of Changes--continued**

CHANGES	FY 2006 Appropriation		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	363	\$151,609,000	37	\$5,769,000
b. Competing	178	58,925,000	0	0
c. SBIR/STTR	35	10,800,000	0	0
Total	576	221,334,000	37	5,769,000
2. Research centers	35	41,892,000	0	(192,000)
3. Other research	103	16,548,000	4	806,000
4. Research training	490	19,188,000	(2)	(96,000)
5. Research and development contracts	116	152,119,000	(6)	(11,458,000)
Subtotal, extramural				(5,171,000)
	<u>FTEs</u>		<u>FTEs</u>	
6. Intramural research	559	167,583,000	3	(5,703,000)
7. Research management and support	93	16,739,000	0	(336,000)
8. NIH Roadmap for Medical Research	0	5,729,000	0	1,964,000
Subtotal, program		641,132,000		(9,246,000)
Total changes				(3,809,000)

**NATIONAL INSTITUTES OF HEALTH**  
**National Institute of Environmental Health Sciences**  
**Budget Authority by Object**

	FY 2006 Appropriation	FY 2007 Estimate	Increase or Decrease
<b>Total compensable workyears:</b>			
Full-time employment	652	655	3
Full-time equivalent of overtime & holiday hours	2	2	0
Average ES salary	\$135,000	\$138,000	\$3,000
Average GM/GS grade	11.2	11.2	0.0
Average GM/GS salary	\$73,330	\$74,940	\$1,610
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	\$91,600	\$93,600	\$2,000
Average salary of ungraded positions	111,300	113,800	2,500
<b>OBJECT CLASSES</b>	<b>FY 2006 Appropriation</b>	<b>FY 2007 Estimate</b>	<b>Increase or Decrease</b>
<b>Personnel Compensation:</b>			
11.1 Full-Time Permanent	\$35,290,000	\$37,135,000	\$1,845,000
11.3 Other than Full-Time Permanent	16,630,000	17,503,000	873,000
11.5 Other Personnel Compensation	865,000	912,000	47,000
11.7 Military Personnel	905,000	956,000	51,000
11.8 Special Personnel Services Payments	9,869,000	10,126,000	257,000
<b>Total, Personnel Compensation</b>	<b>63,559,000</b>	<b>66,632,000</b>	<b>3,073,000</b>
12.0 Personnel Benefits	14,600,000	15,367,000	767,000
12.2 Military Personnel Benefits	520,000	550,000	30,000
13.0 Benefits for Former Personnel	23,000	24,000	1,000
<b>Subtotal, Pay Costs</b>	<b>78,702,000</b>	<b>82,573,000</b>	<b>3,871,000</b>
21.0 Travel & Transportation of Persons	2,085,000	2,140,000	55,000
22.0 Transportation of Things	340,000	345,000	5,000
23.1 Rental Payments to GSA			0
23.2 Rental Payments to Others	21,000	21,000	0
23.3 Communications, Utilities & Miscellaneous Charges	1,260,000	1,310,000	50,000
24.0 Printing & Reproduction	230,000	235,000	5,000
25.1 Consulting Services	1,350,000	1,380,000	30,000
25.2 Other Services	24,011,000	17,664,000	(6,347,000)
25.3 Purchase of Goods & Services from Government Accounts	90,180,000	89,054,000	(1,126,000)
25.4 Operation & Maintenance of Facilities	500,000	515,000	15,000
25.5 Research & Development Contracts	113,596,000	104,933,000	(8,663,000)
25.6 Medical Care	115,000	116,000	1,000
25.7 Operation & Maintenance of Equipment	2,175,000	2,216,000	41,000
25.8 Subsistence & Support of Persons			0
<b>25.0 Subtotal, Other Contractual Services</b>	<b>231,927,000</b>	<b>215,878,000</b>	<b>(16,049,000)</b>
26.0 Supplies & Materials	16,770,000	16,780,000	10,000
31.0 Equipment	10,080,000	10,080,000	0
32.0 Land and Structures			0
33.0 Investments & Loans			0
41.0 Grants, Subsidies & Contributions	293,988,000	300,268,000	6,280,000
42.0 Insurance Claims & Indemnities			0
43.0 Interest & Dividends			0
44.0 Refunds			0
<b>Subtotal, Non-Pay Costs</b>	<b>556,701,000</b>	<b>547,057,000</b>	<b>(9,644,000)</b>
<b>NIH Roadmap for Medical Research</b>	<b>5,729,000</b>	<b>7,693,000</b>	<b>1,964,000</b>
<b>Total Budget Authority by Object</b>	<b>641,132,000</b>	<b>637,323,000</b>	<b>(3,809,000)</b>

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research

**NATIONAL INSTITUTES OF HEALTH**  
**National Institute of Environmental Health Sciences**

**Salaries and Expenses**

OBJECT CLASSES	FY 2006 Appropriation	FY 2007 Estimate	Increase or Decrease
<b>Personnel Compensation:</b>			
Full-Time Permanent (11.1)	\$35,290,000	\$37,135,000	\$1,845,000
Other Than Full-Time Permanent (11.3)	16,630,000	17,503,000	873,000
Other Personnel Compensation (11.5)	865,000	912,000	47,000
Military Personnel (11.7)	905,000	956,000	51,000
Special Personnel Services Payments (11.8)	9,869,000	10,126,000	257,000
<b>Total Personnel Compensation (11.9)</b>	<b>63,559,000</b>	<b>66,632,000</b>	<b>3,073,000</b>
Civilian Personnel Benefits (12.1)	14,600,000	15,367,000	767,000
Military Personnel Benefits (12.2)	520,000	550,000	
Benefits to Former Personnel (13.0)	23,000	24,000	1,000
<b>Subtotal, Pay Costs</b>	<b>78,702,000</b>	<b>82,573,000</b>	<b>3,871,000</b>
Travel (21.0)	2,085,000	2,140,000	55,000
Transportation of Things (22.0)	340,000	345,000	5,000
Rental Payments to Others (23.2)	21,000	21,000	0
Communications, Utilities and Miscellaneous Charges (23.3)	1,260,000	1,310,000	50,000
Printing and Reproduction (24.0)	230,000	235,000	5,000
<b>Other Contractual Services:</b>			
Advisory and Assistance Services (25.1)	450,000	465,000	15,000
Other Services (25.2)	24,011,000	17,664,000	(6,347,000)
Purchases from Govt. Accounts (25.3)	55,992,000	57,659,000	1,667,000
Operation & Maintenance of Facilities (25.4)	500,000	515,000	15,000
Operation & Maintenance of Equipment (25.7)	2,175,000	2,216,000	41,000
Subsistence & Support of Persons (25.8)			0
<b>Subtotal Other Contractual Services</b>	<b>83,128,000</b>	<b>78,519,000</b>	<b>(4,609,000)</b>
Supplies and Materials (26.0)	16,770,000	16,780,000	10,000
<b>Subtotal, Non-Pay Costs</b>	<b>103,834,000</b>	<b>99,350,000</b>	<b>(4,484,000)</b>
<b>Total, Administrative Costs</b>	<b>182,536,000</b>	<b>181,923,000</b>	<b>(613,000)</b>

## NATIONAL INSTITUTES OF HEALTH

### National Institute of Environmental Health Sciences

#### SIGNIFICANT ITEMS IN HOUSE AND SENATE APPROPRIATIONS COMMITTEE REPORTS

##### FY 2006 House Appropriations Committee Report Language (H. Rpt. 109-143)

***Parkinson's disease*** – The Committee encourages NIEHS to continue funding research into environmental influences of Parkinson's disease. The causes of Parkinson's and other neurodegenerative disorders are increasingly shown to be a result of the inter-relation of environment and genes. Possible environmental triggers of Parkinson's are pesticides and/or heavy metals. If these environmental toxins can be identified and the mechanisms elucidated, appropriate prevention or treatment may prevent many cases of Parkinson's, especially concerning increasingly younger persons at risk. (p. 85)

##### Action taken or to be taken

Parkinson's and other neurodegenerative diseases continue to be priority areas for NIEHS and a number of mechanisms are used to encourage research in this area. NIEHS currently supports a significant number of investigator-initiated studies in Parkinson's disease. Additional applications are solicited actively through a Program Announcement with a \$2 million dollar set-aside, PAS 03-160: "Gene-Environment Interactions in Neurodegenerative Disease." NIEHS supports a national network, the Collaborative Centers for Parkinson's Disease Environmental Research (CCPDER). These Centers focus on gene-environment interactions in disease etiology; pesticides and metals are among the toxicants under study. In addition to providing support for self-contained research conducted at each CCPDER, NIEHS has made additional funds available to CCPDER investigators to support several network projects. These collaborative projects are aimed at (1) developing improved animal models; (2) creating a screening battery for identifying potential environmental toxicants that may contribute to Parkinson's; and (3) developing a risk factor instrument that will facilitate data sharing and pooling among epidemiologists studying Parkinson's. Finally, NIEHS continues to support meetings and conferences that focus on environmental aspects of Parkinson's.

##### Item

***Mercury*** – In order to properly research gaps in the area of mercury exposure and brain chemistry, and given recent hearings on mercury exposure and relationships between autism and Alzheimer's disease and mercury exposure, NIEHS is encouraged to pursue studies of how inorganic mercury and organic mercury compounds (including ethyl, methyl, and other forms of mercury from all sources) are processed in the bodies of children and adults. NIEHS is also encouraged to support studies of the toxic effects of inorganic mercury and organic mercury

compounds on the nervous systems of young children, adults, and the elderly and methods of properly removing mercury and mercury-containing compounds from the brains of affected humans. (p. 85)

#### Action taken or to be taken

NIEHS recognizes that environmental mercury exposure is an important public health concern and provides ongoing funding for a number of studies in this area. Together with the US EPA, NIEHS funds a large epidemiologic investigation to determine the relationship between a range of environmental exposures, including mercury and other metals, and the risk of autism spectrum disorders (ASD). NIEHS has provided additional funding to investigators to support a replication study of the recent published finding by another group of investigators of strain-dependent differences in sensitivity to the mercury-based preservative thimerosal.

Within the autism arena, NIEHS works collaboratively with other NIH institutes and federal agencies to support a number of autism research initiatives and activities. NIEHS is a cosponsor of a broadly-based program announcement that encourages investigators to submit new applications addressing autism etiology, treatment and other priority items relevant to autism. NIEHS plans to contribute to the funding of the new NIH Autism Centers of Excellence Program that is being developed and will encourage applicants to include studies that address environmental influences in autism. Finally, NIEHS is working collaboratively with the National Institute of Mental Health (NIMH) to explore the feasibility of conducting a small clinical trial of chelation therapy with succimer in individuals with autism. NIEHS has significant expertise in this area and supported the development and application of succimer as a treatment for heavy metal poisoning.

NIEHS continues to support very basic research to appreciate at the molecular level, the toxicity of mercury to the brain, especially the developing brain. These range from the methylmercury effect on mitochondrial oxidative function, on the extreme sensitivity of the GABAA transmitter receptor, on the development of microphthalmia in children, on the relative contributions of different forms of mercury on neurobehavioral defects as well as a potential biomarker for a possible predisposition to altered mercury susceptibility in humans. A project examining the mechanism(s) by which methylmercury is transported into the cell has identified a novel antidote/chelator for removal of methylmercury from the body using N-acetylcysteine.

NIEHS supports studies examining the effects of dietary ingestion of methylmercury on the developing brain. Two are studying whether there are any lasting effects of mercury exposure in what are now adolescents and they will be able to correlate their findings to school performance. Two others center on whether nutrients from a fish diet can mitigate the effects of methylmercury exposure. This is especially relevant since a small pilot study has shown that the offspring of mothers who eat fish have better cognition at age two. But the two year-old offspring of mothers who have high exposure to mercury have poorer cognition.

NIEHS plans to continue to encourage investigator-initiated research in the field of mercury research including its effect on the immune system as well as the brain.

## Item

***Toxic exposure and brain development*** – Notwithstanding the Institute of Medicine May 2004 report on autism, the Committee believes it is important to develop a more complete understanding of the impact that toxic exposures may have on brain development. There is a convergence of findings from tissue culture studies, animal models, and clinical studies of immune dysfunction in children with autism and other neurodevelopmental disorders (NDDs) that suggests a biological link between genetic sensitivity and damage to developing brains from certain toxins. It is important that NIH continue this research to better understand the impact that exposures to mercury (including thimerosal) and other toxins have on brain development. A more complete understanding of the impact of these exposures through research, including animal models, will help to develop more effective interventions. (p. 85)

## Action taken or to be taken

NIEHS recognizes the importance of understanding how a broad range of environmental exposures affect aspects of early development. Individual differences in susceptibility to exposure are a central theme in many NIEHS-supported research efforts. NIEHS, together with the Environmental Protection Agency (EPA), supports a national network of Children's Centers for Environmental Health and Disease Prevention. Several of these Centers focus on environmental contributors to neurodevelopmental disorders, including autism. NIEHS and EPA recently announced a new round of competition for these Centers; existing Centers and new teams of investigators are encouraged to apply; applicants are required to focus on neurodevelopmental and/or endocrine disorders. NIEHS and EPA expect to fund four Centers for a period of five years, contingent on a sufficient number of meritorious applications.

In addition to this Centers program, NIEHS supports many investigator-initiated grants in the area of neurodevelopment. These studies include population-based epidemiologic investigations in infants and children to animal and cellular models of toxicant action in developing brain.

NIEHS continues to provide support for a study aimed at determining the reliability of a recent finding demonstrating strain-dependent sensitivity to thimerosal administration in mice. This study will be completed within the next six months and submitted for publication in a peer-reviewed journal within a year. NIEHS also plans to provide expert advice for a study that will examine the brains of non-human primates exposed to thimerosal or methyl mercury early in development to determine any effects on cell type and number.

NIEHS is aware of the emerging findings of immune dysfunction in ASD. To encourage neurotoxicologists to study the interaction of environmental agents with the immune systems during early brain development, NIEHS sponsored a scientific session at the International Neurotoxicology Society meeting on September 12, 2005. This session was entitled: "Environmental Perturbations of the Immune System: Implications for Autism and Other Neurodevelopmental Disorders." The scientific session was followed by a small workshop of

scientific experts in this area to identify research needs and opportunities. The results of this workshop will be used in planning future NIEHS activities.

#### Item

***Toxicology validation reviews*** – In order for the Interagency Coordinating Committee for the Validation of Alternative Methods (ICCVAM) to carry out its responsibilities under the ICCVAM Authorization Act of 2000, the Committee encourages NIEHS to strengthen the resources for methods validation reviews in fiscal year 2006. The Committee is encouraged by the National Toxicology Program's Road Map and Vision for NTP's toxicology program in the twenty-first century and encourages NIEHS to move rapidly to implement the programs, especially those directly aimed at strengthening the scientific basis for many alternative methods (such as Quantitative Structure-Activity Relationships), mechanistic screens, high throughput assays, and toxicogenomics). (p. 85/86)

#### Action taken or to be taken

The development, validation, acceptance and harmonization of new, alternative, and revised toxicological test methods is coordinated within the federal government by ICCVAM, a permanent interagency committee of NIEHS under the National Toxicology Program Interagency Center for Evaluation of Alternative Toxicological Methods (NICEATM). NICEATM administers ICCVAM and provides scientific support for ICCVAM and ICCVAM-related activities including coordination of independent validation studies to evaluate the usefulness and limitations of proposed test methods. NICEATM has several goals for FY2006, all of which are supported by NIEHS: (1) Standardize and plan validation studies on a non-animal/non-radioisotopic estrogen receptor transcriptional activation test method to determine if this test method can replace current methods that require surgically manipulated animals; (2) Finalize and forward ICCVAM test method recommendations for four non-animal methods for identifying severe ocular irritants and corrosives; (3) Complete independent peer review evaluation of two *in vitro* cytotoxicity methods proposed for reducing the number of animals required for acute systemic toxicity studies and convene an expert workshop to identify the highest priority R&D and validation studies necessary to further reduce the number of animals required for acute toxicity; (4) Convene an expert workshop to identify high priority R&D and validation studies needed to further reduce animal use needed to determine the potency of botulinum toxin preparations; and (5) Identify priority validation needs for *in vitro* ocular irritancy testing and initiate planning of needed studies.

NIEHS appointed a new Deputy Director for NICEATM in June 2005. This additional person will allow for expansion of NICEATM activities and facilitate integration of NICEATM in the NTP Roadmap initiative on high throughput screening. NTP is working to identify or develop rapid, mechanism-based assays that can be used to screen large numbers of environmental substances for their potential biological activity. NTP plans to explore the use of this technology to predict how substances might react in biological systems and prioritize them for more extensive toxicological evaluation using fewer laboratory animals.



### Item

***Risk analysis*** – The Committee encourages NIEHS to establish a competitive, peer-reviewed extramural program of centers for risk sciences to conduct research in risk sciences, including assessment, management analysis, and communication of risks from exposure to environmental chemicals. NIEHS is encouraged to work with these centers to develop scientifically-based methodologies used to determine, quantify, and communicate risk to the public's health. (p. 86)

### Action taken or to be taken

NIEHS, through the Superfund Basic Research Program (SBRP), supports a multidisciplinary research focus in the assessment of risk. This program was established under the Superfund Amendments and Reauthorization Act (SARA) of 1986 with specific mandates to develop a research program that, in part, advances techniques for the detection, assessment, and evaluation of the effects on human health of hazardous substances and develops methods to assess the risks to human health presented by hazardous substances. Through this research program, we encourage the development of new risk assessment models that describe risk from the source of contamination, through the movement of contaminants within environmental media, to its uptake by biological receptors (i.e., human or wildlife) and the effect within biological receptors on complex cellular and molecular pathways to the incipience of dysfunction or disease. SBRP also supports community outreach and research translation activities that include the development of risk communication strategies. In parallel efforts, NIEHS invests in basic research in exposure assessment and statistical methods that advances the underlying data necessary to develop and conduct scientifically sound risk assessments. Through initiatives such as the Community-Based Participatory Research Program, NIEHS conducts evaluation of risk communication strategies.

NIEHS supports these research efforts through a competitive peer-review process. NIEHS will continue to encourage anticipatory research and identify “emerging” issues, especially in pivotal sources of uncertainty that might affect the risk sciences.

### Item

***Asthma*** – Given the link between environmental factors and the onset of asthma, COPD, and pulmonary fibrosis, the Committee encourages NIEHS to further develop research initiatives, such as a large multi-center, long-term longitudinal, and maternal/birth cohort to understand the environmental and genetic risk factors for predisposing some individuals to and in controlling the severity of these lung diseases. (p. 86)

### Action taken or to be taken

NIEHS agrees with the Committee that multidisciplinary research on the environmental and genetic factors that contribute to the development of asthma, COPD, and pulmonary fibrosis is an important priority and supports numerous multi-disciplinary, longitudinal research programs that include human populations and animal models. NIEHS supports the Children's Environmental Health and Disease Prevention Research Centers and investigator-initiated

research grants that focus on the role of ambient air and environmental home contaminants on the development and severity of childhood asthma. In a longitudinal study of school children in twelve communities with varying levels of air pollution, the addition of genetic markers that may modulate the biological response to toxicants are examined. Deficits in lung growth and function have been associated with increased levels of air pollutants. Interactions between genes involved with metabolism and detoxification of these toxicants and oxidant stress are being examined. In epidemiologic and intervention research supported by NIEHS, exposures such as indoor allergens, and chemicals such as insecticides, pesticides, and phthalates are being examined as children grow and develop. Diesel exhaust particles, a constituent of truck exhaust, have been implicated in the development and exacerbation of lung diseases. Using a birth cohort design, NIEHS-funded researchers are examining the health risk to children residing near interstate highways who are exposed to high levels of diesel exhaust particles and finding allergic and respiratory responses in those highly exposed.

Animal models provide the opportunity to examine the cellular and molecular mechanisms through which environmental exposures induce lung disease. The neonatal response to oxidant air pollutants and allergens and the relationship of these exposures to development of childhood and adult asthma is being studied in a rhesus monkey model. Research will identify developmental “windows of susceptibility” in the first year of life and structural and functional changes in the neonatal lung that predispose individuals to pulmonary disease. Using clinical research tools, the genetics of complex lung disease are investigated through studies that model biologically unique gene-environment disease phenotypes. NIEHS research is exploring the role of the Toll-like Receptor 4 in airway responsiveness to endotoxin and the role of S-nitrosylation in the inflammatory component of lung disease. NIEHS has also initiated a program to investigate the effect of fetal exposure to environmental pollutants on the development of adult disease, including lung disease. Environmental pollutants employed in NIEHS animal studies include diesel exhaust particles, ozone, heavy metals, manufacturing chemicals such as toluene diisocyanate and dioxin, and environmental tobacco smoke. State-of-the-art technologies are encouraged, including genomics, to assess exposure-initiated changes in gene expression, proteomics to identify changes in the proteins that affect the response to exposure, and computer models to link *in vitro* and *in vivo* studies. It is through longitudinal human populations studies, clinical based inquires and laboratory based experimental research that advances in our understanding of the mechanisms of environmental exposures can be applied to the prevention and treatment of lung disease in children and adults.

#### FY 2006 Senate Appropriations Committee Report Language (S. Rpt. 109-103)

##### Item

**Asthma** – Given the link between environmental factors and the onset of asthma, COPD, and pulmonary fibrosis, the Committee encourages NIEHS to further develop research initiatives, such as a large multi-center, long-term longitudinal, and maternal/birth cohort to understand the environmental and genetic risk factors for predisposing some individuals to and in controlling the severity of these lung diseases. (p. 128)

#### Action taken or to be taken

Please refer to the item regarding *Asthma* on pages NIEHS-33 and NIEHS-34 of this document for response to this Significant Item.

#### Item

***Basic Behavioral and Social Sciences Research*** – The Committee encourages NIEHS to participate in trans-institute initiatives organized by OBSSR or another institute to strengthen basic behavioral or social science research, and to enhance opportunities for behavioral and social science research training. (p.128)

#### Action taken or to be taken

Over the past ten years, NIEHS and OBSSR have been strong partners in a number of joint initiatives. We have participated in a number of program announcements and Requests for Applications (RFAs) which have brought behavioral and social science research into the spectrum of disciplines in the environmental health sciences. Many of the NIEHS programs in environmental justice, community-based participatory research, and health disparities have been strengthened by working with OBSSR on these important issues. During 2005, NIEHS has been a member of the trans-NIH committee on behavioral and social sciences and will continue to devote staff time and resources to maintain our involvement with this group. During the last year, NIEHS participated with OBSSR and other ICs on a program announcement on health literacy, an RFA on obesity and the built environment, and a three-year program announcement to stimulate continued growth and application of community-based participatory research methods to study human health and disease. In each activity NIEHS is particularly interested in the application of intervention and behavioral methods to environmental health questions.

#### Item

***Breast Cancer*** – The Committee believes that it is essential to support research on environmental factors that may be related to the etiology of breast cancer. The Committee recognizes the important first step the Institute has taken with its recently awarded grants to four research centers to begin to study the prenatal-to-adult environmental exposures that may predispose a woman to breast cancer. However, the recent awards are only a small down payment in terms of dollars, process, and focus on the comprehensive and collaborative research that is needed. The need for more funding and a comprehensive research strategy, as outlined by the Breast Cancer and Environmental Research Act, is clear. The Committee understands that the Institute will establish an advisory board to make recommendations to the Director with regard to the development of the research centers. The Committee is pleased that the board will include representatives from the breast cancer community who have had the disease. The Committee asks that the director provide an update in the fiscal year 2007 appropriations justification on the progress of the centers. (p.128)

### Action taken or to be taken

NIEHS and NCI are partnering to support a network of research centers in which multidisciplinary teams of scientists, clinicians, and breast cancer advocates work collaboratively on understanding the impact of early life exposures on breast cancer risk.

An epidemiological study is underway to determine how environmental factors that are local to where young women live and learn may change the timing of puberty. Twelve hundred girls (ages 8 - 14) of diverse background are being evaluated to determine whether exposures and nutrition contribute to early onset of puberty, an established risk factor for breast cancer. Candidate exposures are also studied in depth using laboratory animals to better understand their mechanisms of action, genomic features, and tumor-promoting potential.

Results of preliminary studies are encouraging and are providing new insights into the interactions of genes and the environment. In a pilot study to determine which genes might interact with environmental conditions to predispose girls to earlier puberty, naturally-occurring variations in six estrogen-synthesis and -metabolizing genes were compared. An association was found between obesity and earlier breast development, but only among girls with a slow "estrogen synthesis allele profile," especially those girls with variations in the gene (Cyp19) that plays a role in testosterone-to-estrogen conversion.

In concert with the puberty study, Breast Cancer and Environmental Research Centers (BCERC) laboratory researchers are investigating the impact of diet and common exposures on the architecture and development of mammary glands in animal models. An important study - recently published by the Center at Michigan State University - characterizes the levels of cell receptor sub-types that modulate the effects of progesterone, a hormone that, together with estrogen, guides central processes in female development. The report is the first to demonstrate that the distribution of progesterone receptors changes during puberty and pregnancy and correlate with the appearance of specific structures within the mammary gland.

Another study revealed intriguing effects of phthalates and other endocrine disruptors, chemicals that leach out of plastic, on gene activity in rat mammary glands. The investigators saw changes in activity of a number of known and, as yet, unknown genes following treatment of nursing dams with bis-phenol A (BPA) or n-butyl benzyl phthalate (BBP). Surprisingly, a single gene appears to be continually down-modulated in the offspring under both these treatment conditions. Ongoing studies are being performed to confirm these observations and to determine the significance of the findings for the architecture of the mammary gland, onset and progression through puberty, and ultimately, the influence on breast tumor development.

### Item

***Built Environment*** – The Committee is pleased with the research that NIEHS is supporting on environmental factors, including built environment, and their relationship to the rising prevalence of obesity among youth and adults. The Committee urges NIEHS to continue work in this area, including transportation choices and their impact on public health outcomes. (p. 129)

#### Action taken or to be taken

On August 20, 2004, NIEHS, the National Cancer Institute (NCI), The National Institute of Child Health and Human Development (NICHD), the NIH Office of Behavioral and Social Sciences Research (OBSSR), and two Centers within the Centers for Disease Control (CDC) released RFA-ES-003, "Obesity and the Built Environment," to begin building a program of R01 and R21 research projects in two specific areas related to the built environment and obesity: understanding the role of the built environment in causing/exacerbating obesity and related co-morbidities; and developing, implementing, and evaluating prevention/intervention strategies that influence parameters of the built environment in order to reduce the prevalence of overweight, obesity and co-morbidities.

NIEHS committed \$3 million to fund five R01 and three R21 grant proposals. In addition, NIEHS will administer three CDC-funded R21 projects. The purpose of the R01 studies, with up to five years of funding, is to provide solutions for alleviating the burden of obesity and being overweight in the U.S. by providing insights into treatment mechanisms or developing models for prevention. The purpose of the two-year R21 studies is to develop and validate built environment measures and methods of data collection. Applications selected for funding included longitudinal, cross-sectional and intervention studies in rural, urban and suburban areas and were chosen to create a diverse, balanced portfolio that will enable NIEHS to contribute significantly to the scientific understanding of environment-obesity interactions. Program funding began in September 2005. An Annual Meeting for the project investigators and NIH and CDC program staff is planned for Winter/Spring 2006. By funding this set of awards, NIEHS created a fully integrated research program to better understand how the environment has contributed to obesity and how environmental interventions can prevent or treat this condition.

#### Item

***Interagency Coordinating Committee for the Validation of Alternative Methods [ICCVAM]*** – In order for the Interagency Coordinating Committee for the Validation of Alternative Methods [ICCVAM] to carry out its responsibilities under the ICCVAM Authorization Act of 2000, the Committee encourages the NIEHS to strengthen the resources for the National Toxicology Program's Interagency Center for the Evaluation of Alternative Toxicological Methods [NICEATM] for ICCVAM for methods validation reviews in fiscal year 2006. The Committee is encouraged by the National Toxicology Program's [NTP] Road Map and Vision for NTP's toxicology program in the 21st century and encourages NIEHS to move rapidly to implement the programs, especially those directly aimed at strengthening the scientific basis for many alternative methods (such as Quantitative Structure-Activity Relationships), mechanistic screens, high throughput assays, and toxicogenomics. (p. 129)

#### Action taken or to be taken

Please refer to the item regarding ***Toxicology validation reviews*** on page NIEHS-32 of this document for response to this Significant Item.

#### Item

***Parkinson's Disease*** – The Committee encourages NIEHS to continue funding research into environmental influences of Parkinson's disease. The causes of Parkinson's and other neurodegenerative disorders are increasingly shown to be a result of the inter-relation of environment and genes. Possible environmental triggers of Parkinson's are pesticides and/or heavy metals. If these environmental toxins can be identified and the mechanisms elucidated, appropriate prevention or treatment may prevent many cases of Parkinson's, especially concerning increasingly younger persons at risk. (p. 129)

#### Action taken or to be taken

Please refer to the item regarding ***Parkinson's disease*** on page NIEHS-29 of this document for response to this Significant Item.

#### Item

***Pacific Center for Environmental Health*** – The Committee commends the NIEHS for its prompt attention to the concerns of the citizens of Hawaii related to volcanic emissions, food and waterborne illnesses, fish contamination by pesticides and heavy metals, and pesticide residue in food and water. The Committee urges NIEHS to pursue an Environmental Health Sciences Center in Hawaii to research and address these environmental concerns and to seek workable solutions to improve the health of Pacific Islanders. (p. 129)

#### Action taken or to be taken

In 2005, NIEHS re-announced the NIEHS Core Centers grant program with changes which provide for a renewed focus on translation of basic environmental health science research to clinical and public health applications. This yearly competition is open to all universities submission of applications from universities which do not yet have a P30 grant from NIEHS is encouraged. In the past, NIEHS staff has worked with investigators from the University of Hawaii who were interested in environmental health concerns unique to the Pacific Islands. NIEHS funded a Center for Oceans and Human Health at the University of Hawaii combining the research of talented marine biologists and toxicologists. NIEHS also supports a community based participatory research program focusing on the respiratory health effects of exposure to volcanic emissions. NIEHS would welcome an application from the University of Hawaii and their collaborators for a Core Center grant and continues to be willing to discuss these possibilities with their lead researchers.

#### Item

***Perchlorate*** – The Committee encourages the Institute to support clinical, mechanistic, and epidemiological studies that focus on establishing a better understanding of the long-term health effects of perchlorate exposure on humans and determining with greater certainty what

perchlorate exposures are safe for the most vulnerable populations. The Committee encourages the NIEHS to give priority in the following areas: (1) clinical studies on humans or primates designed to provide information on the effects of long-term exposures to low doses of perchlorate; (2) the design and implementation of innovative epidemiological studies that assess the possible health effects of perchlorate exposure on the most vulnerable populations, including pregnant women and their fetuses and newborns, and involve appropriate control populations; and/or (3) in vitro studies of the perchlorate influence on placental and breast iodide transport using human tissues and animals studies, and the effects of perchlorate on development independent of effects on iodide transport. (p. 129-130)

#### Action taken or to be taken

NIEHS recognizes the importance of research to understand the long-term health effects of perchlorate on humans. We are working proactively with the extramural research community to encourage research applications on perchlorate toxicity in human and animal models. In this regard, we have communicated with all grantees studying the developmental basis of disease requesting that they consider studying developmental exposure to perchlorate and its potential links to disease and dysfunction later in life. We are planning to sponsor a symposium next year on Thyroid Function; Basic Biology, Toxicology and Translation to Human Risk, which will include a session on perchlorate toxicity to the human thyroid system. Finally, we will be publishing an article on perchlorate toxicity and our continuing interest in funding perchlorate research in the journal *Environmental Health Perspectives*. This journal reaches toxicology and environmental health researchers across the country and should stimulate additional grant applications in this important area.

#### Item

**Risk Sciences** – The Committee encourages NIEHS to establish a competitive, peer-reviewed extramural program to conduct research in risk sciences, including methodologies for assessment, management, analysis, and communication of risks from exposure to environmental chemicals. (p. 130)

#### Action taken or to be taken

Please refer to the item regarding **Risk analysis** on pages NIEHS-33 of this document for response to this Significant Item.

**NATIONAL INSTITUTES OF HEALTH**  
**National Institute of Environmental Health Sciences**

**Authorizing Legislation**

	PHS Act/ Other Citation	U.S. Code Citation	2006 Amount Authorized	FY 2006 Appropriation	2007 Amount Authorized	FY 2007 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite	\$621,944,000	Indefinite	\$618,231,000
Environmental Health Sciences	Section 41B	42§285b	Indefinite		Indefinite	
National Research Service Awards	Section 487(d)	42§288	a/	19,188,000		19,092,000
Total, Budget Authority				641,132,000		637,323,000

a/ Amounts authorized by Section 301 and Title IV of the Public Health Act.



**NATIONAL INSTITUTES OF HEALTH**  
**National Institute of Environmental Health Sciences**

**Appropriations History**

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation <sup>1/</sup>
1998	313,583,000 <sup>2/</sup>	328,583,000	331,969,000	330,108,000
1999	349,021,000 <sup>2/ 3/</sup>	356,047,000	375,743,000	375,743,000
Rescission				(249,000)
2000	390,718,000 <sup>2/</sup>	421,109,000	436,113,000	444,817,000
Rescission				(2,368,000)
2001	460,971,000 <sup>2/</sup>	506,730,000	508,263,000	502,549,000
Rescission				(495,000)
2002	561,570,000	557,435,000	585,946,000	566,639,000
Rescission				(1,942,000)
2003	609,705,000	609,705,000 <sup>4/</sup>	6,147,258,000	618,258,000
Rescission				(4,019,000)
2004	630,774,000	630,774,000	637,074,000	636,974,000
Rescission				(4,582,000)
2005	650,027,000	650,027,000	655,100,000	650,027,000
Rescission				(5,522,000)
2006	647,608,000	647,608,000	667,372,000	647,608,000
Rescission				(6,476,000)
2007	637,323,000			

<sup>1/</sup> Reflects enacted supplementals, rescissions, and reappropriations.

<sup>2/</sup> Excludes funds for HIV/AIDS research activities consolidated in the NIH Office of AIDS Research

<sup>3/</sup> Reflects a decrease of \$931,000 for the budget amendment for Bioterrorism

<sup>4/</sup> Reflects the President's Budget Request

**NATIONAL INSTITUTES OF HEALTH**  
**National Institute of Environmental Health Sciences**

**Detail of Full-Time Equivalent Employment (FTEs)**

OFFICE/DIVISION	FY 2005 Actual	FY 2006 Appropriation	FY 2007 Estimate
Office of the Director	14	14	14
Division of Research Coordination, Planning, and Translation	38	38	38
Division of Intramural Research	458	459	462
Division of Extramural Research and Training	54	54	54
Office of Management	87	87	87
<b>Total</b>	<b>651</b>	<b>652</b>	<b>655</b>
Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research FTEs supported by funds from Cooperative Research and Development Agreements			
	(0)	(0)	(0)
FISCAL YEAR	Average GM/GS Grade		
2003	10.1		
2004	11.1		
2005	11.2		
2006	11.2		
2007	11.2		

**NATIONAL INSTITUTES OF HEALTH**  
**National Institute of Environmental Health Sciences**

**Detail of Positions**

GRADE	FY 2005 Actual	FY 2006 Appropriation	FY 2007 Estimate
Total - ES Position	0	1	1
Total - ES Salary	\$0	\$135,000	\$138,000
GM/GS-15	40	40	40
GM/GS-14	62	62	62
GM/GS-13	67	67	67
GS-12	75	75	75
GS-11	114	114	115
GS-10	2	2	2
GS-9	71	71	71
GS-8	19	19	19
GS-7	28	28	28
GS-6	10	10	10
GS-5	1	1	1
GS-4	10	10	10
GS-3	2	2	2
GS-2	1	1	1
GS-1	1	1	1
Subtotal	503	503	504
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General			
Director Grade	8	8	8
Senior Grade			
Full Grade			
Senior Assistant Grade			
Assistant Grade			
Subtotal	8	8	8
Ungraded	167	168	170
Total permanent positions	493	494	497
Total positions, end of year	678	679	682
Total full-time equivalent (FTE) employment, end of year	651	652	655
Average ES salary	\$0	\$135,000	\$138,000
Average GM/GS grade	11.2	11.2	11.2
Average GM/GS salary	\$69,430	\$73,330	\$74,940

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research

**NATIONAL INSTITUTES OF HEALTH  
National Institute of Environmental Health Sciences**

**New Positions Requested**

	FY 2007		
	Grade	Number	Annual Salary
Clinical Investigator	Title 42	1	\$170,000
Staff Scientist	Title 42	1	80,000
Tenure Track Investigator	Title 42	1	100,000
Research Fellow	Title 42	1	60,000
Clinical Technician	GS-9	1	45,000
Total Requested		5	