DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

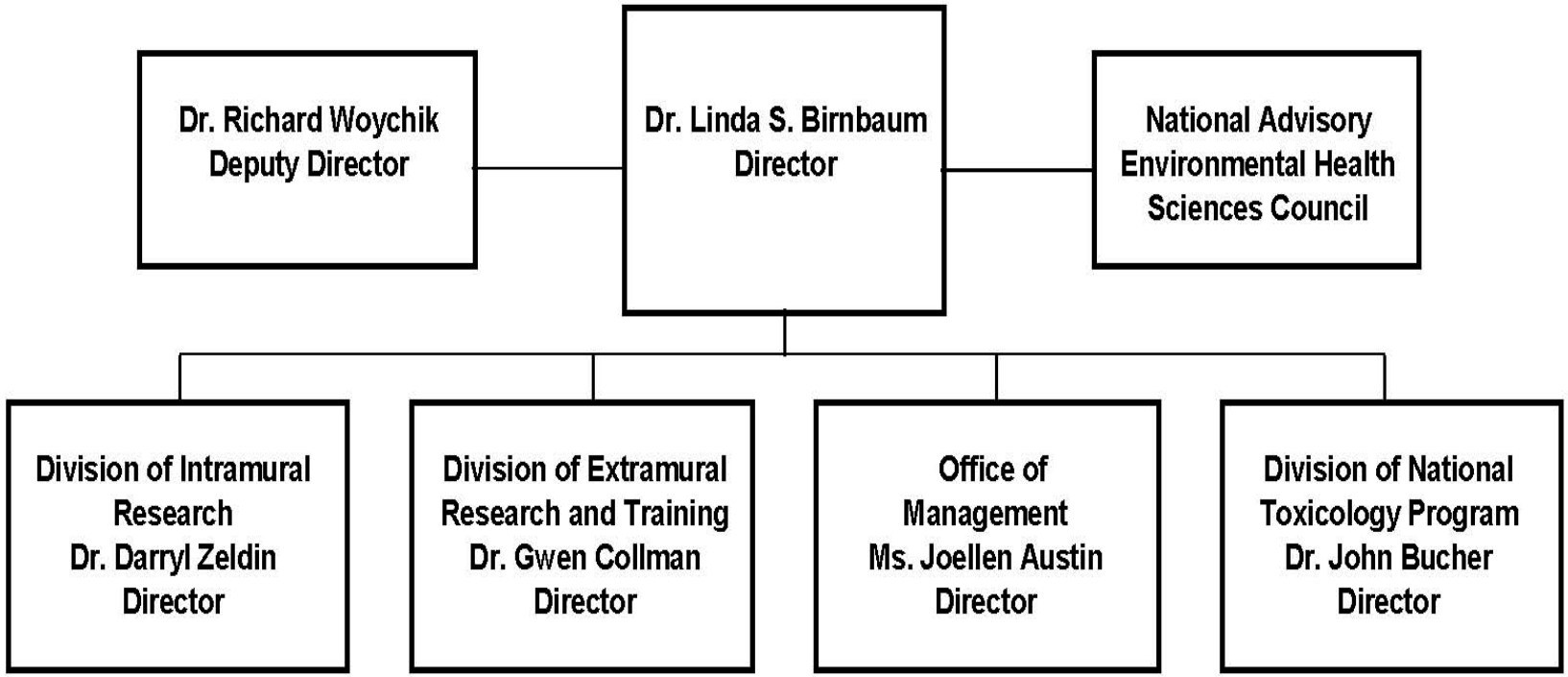
National Institute of Environmental Health Sciences (NIEHS)

FY 2013 Budget — Page No.

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 section 301 and title IV of the Public Health Services Act with respect to environmental health sciences, **[**$686,869,000**]** *$684,030,000. (Department of Health and Human Services Appropriations Act, 2012.)*

NATIONAL INSTITUTES OF HEALTH
National Institute of Environmental Health Sciences

Amounts Available for Obligation [1]
(Dollars in Thousands)

Source of Funding	FY 2011 Actual	FY 2012 Enacted	FY 2013 PB
Appropriation	689,781	686,869	684,030
Type 1 Diabetes	0	0	0
Rescission	(6,057)	(1,298)	0
Supplemental	0	0	0
Subtotal, adjusted appropriation	683,724	685,571	684,030
Real transfer under Director's one-percent transfer authority (GEI)	0	0	0
Real transfer under Secretary's transfer authority	0	(195)	0
Comparative Transfers for NCATS reorganization	0	0	0
Comparative Transfers to NCATS for Therapeutics and Rare and Neglected Diseases (TRND)	(555)	0	0
Comparative Transfers to NLM for NCBI and Public Access	(587)	(621)	0
Subtotal, adjusted budget authority	682,582	684,755	684,030
Unobligated balance, start of year	0	0	0
Unobligated balance, end of year	0	0	0
Subtotal, adjusted budget authority	682,582	684,755	684,030
Unobligated balance lapsing	(167)	0	0
Total obligations	682,415	684,755	684,030

[1] Excludes the following amounts for reimbursable activities carried out by this account:
FY 2011 - $2,799,000 FY 2012 - $4,800,000 FY 2013 - $4,800,000
Excludes $234,251 in FY2011 and $399,045 in FY2012 for royalties.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Budget Mechanism - Total [1/]

(Dollars in Thousands)

MECHANISM	FY 2011 Actual		FY 2012 Enacted		FY 2013 PB		Change vs. FY 2012	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Grants								
Research Projects								
Noncompeting	450	$192,899	451	$191,520	467	$188,604	16	($2,916)
Administrative Supplements	*35*	2,364	*30*	2,000	*20*	1,500	*(10)*	(500)
Competing:								
Renewal	25	11,678	21	10,349	20	8,729	(1)	(1,620)
New	134	43,548	142	45,955	144	47,319	2	1,364
Supplements	0	0	3	1,179	1	393	(2)	(786)
Subtotal, Competing	159	$55,226	166	$57,483	165	$56,441	(1)	($1,042)
Subtotal, RPGs	609	$250,489	617	$251,003	632	$246,545	15	($4,458)
SBIR/STTR	39	$12,666	43	$13,803	44	$14,218	1	$415
Research Project Grants	648	$263,155	660	$264,806	676	$260,763	16	($4,043)
Research Centers								
Specialized/Comprehensive	29	$35,393	29	$35,393	29	$35,060	0	($333)
Clinical Research	0	0	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0	0	0
Comparative Medicine	0	0	0	0	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	29	$35,393	29	$35,393	29	$35,060	0	($333)
Other Research								
Research Careers	45	$6,321	45	$6,321	45	$6,262	0	($59)
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	0	0	0	0	0	0	0	0
Biomedical Research Support	0	0	0	0	0	0	0	0
Minority Biomedical Research Support	0	188	0	188	0	186	0	(2)
Other	35	2,921	35	2,921	35	2,894	0	(27)
Other Research	80	$9,430	80	$9,430	80	$9,342	0	($88)
Total Research Grants	757	$307,978	769	$309,629	785	$305,165	16	($4,464)
Research Training	FTTPs		FTTPs		FTTPs			
Individual Awards	50	$2,010	49	$2,010	48	$1,991	(1)	($19)
Institutional Awards	421	16,980	416	16,980	408	16,820	(8)	(160)
Total Research Training	471	$18,990	465	$18,990	456	$18,811	(9)	($179)
Research & Development Contracts	99	$147,070	99	$147,592	99	$151,510	0	$3,918
SBIR/STTR	*6*	*$499*	*0*	*$167*	*0*	*$167*	*0*	*$0*
	FTEs		FTEs		FTEs		FTEs	
Intramural Research	537	$184,771	537	$184,771	531	$184,771	(6)	$0
Research Management and Support	139	23,773	139	23,773	138	23,773	(1)	0
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, NIEHS	676	$682,582	676	$684,755	669	$684,030	(7)	($725)

1/ All items in italics are "non-adds"; items in parenthesis are subtractions.

Major Changes in the Fiscal Year 2013 President's Budget Request

Major changes by budget mechanism and/or budget program detail are briefly described below. Note that there may be overlap between budget mechanism and activity detail and these highlights will not sum to the total change for the FY 2013 President's Budget request for NIEHS, which is $725 thousand less than the FY 2012 Enacted level, for a total of $684.030 million.

Research Project Grants (RPGs) (-$4.043 million; total $260.763 million): NIEHS expects to support a total of 676 RPG awards in FY 2013. Noncompeting RPGs will increase by 16 awards and decrease by $2.916 million from the FY 2012 level. Competing RPGs will decrease by one award and $1.042 million. NIH budget policy for RPGs in FY 2013 discontinues inflationary allowances and reduces the average cost of noncompeting and competing RPGs by one percent below the FY 2012 level. NIEHS will continue to support new investigators in FY 2013.

Clinical and Translational Research: Bench to Bedside to Public Health (+$9.153 million; total $202.131 million): Additional funding in this program will be used to support several programs. The Virtual Consortium for Translational/Transdisciplinary Environmental Research (ViCTER) program is being expanded, along with research on Climate Change and Health.

Exposure Biology/Exposure Measurement (-$7.602 million; total $23.110 million): The decrease in this program is due to the completion of the Disease Investigation through Specialized Clinically-Oriented Ventures in Environmental Research (DISCOVER) grants. Also, exposure detection technology work is progressing to the point where plans for FY 2013 and beyond call for reducing investment in new tools and focusing resources on validation and field testing of the new exposure assessment tools and biomarkers that have been identified through previous work.

NATIONAL INSTITUTES OF HEALTH
National Institute of Environmental Health Sciences
Summary of Changes
(Dollars in Thousands)

FY 2012 Enacted				**$684,755**
FY 2013 President's Budget				**$684,030**
Net change				**($725)**
	2013 President's Budget		**Change from FY 2012**	
CHANGES	**FTEs**	**Budget Authority**	**FTEs**	**Budget Authority**
A. Built-in:				
1. Intramural Research:				
a. Annualization of January 2012 pay increase & benefits		$77,975		$3
b. January FY 2013 pay increase & benefits		77,975		242
c. One more day of pay		77,975		300
d. Annualization of PY net hires		77,975		0
e. Payment for centrally furnished services		25,035		0
f. Increased cost of laboratory supplies, materials, other expenses, and non-recurring costs		81,761		0
Subtotal				$545
2. Research Management and Support:				
a. Annualization of January 2012 pay increase & benefits		$15,067		$1
b. January FY 2013 pay increase & benefits		15,067		45
c. One more day of pay		15,067		58
d. Annualization of PY net hires		15,067		0
e. Payment for centrally furnished services		2,427		0
f. Increased cost of laboratory supplies, materials, other expenses, and non-recurring costs		6,279		0
Subtotal				$104
Subtotal, Built-in				$649

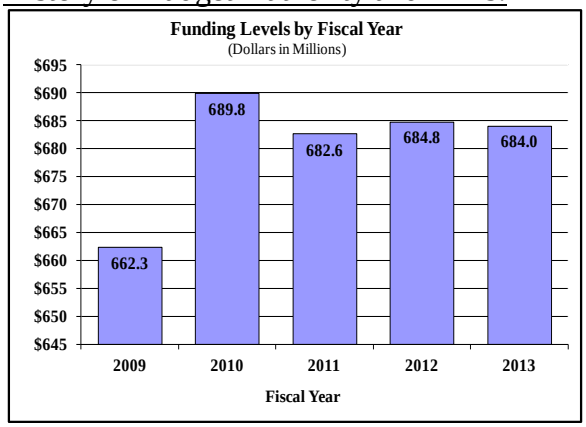
NATIONAL INSTITUTES OF HEALTH
National Institute of Environmental Health Sciences

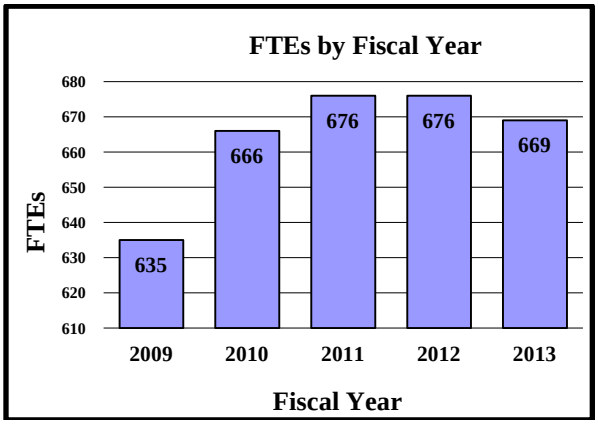
Summary of Changes--continued

CHANGES	2013 President's Budget No.	2013 President's Budget Amount	Change from FY 2012 No.	Change from FY 2012 Amount
B. Program:				
1. Research Project Grants:				
a. Noncompeting	467	$190,104	16	($3,416)
b. Competing	165	56,441	(1)	(1,042)
c. SBIR/STTR	44	14,218	1	415
Total	676	$260,763	16	($4,043)
2. Research Centers	29	$35,060	0	($333)
3. Other Research	80	9,342	0	(88)
4. Research Training	456	18,811	(9)	(179)
5. Research and development contracts	99	151,510	0	3,918
Subtotal, Extramural		$475,486		($725)
	FTEs		FTEs	
6. Intramural Research	531	$184,771	(6)	($545)
7. Research Management and Support	138	23,773	(1)	(104)
8. Construction		0		0
9. Buildings and Facilities		0		0
Subtotal, program	669	$684,030	(7)	($1,374)
Total changes				($725)

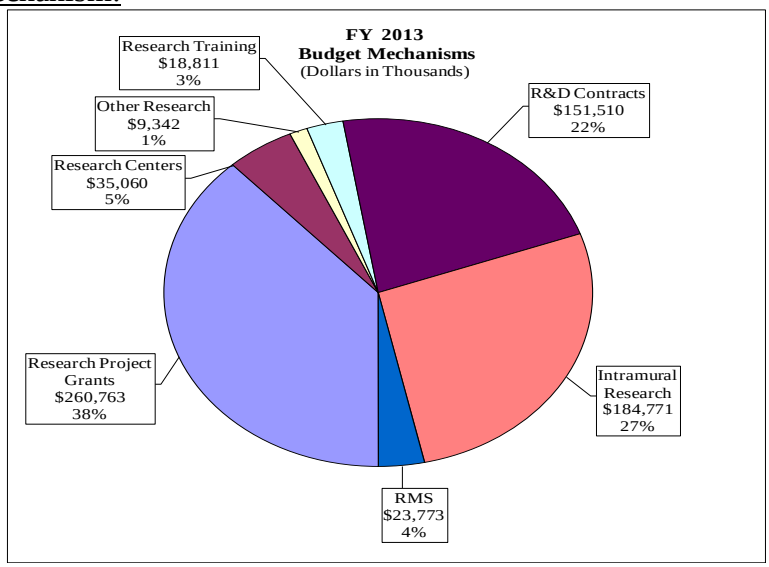
FY 2013 Budget Graphs

History of Budget Authority and FTEs:

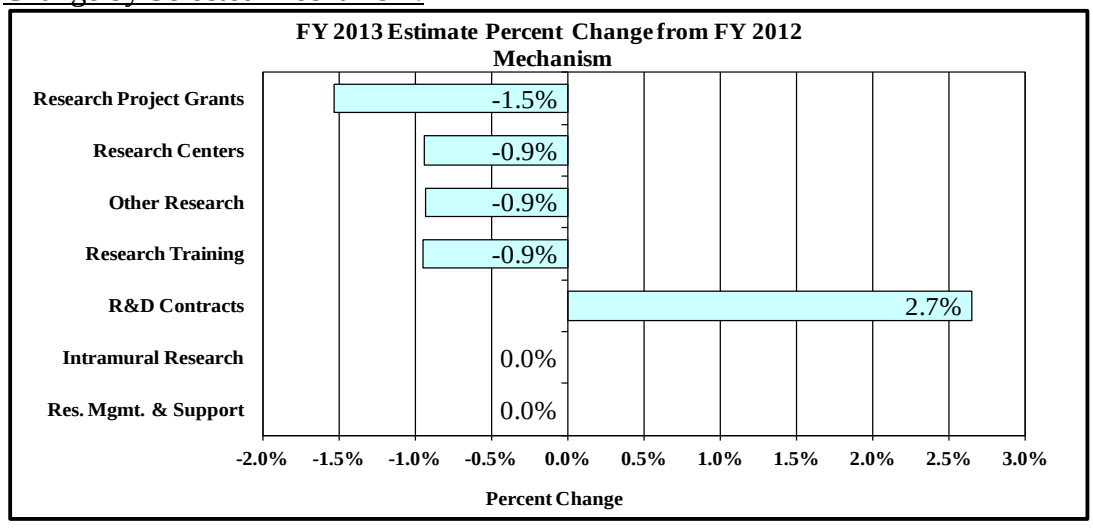




Distribution by Mechanism:



Change by Selected Mechanism:



NATIONAL INSTITUTES OF HEALTH
National Institute of Environmental Health Sciences
Budget Authority by Activity
(Dollars in Thousands)

	FY 2011 Actual		FY 2012 Enacted		FY 2013 PB		Change vs. FY 2012 Enacted	
Extramural Research	**FTEs**	**Amount**	**FTEs**	**Amount**	**FTEs**	**Amount**	**FTEs**	**Amount**
Detail:								
Clinical and Translational Research:								
Bench to Bedside to Public Health		181,021		192,978		202,131		9,153
Toxicity Testing and Evaluation		88,887		89,122		88,943		(179)
Basic Mechanism in Human Biology		135,975		128,557		126,799		(1,758)
Exposure Biology/Exposure Measurement		32,998		30,712		23,110		(7,602)
Pathways for Future Environmental Health Scientists		35,157		34,842		34,503		(339)
Subtotal, Extramural		$474,038		$476,211		$475,486		($725)
Intramural Research	537	$184,771	537	$184,771	531	$184,771	(6)	$0
Research Management & Support	139	$23,773	139	$23,773	138	$23,773	(1)	$0
TOTAL	676	$682,582	676	$684,755	669	$684,030	(7)	($725)

1. Includes FTEs which are reimbursed from the NIH Common Fund.
2. Includes Real Transfers and Comparable Adjustments as detailed in the "Amounts Available for Obligation" table.

NATIONAL INSTITUTES OF HEALTH
National Institute of Environmental Health Sciences

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2012 Amount Authorized	FY 2012 Enacted	2013 Amount Authorized	FY 2013 PB
Research and Investigation	Section 301	42§241	Indefinite	$684,755,000	Indefinite	$684,030,000
National Institute of Environmental Health Sciences	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				$684,755,000		$684,030,000

NATIONAL INSTITUTES OF HEALTH
National Institute of Environmental Health Sciences

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
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	$637,323,000	$641,292,000	$642,002,000
Rescission				$0
2008	$637,406,000	$652,303,000	$656,176,000	$653,673,000
Rescission				($11,420,000)
Supplemental				$3,416,000
2009	$642,875,000	$664,980,000	$660,767,000	$662,820,000
Rescission				$0
2010	$684,257,000	$695,497,000	$683,149,000	$689,781,000
Rescission				$0
2011	$707,339,000		$706,227,000	$689,781,000
Rescission				($6,057,112)
2012	$700,537,000	$700,537,000	$676,033,000	$686,869,000
Rescission				($1,298,182)
2013	$684,030,000			

Justification of Budget Request

National Institute of Environmental Health Sciences

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

Budget Authority:

	FY 2011 Actual	FY 2012 Enacted	FY 2013 President's Budget	FY 2013 +/- FY 2012
BA	$682,582,000	$684,755,000	$684,030,000	-$725,000
FTE	676	676	669	-7

Program funds are allocated as follows: Competitive Grants/Cooperative Agreements; Contracts; Direct Federal/Intramural and Other.

Director's Overview

The National Institute of Environmental Health Sciences (NIEHS) exists to support the very best science seeking to discover how the environment affects people's health, and to communicate the results of that science to individuals, communities, and policymakers with the goal of preventing disease and promoting healthier lives. Within the NIH, NIEHS occupies a special place: not devoted to a specific organ or disease, but uniquely empowered to follow the lines of scientific evidence of environmental influences wherever they might lead. The breadth of this mission has served NIEHS and the nation well; for example, our comprehensive understanding of the basic mechanisms of environmental contaminants like dioxin and lead allows us insight into a myriad of health outcomes such as cancer or developmental problems. Similarly, studying air pollution or diesel exhaust particulates can lead us to an understanding of respiratory outcomes, cognitive deficits, and cardiovascular health. Approximately 83 million Americans suffer some form of cardiovascular disease,[1] with significant associated costs in terms of human suffering, health care costs, and lost productivity (the costs for cardiovascular disease and stroke alone were estimated in 2007 at nearly $286 billion a year).[2] This focus, at the nexus of exposure and disease, gives NIEHS research its value as the foundation of good public health decision making in the prevention of environmentally-related diseases and disabilities.

NIEHS has embarked on a 15-month process of Strategic Planning for the next five years. In consultation with our scientists and key outside stakeholders, we have reaffirmed our mission and vision and are developing a set of Strategic Pillars and Goals to guide and optimize our research investments. The vision of the NIEHS is to provide the nation's leadership for innovative scientific research that result in improved public health through preventing disease and disability caused by the environment.

[1] American Heart Association. Heart disease and stroke statistics—2011 update. (cited 2011 December 2); available from http://www.circ.ahajournals.org/content/123/4/e18.full.pdf.
[2] Ibid.

Theme 1: Investing in Basic Research: Some of the most important issues in basic biomedical research are also at the heart of how the environment influences human biology and health. For example, the science of epigenetics is growing in importance for our understanding of how all genes are regulated. Epigenetics is the study of changes to the packaging of the DNA molecules; these changes in packaging and other DNA modifications influence the expression of genes and thus all the normal and pathogenic processes for which genes are responsible. Research on models of epigenetic processes has been demonstrating a key role for effects of environmental exposures through epigenetic mechanisms.[3,4,5,6] NIEHS has led a trans-NIH Common Fund initiative in the area of epigenetics research, and is continuing its own robust investment in this area.

Theme 2: Accelerating Discovery Through Technology*:* NIEHS stands at the forefront of applying state-of-the-art biomedical science tools to critical questions in environmental health. Proteomics, genomics, and metabolomics are all examples of the comprehensive or "omics" approaches to biology, making new discoveries and understanding of proteins, genes, and metabolism possible. For example, the rapidly developing field of proteomics (study of the "proteome" or entire set of proteins expressed by a cell, tissue or organism) uses new mass spectrometry-based methodologies to identify "protein signatures"—hundreds to thousands of individual proteins expressed in combination that can be identified and measured—that can be used to link specific environmental exposures with certain disease outcomes. One such NIEHS-funded research effort is focusing on understanding how children's early exposure to pet dander creates a protective effect against later development of asthma by looking at specific proteomic signatures. Another project is using proteomics and genomics technologies, including the breakthrough technology of toxicity assays that can test thousands of chemical samples on tiny microchips, to identify biological markers of exposure to chemicals such as bisphenol A (BPA) and genistein. This NIEHS-funded group is using a microchip assay approach to create a high-throughput system that will allow us to measure DNA damage far more rapidly than before.

Theme 3: Advancing Translational Sciences: NIEHS research priorities are established with the goal of solving real-world problems in environmental health. One of the critical areas in translational environmental health science is predictive toxicology, or how to incorporate our knowledge of key pathways, molecular events, and processes linked to disease or injury into a research and testing framework that will enable us to predict health outcomes and take preventive action to avoid adverse effects. NIEHS/NTP (National Toxicology Program) has partnered with the National Human Genome Research Institute, the Environmental Protection Agency, and the Food and Drug Administration to incorporate or integrate this knowledge into a new testing paradigm that uses quantitative high-throughput screening assays to test a large number of chemicals for their ability to affect important cellular pathways and biological

[3] Barr FD, Krohmer LJ, Hamilton JW, Sheldon LA. Disruption of histone modification and CARM1 recruitment by arsenic represses transcription at glucocorticoid receptor-regulated promoters. PLoS One. 2009 Aug 26;4(8):e6766.
[4] Ke Q, Davidson T, Chen H, Kluz T, Costa M. Alterations of histone modifications and transgene silencing by nickel chloride. Carcinogenesis. 2006 Jul;27(7):1481-8. Epub 2006 Mar 7.
[5] Guerrero-Bosagna C, Settles M, Lucker B, Skinner MK. Epigenetic transgenerational actions of vinclozolin on promoter regions of the sperm epigenome. PLoS One. 2010 Sep 30;5(9). pii: e13100.
[6] Koturbash I, Scherhag A, Sorrentino J, Sexton K, Bodnar W, Tryndyak V, Latendresse JR, Swenberg JA, Beland FA, Pogribny IP, Rusyn I. Epigenetic alterations in liver of C57BL/6J mice after short-term inhalational exposure to 1,3-butadiene.

processes. As we build a knowledge base of these results across chemicals and across testing screens, we will be able to create a framework for making better predictions about the toxic properties of the large numbers of chemicals and drugs that have not been adequately tested.

Theme 4: Encouraging New Investigators and New Ideas: NIEHS actively seeks to develop the pipeline of talented new scientists for the field of environmental health research. NIEHS programs are aimed at fostering interest in science and discovery at all levels, from K-12 through college, graduate study, and postdoctoral training. NIEHS pioneered the establishment of transition-to-independence awards that are targeted to the needs of early investigators just emerging from postdoctoral study and attempting to establish their own labs. In order to solve the complex and widely varying nature of environmental health problems, NIEHS supports training programs in multiple disciplines including genetics, cell and molecular biology, toxicology, exposure science, epidemiology, and others.

NIEHS is proud to be at the forefront of the use of state-of-the-art biomedical science to understand exposure-disease relationships and create the knowledge necessary to solve current and future problems in environmental public health.

Budget Policy: The FY 2013 President's Budget request for NIEHS is $684.030 million, a decrease of $725 thousand, or 0.1 percent from the FY 2012 Enacted level. NIEHS will continue to support new investigators and to maintain the number of competing RPGs. In FY 2013, no inflationary increase will be provided for non-competing grants and they will be reduced one percent below the FY 2012 Enacted level. NIEHS will also reduce the average cost of competing grants one percent below the FY 2012 Enacted level. In addition, NIEHS has targeted a portion of the funds available for competing research project grants to support high priority projects outside of the payline, including awards to new investigators and early stage investigators. The Institute also seeks to maintain a balance between solicitations issued to the extramural community in areas that need stimulation and funding made available to support investigator-initiated projects.

NIH will provide an across-the-board increase in FY 2013 of 2.0 percent for stipends levels under the Ruth L. Kirschstein National Research Service Award training program consistent with recommendations from the National Academy of Sciences. This will build on the 2.0 percent increase in stipend levels for FY 2012. Stipend levels were largely flat for several years, and the requested increase will help to sustain the development of a highly qualified biomedical research workforce.

Intramural Research and Research Management and Support are funded at the same level in FY 2013 as in FY 2012. Funds are included in R&D contracts to support trans-NIH initiatives, such as the Basic Behavioral and Social Sciences Opportunity Network (OppNet).

Program Descriptions and Accomplishments

Clinical and Translational Research: Bench to Bedside to Public Health: This program encourages integration of clinical, population, and community-based research to translate findings into improved public health practice and disease prevention. Genome-wide association studies (GWAS) have been successfully used to identify susceptibility genes for many common diseases. Unfortunately, genes that influence disease through their interactions with other genes or with environmental factors are difficult to detect through GWAS. In August 2011, a group of NIEHS-funded researchers and others published a groundbreaking study using a novel method called Genome-Wide Association and Interaction Study (GWAIS) to identify gene-environment interactions in Parkinson's Disease (PD).[7] These researchers focused on PD as an important disease with known associations to both specific genes and specific environmental influences (having both protective effects and deleterious effects). Using several cohorts, they checked the interaction of over 800,000 gene variants against consumption of caffeinated coffee by the individual subjects. The findings identified a novel PD modifier gene, called *GRIN2A*. This gene encodes a portion of a neurological receptor, the NMDA-glutamate-receptor known for regulating some types of neurotransmission in the brain and controlling movement and behavior. The gene had not turned up in previous GWAS studies of PD because its effect is small when considered independently of the interaction with coffee. This study is proof of concept that inclusion of environmental factors can help identify genes that are missed in GWAS. *GRIN2A* may be a useful pharmacogenetic marker for subdividing individuals in clinical trials to determine which medications might work best for which patients.

Budget Policy: The FY 2013 President's Budget request for this program is $202.131 million, an increase of $9.153 million, or 4.7 percent over the FY 2012 Enacted level. Research will be used to support a variety of clinical and translational research activities, including the increasing translational research capacity through our new translational research consortia.

[7] Hamza TH, Chen H, Hill-Burns EM, Rhodes SL, Montimurro J, Kay DM, Tenesa A, Kusel VI, Sheehan P, Eaaswarkhanth M, Yearout D, Samii A, Roberts JW, Agarwal P, Bordelon Y, Park Y, Wang L, Gao J, Vance JM, Kendler KS, Bacanu SA, Scott WK, Ritz B, Nutt J, Factor SA, Zabetian CP, Payami H. Genome-wide gene-environment study identifies glutamate receptor gene GRIN2A as a Parkinson's disease modifier gene via interaction with coffee. PLoS Genet. 2011 Aug;7(8):e1002237. Epub 2011 Aug 18

Program Portrait: Environment and Autism

FY 2012 Level: $6.3 million
FY 2013 Level: $6.3 million
Difference: $0.0 million

The number of children diagnosed with autism spectrum disorder (ASD) has increased in the U.S. in the past several years. NIEHS conducts and funds multiple projects investigating environmental links to autism, and actively participates in the Interagency Autism Coordinating Committee, a group of Federal agencies and public members (parents and people living with autism) that works to coordinate scientific research on this disorder. NIEHS's two largest efforts on autism are the Childhood Autism Risks from Genes and the Environment (CHARGE) study, and the Early Autism Risk Longitudinal Investigation (EARLI) study. In the CHARGE study, led by the Children's Center at the University of California at Davis, researchers are looking at more than 1,600 children in three groups: children with autism, children with developmental delay who do not have autism, and children from the general population. All of the children are evaluated for a broad array of environmental exposures and susceptibilities with the goal of better understanding the causes and contributing factors for autism or developmental delay. A significant recent finding is that 40 percent of children with autism show evidence of regression, defined alternatively as the loss of language and social skills after developing normally up to that point, or loss only of social skills. This is much higher than previously thought and indicates that requiring loss of language in the definition significantly underestimates the frequency of developmental regression. In the EARLI study, researchers at the Drexel University School of Public Health are enrolling 1,000 mothers who have a child with autism and who are pregnant again. The study, which is part of the trans-NIH Autism Centers of Excellence (ACE) Program, will follow the mothers during their pregnancy and their new babies through age three to identify in real time prenatal, neonatal, and early postnatal environmental exposures that may influence their risk of developing autism. NIEHS also partnered with UC-Davis and Autism Speaks on a workshop that brought together parents, educators, community clinicians, scientists, media, and policy makers to explore issues surrounding the ethics of communicating scientific findings on autism risk.

[1] http://www.cdc.gov/ncbddd/autism/data.html "State of Research on Potential Environmental Health Factors with Autism and Related Neurodevelopment Disorders" Senate Environment and Public Works Subcommittee on Children's Health August 3, 2010

Toxicity Testing and Evaluation: This program comprises the NIEHS extramural research investment of the National Toxicology Program, whose mission is to evaluate environmental agents of public health concern, and generate information to be used by health regulatory agencies to make informed decisions affecting public health. NTP also works to develop new and improved test methods, including alternatives to animal testing and high-throughput methods to test substances faster, in order to disseminate useful public health information more rapidly. NTP research also helps to develop new and improved models of toxicity that can help to predict cancer and other adverse health outcomes that may result from fetal or early life exposures. For example, a mouse transplacental model has been developed in which maternal exposure to inorganic arsenic either acts as a complete carcinogen or enhances carcinogenic response to other agents to which the offspring are subsequently exposed to produce tumors during adulthood.[8] This model suggests that arsenic acts to enhance the number and survival of cancer stem cells. Because inorganic arsenic causes cancer in multiple human tissues including the bladder, skin, and lung, as well as the liver, kidney, and prostate, this model should provide useful information on stem cell-based cancers caused by developmental exposure to other toxicants as well.

[8] Tokar EJ, Qu W, Waalkes MP. Arsenic, stem cells, and the developmental basis of adult cancer. Toxicol Sci. 2011 Mar;120 Suppl 1:S192-203.

Budget Policy: The FY 2013 President's Budget request for this program is $88.943 million, a decrease of $0.179 million, or 0.2 percent below the FY 2012 Enacted level. Resources in this program are supporting novel toxicology methods to improve our ability to assess risk and to understand toxic effects at the cellular and molecular level.

Basic Mechanisms in Human Biology: Environmental toxicants can interrupt normal biological processes and initiate events leading to disease. This program uses environmental toxicants as laboratory probes for studying the complex molecular pathways that lead to chronic disease, identifies methods to diagnose these diseases before they are clinically evident, and develops early interventions to prevent progression to end-stage disease.

NIEHS-supported researchers reported in the November 2011 issue of Nature Nanotechnology[9] the mechanics of how cells are doomed to fail when attempting to engulf carbon nanotubes specifically due to the shape of the nanomaterial. Carbon nanotubes have a variety of uses in materials science because of their high strength to weight characteristics and in medicine as targeted drug delivery devices. Carbon nanotubes that are closed on one end appear like spheres to the cells. In the process described in the paper, cells begin to engulf the rounded end and often orient the nanotube so that it is perpendicular to the cell membrane. As the nanotube brushes up against the membrane, special receptors send signals that cause the cell to wrap its membrane around the nanotube. As this occurs, the nanotube is tipped to a 90 degree angle, effectively reducing the amount of energy needed for the cell to engulf what it inaccurately senses is a small particle. Within minutes, the cell senses it will not be able to completely engulf the nanotube, but once the engulfing process begins, there is no corresponding signal to stop and reverse the process. The cell then mounts an immune response that results in chronic inflammation. As this process is very similar to the reaction of cells to asbestos, it has potentially high applicability to existing environmental health problems. This research also is important for scientists to fully understand how cells and nanomaterials interact so that nanostructures can be designed safely.

Budget Policy: The FY 2013 President's Budget request for this program is $126.799 million, a decrease of $1.758 million, or 1.4 percent below the FY 2012 Enacted level. In large part, this decrease represents the completion of several earlier initiatives.

Exposure Biology/Exposure Measurement: This program seeks to develop improved methods to detect and measure environmental exposures in humans or other organisms. Identifying hazardous agents in the environment can be a difficult task; many environmental factors that pose significant risks to human health are actually non-toxic in the form to which humans are exposed but are metabolized by the body's enzymes into highly reactive, toxic compounds. Through a series of publications this past year, an NIEHS-funded researcher and colleagues demonstrated the power of a new technology to detect such compounds and predict their toxicological potential. The technology is based on the ability to embed the human metabolic enzymes in a nanoscale film on an electrochemical sensor in a technology called a microfluidic array. Essentially, non-toxic agents that can be metabolized by the body into toxic forms are applied to the assay film. The technology generates an electrical current when the enzymes metabolize the non-toxic compounds into a toxic form, thereby identifying the conditions under

[9] Shi X, von dem Bussche A, Hurt RH, Kane AB, Gao H. Cell entry of one-dimensional nanomaterials occurs by tip recognition and rotation. Nat Nanotechnol. 2011 Sep 18. doi: 10.1038/nnano.2011.151.

which they are metabolized.[10, 11] This research group has recently shown the ability to detect compounds using this technology by demonstrating its success using pollutants that are known to metabolize into toxic forms. This microfluidic array is the first demonstration of the use of an electrochemical sensor system to assess the metabolism of potentially harmful environmental compounds.

Budget Policy: The FY 2013 President's Budget request for this program is $23.110 million, a decrease of $7.602 million, or 24.75 percent below the FY 2012 Enacted level. A large portion of this decrease is due to the ending of the previous RFA known as DISCOVER. In addition, exposure detection technology work is proceeding to the point where plans for FY2013 and beyond call for reducing investment in new tools and focusing resources on validation and field testing of the new exposure assessment tools and biomarkers that have been identified through previous work.

Program Portrait: Next Phase of the Exposure Biology Program/Genes, Environment and Health Initiative

FY 2012 Level: $7.1 million
FY 2013 Level: $6.5 million
Difference: -$0.6 million

The Genes, Environment and Health Initiative (GEI) was started in 2007 to create a technological foundation for investigating the interaction between environmental and genetic underpinnings of human disease. The Initiative consisted of two major components: identifying genetic susceptibility factors for diseases with high public health impact and developing new technologies for accurate measurement of environmental exposures and lifestyle factors. The Exposure Biology Program (EBP) was established to develop a set of tools for assessing individual exposure to environmental stressors, including airborne toxic chemicals, psychosocial stress, addictive substances, and diet and physical activity, as well as measures of the biological response to those stressors. A number of exciting technologies have been created or adapted under this program, including dietary assessment methods using cell phone and digital imaging; miniaturized personal monitors for black carbon and other air pollutants; early disease biomarkers for PCB exposure; and an integrated measurement system to assess physical activity. The evolution of this program builds on the success of the initial phase in creating these prototype technologies. In FY 2013, the EBP will focus on:

--Validation of tools and candidate biomarkers for exposure biology, including assessment of the scientific value of the tools in an epidemiological setting.
--Development of wearable tools for characterization of the personal environment that are minimally intrusive and encourage full use so that researchers can assess exposure to multiple factors in the wearer's environment simultaneously.
--Field deployable tools for multi-analyte biomonitoring of environmental exposures, to develop a new set of tools based on in vitro diagnostic or lab-on-a-chip technologies to assay the levels of environmental factors in readily accessible biological samples.

NIEHS will also continue work under this program to promote new methodologies for studies of gene-environment interactions by integrating environmental measures into analyses of human population studies.

[10] Krishnan S, Wasalathanthri D, Zhao L, Schenkman JB, Rusling JF. Efficient bioelectronics actuation of the natural catalytic pathway of human metabolic cytochrome P450s. dx.doi.org/10.1021/ja108637s | J. Am. Chem. Soc. 2011, 133, 1459–1465

[11] Krishnan S, Schenkman JB, Rusling JF. Bioelectronic delivery of electrons to cytochrome P450 enzymes. J Phys Chem B. 2011 Jul 7;115(26):8371-80. Epub 2011 May 17.

Pathways for Future Environmental Health Scientists: This program's goal is to attract the brightest students and scientists into the environmental health sciences field to ensure a cadre of professionals to conduct the interdisciplinary research necessary to solve critical environmental health problems. This program includes efforts at the high school and undergraduate levels (opportunities for laboratory-based training), the graduate level (institutional and individual training grants), and the faculty level (grants for young investigators and short term sabbatical awards). The Mentored Clinical Scientist Development Award program supports the development of outstanding clinician research scientists who demonstrate the potential to develop into independent investigators. One scientist currently supported under this program is investigating immune responses and human airway disease from exposure to organic dust in swine confinement facilities. This researcher has developed an *in vivo* mouse model of intranasal dust exposure that results in exaggerated airway inflammation and tissue injury.[12] This model, which appears to mimic the well-recognized adaptation response described in humans, will allow for qualitative and quantitative measures of dust-induced inflammation useful for studying mechanistic regulation of environmentally triggered lung disease. This research has demonstrated novel aspects related to organic dust-induced inflammation that are relevant to human airway disease. In particular, in contrast to the current dogma which focuses on endotoxin-driven mechanisms, this study strongly suggests that Gram-positive bacteria cell wall products may be the principal drivers of inflammation. This result could have important consequences for environmental sampling strategies and targets for potential prevention and therapeutic interventions in humans.

Budget Policy: The FY 2013 President's Budget request for this program is $34.503 million, a decrease of $0.339 million, or 0.97 percent below the FY 2012 Enacted level. Resources will be used to continue ongoing training programs at undergraduate, doctoral, postdoctoral, and early- and mid-career levels.

Intramural Research: The mission of the NIEHS intramural research program is to investigate the role of environmental agents in human disease and dysfunction and define the important biological and chemical processes that these agents affect. NIEHS intramural research studies are often longitudinal and not immediately translatable into diagnostic or therapeutic tools, and comprise unique components, such as NIEHS contribution to the NTP, epidemiological studies of environmentally associated diseases and exposures (including the new study of individuals exposed by the Gulf oil spill), and intervention and prevention studies in humans to reduce the effects of exposures to hazardous environments. The NIEHS Clinical Research Unit provides opportunities for clinical and basic scientists in the Intramural Program to collaborate and learn how environmental exposures influence human health and disease. Among many important lines of research, NIEHS intramural scientists are studying the mechanisms that control the ability of environmental substances to cross from the blood into the brain. The body has a remarkable blockade system to prevent access to the brain, termed the "blood-brain barrier." Cellular proteins called "transporters" are required to move substances in and out of the brain. A recent finding identified a common cellular receptor protein as a mediator of the action of these transporters. This protein, termed the Aryl Hydrocarbon Receptor or AhR, senses the presence

[12] Poole JA, Kielian T, Wyatt TA, Gleason AM, Stone J, Palm K, West WW, Romberger DJ. Organic dust augments nucleotide-binding oligomerization domain expression via an NF-{kappa}B pathway to negatively regulate inflammatory responses. Am J Physiol Lung Cell Mol Physiol. 2011 Sep;301(3):L296-306.

of many deleterious toxic chemicals, including dioxin. NIEHS intramural scientists demonstrated that when dioxin was bound to AhR in rat brain capillaries, there was an associated increase in activity and expression of the P-glycoprotein transporter molecules, leading to changes to the accessibility of the drugs and environmental agents to the brain that are affected by this transporter.[13] These findings introduce a completely new framework for understanding how environmental exposures affect health – by altering the vulnerability of the brain itself.

Budget Policy: The FY 2013 President's Budget request for this program is $184.771 million, the same as the FY 2012 Enacted level. Resources will be continue to support the demand for bioinformatics in high-throughput screening, toxicogenomics, epigenomics, systems biology and database integration.

Program Portrait: Understanding Environmental Influences on Chemical "Marks" in DNA that Modify Gene Expression: the "Methylome Project"

FY 2012 Level: $0.9 million
FY 2013 Level: $0.3 million
Difference: -$0.6 million

Recent advances in DNA molecular biology have identified many enzymes that can chemically modify the four DNA bases. Some of these modifications affect the activity of the genes in the cell in which they are found. Most prominent is methylation -- the attachment of a simple methyl group [CH_3] to certain cytosines. Some methylation patterns are associated with production of liver tumors in laboratory mice. Because strains of mice differ in the likelihood that they will develop liver tumors, investigators hypothesize that the patterns of methylated cytosines in the livers of each strain also may be different. The NIEHS "Mouse Methylome Project" has been developed to answer these questions.

The primary goal will be to use high throughput ["NextGen"] DNA sequencing machines to create a high resolution map of the mouse liver methylome from three different mouse stains. These strains show dramatically different incidences of spontaneous liver tumors. A major premise of this project is that the variable cancer incidence among these mouse strains may be due in part to differential cytosine methylation in critical tumor suppressor genes and other regulatory regions of the genome that affect associated pathways for liver cancer susceptibility and its heritability across generations.

Two mouse strains and their offspring will be measured. Once the methylation locations are defined, the information will be placed in a publicly-accessible database on the Internet, together with suitable computer programs allowing scientists and the general public to inspect these sequences and further explore the linkage between the methylome and the appearance of liver diseases, including cancers.

Research Management and Support (RMS): The RMS program provides administrative, budgetary, logistical and scientific support in the review, award, and monitoring of research grants and training awards. NIEHS currently oversees approximately 785 research grants and centers. RMS also provides administrative support for the Intramural Research program. Other RMS functions include strategic planning, coordination, and evaluation of NIEHS programs, regulatory compliance, ethics, and liaison with other Federal agencies, Congress, and the public. NIEHS has been conducting an inclusive strategic planning process for almost a year; the

[13] Wang, X., Hawkins, B. T., Miller, D. S. Aryl hydrocarbon receptor-mediated up-regulation of ATP-driven xenobiotic efflux transporters at the blood-brain barrier. FASEB J. 25, 644–652 (2011).

resulting Strategic Plan and Goals, due to be completed this summer, will define the Institute's directions for the next five years.

Budget Policy: The FY 2013 President's Budget request for this program is $23.773 million, the same as the FY 2012 Enacted level. Resources continue to support liaison functions with other government agencies and non-government organizations to improve interagency collaboration and efficiency and optimize use of resources.

NATIONAL INSTITUTES OF HEALTH
National Institute of Environmental Health Sciences

Budget Authority by Object
(Dollars in Thousands)

	FY 2012 Enacted	FY 2013 PB	Increase or Decrease
Total compensable workyears:			
Full-time employment	676	669	(7)
Full-time equivalent of overtime and holiday hours	1	1	0
Average ES salary (*in dollars*)	$168,286	$169,127	$841
Average GM/GS grade	11.5	11.5	0.0
Average GM/GS salary (*in dollars)*	$84,279	$84,700	$421
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207) *(in dollars)*	$99,642	$101,635	$1,993
Average salary of ungraded positions (*in dollars*)	126,697	127,330	633

	OBJECT CLASSES	FY 2012 Enacted	FY 2013 PB	Increase or Decrease
	Personnel Compensation:			
11.1	Full-time permanent	$41,092	$40,820	($272)
11.3	Other than full-time permanent	20,744	20,738	(6)
11.5	Other personnel compensation	1,374	1,374	0
11.7	Military personnel	1,063	1,079	16
11.8	Special personnel services payments	9,187	9,182	(5)
	Total, Personnel Compensation	**$73,460**	**$73,193**	**($267)**
12.0	Personnel benefits	$19,083	$19,015	($68)
12.2	Military personnel benefits	837	834	(3)
13.0	Benefits for former personnel	0	0	0
	Subtotal, Pay Costs	**$93,380**	**$93,042**	**($338)**
21.0	Travel and transportation of persons	$2,042	$1,775	($267)
22.0	Transportation of things	393	393	0
23.1	Rental payments to GSA	3	3	0
23.2	Rental payments to others	29	29	0
23.3	Communications, utilities and miscellaneous charges	1,051	1,051	0
24.0	Printing and reproduction	54	54	0
25.1	Consulting services	859	859	0
25.2	Other services	31,507	31,622	115
25.3	Purchase of goods and services from government accounts	106,214	111,278	5,064
25.4	Operation and maintenance of facilities	4,206	4,206	0
25.5	Research and development contracts	93,647	93,470	(177)
25.6	Medical care	226	226	0
25.7	Operation and maintenance of equipment	3,609	3,495	(114)
25.8	Subsistence and support of persons	0	0	0
25.0	**Subtotal, Other Contractual Services**	**$240,268**	**$245,156**	**$4,888**
26.0	Supplies and materials	$11,491	$11,448	($43)
31.0	Equipment	7,424	7,102	(322)
32.0	Land and structures	0	0	0
33.0	Investments and loans	0	0	0
41.0	Grants, subsidies and contributions	328,619	323,976	(4,643)
42.0	Insurance claims and indemnities	0	0	0
43.0	Interest and dividends	1	1	0
44.0	Refunds	0	0	0
	Subtotal, Non-Pay Costs	**$591,375**	**$590,988**	**($387)**
	Total Budget Authority by Object	**$684,755**	**$684,030**	**($725)**

Includes FTEs which are reimbursed from the NIH Common Fund.

NATIONAL INSTITUTES OF HEALTH
National Institute of Environmental Health Sciences

Salaries and Expenses
(Dollars in Thousands)

OBJECT CLASSES	FY 2012 Enacted	FY 2013 PB	Increase or Decrease
Personnel Compensation:			
Full-time permanent (11.1)	$41,092	$40,820	($272)
Other than full-time permanent (11.3)	20,744	20,738	(6)
Other personnel compensation (11.5)	1,374	1,374	0
Military personnel (11.7)	1,063	1,079	16
Special personnel services payments (11.8)	9,187	9,182	(5)
Total Personnel Compensation (11.9)	**$73,460**	**$73,193**	**($267)**
Civilian personnel benefits (12.1)	$19,083	$19,015	($68)
Military personnel benefits (12.2)	837	834	(3)
Benefits to former personnel (13.0)	0	0	0
Subtotal, Pay Costs	**$93,380**	**$93,042**	**($338)**
Travel (21.0)	$2,042	$1,775	($267)
Transportation of things (22.0)	393	393	0
Rental payments to others (23.2)	29	29	0
Communications, utilities and miscellaneous charges (23.3)	1,051	1,051	0
Printing and reproduction (24.0)	54	54	0
Other Contractual Services:			
Advisory and assistance services (25.1)	859	859	0
Other services (25.2)	31,507	31,622	115
Purchases from government accounts (25.3)	70,339	70,190	(149)
Operation and maintenance of facilities (25.4)	4,206	4,206	0
Operation and maintenance of equipment (25.7)	3,609	3,495	(114)
Subsistence and support of persons (25.8)	0	0	0
Subtotal Other Contractual Services	**$110,520**	**$110,372**	**($148)**
Supplies and materials (26.0)	$11,488	$11,445	($43)
Subtotal, Non-Pay Costs	$125,577	$125,119	($458)
Total, Administrative Costs	**$218,957**	**$218,161**	**($796)**

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Details of Full-Time Equivalent Employment (FTEs)

OFFICE/DIVISION	FY 2011 Actual			FY 2012 Enacted			FY 2013 PB		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Office of the Director									
Direct:	50	2	52	50	2	52	49	2	51
Reimbursable:	1	0	1	1	0	1	1	0	1
Total:	51	2	53	51	2	53	50	2	52
Division of Intramural Research									
Direct:	344	4	348	344	4	348	339	4	343
Reimbursable:	1	0	1	1	0	1	1	0	1
Total:	345	4	349	345	4	349	340	4	344
Division of National Toxicology Program									
Direct:	105	2	107	105	2	107	105	2	107
Reimbursable:	0	0	0	0	0	0	0	0	0
Total:	105	2	107	105	2	107	105	2	107
Division of Extramural Research and Training									
Direct:	54	0	54	54	0	54	54	0	54
Reimbursable:	1	0	1	1	0	1	1	0	1
Total:	55	0	55	55	0	55	55	0	55
Office of Management									
Direct:	110	2	112	110	2	112	109	2	111
Reimbursable:	0	0	0	0	0	0	0	0	0
Total:	110	2	112	110	2	112	109	2	111
Total	666	10	676	666	10	676	659	10	669
Includes FTEs which are reimbursed from the NIH Common Fund.									
FTEs supported by funds from Cooperative Research and Development Agreements	0	0	0	0	0	0	0	0	0

FISCAL YEAR	Average GS Grade
2009	11.3
2010	11.4
2011	11.5
2012	11.5
2013	11.5

NATIONAL INSTITUTES OF HEALTH
National Institute of Environmental Health Sciences

Detail of Positions

GRADE	FY 2011 Actual	FY 2012 Enacted	FY 2013 PB
Total, ES Positions	1	1	1
Total, ES Salary	168,286	168,286	169,127
GM/GS-15	43	43	43
GM/GS-14	59	59	59
GM/GS-13	80	80	80
GS-12	95	95	94
GS-11	109	109	106
GS-10	1	1	1
GS-9	62	62	62
GS-8	16	16	16
GS-7	25	25	25
GS-6	2	2	2
GS-5	0	0	0
GS-4	7	7	7
GS-3	2	2	2
GS-2	1	1	1
GS-1	0	0	0
Subtotal	502	502	498
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	1	1	1
Director Grade	5	5	5
Senior Grade	2	2	2
Full Grade	2	2	2
Senior Assistant Grade	0	0	0
Assistant Grade	0	0	0
Subtotal	10	10	10
Ungraded	212	212	209
Total permanent positions	493	493	493
Total positions, end of year	705	705	705
Total full-time equivalent (FTE) employment, end of year	676	676	669
Average ES salary	168,286	168,286	169,127
Average GM/GS grade	11.5	11.5	11.5
Average GM/GS salary	84,279	84,279	84,700

Includes FTEs which are reimbursed from the NIH Common Fund.