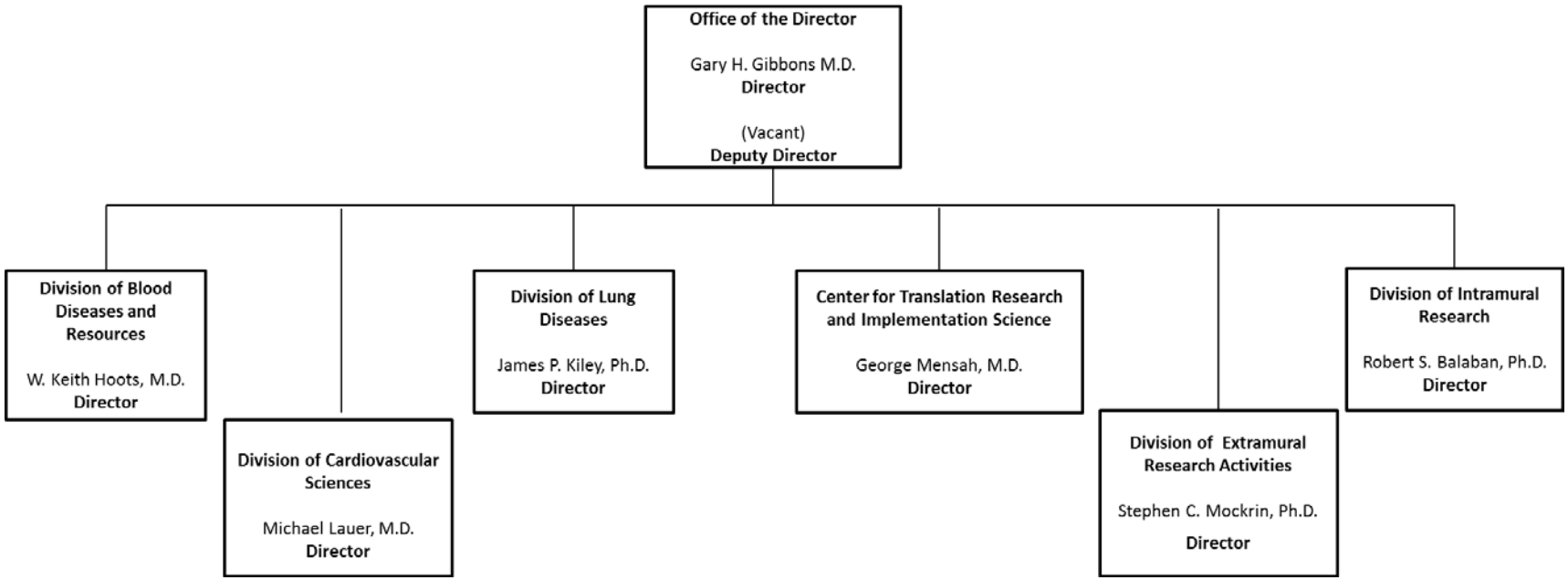
DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Heart, Lung, and Blood Institute (NHLBI)

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood, Institute



NATIONAL INSTITUTES OF HEALTH

National Heart, Lung, and Blood Institute

For carrying out section 301 and title IV of the PHS Act with respect to cardiovascular, lung, and blood diseases, and blood and blood products, [$2,997,870,000]*$3,071,906,000*.

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

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

Source of Funding	FY 2014 Actual	FY 2015 Enacted	FY 2016 President's Budget
Appropriation	$2,988,605	$2,997,870	$3,071,906
Type 1 Diabetes	0	0	0
Rescission	0	0	0
Sequestration	0	0	0
FY 2014 First Secretary's Transfer	-7,502	0	0
FY 2014 Second Secretary's Transfer	-585	0	0
Subtotal, adjusted appropriation	$2,980,518	$2,997,870	$3,071,906
OAR HIV/AIDS Transfers	-1,756	-2,005	0
National Children's Study Transfers	9,822	0	0
Subtotal, adjusted budget authority	$2,988,584	$2,995,865	$3,071,906
Unobligated balance, start of year	0	0	0
Unobligated balance, end of year	0	0	0
Subtotal, adjusted budget authority	$2,988,584	$2,995,865	$3,071,906
Unobligated balance lapsing	-169	0	0
Total obligations	$2,988,415	$2,995,865	$3,071,906

[1] Excludes the following amounts for reimbursable activities carried out by this account:
FY 2014 - $15,768 FY 2015 - $15,839 FY 2016 - $15,510

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Budget Mechanism - Total[1]

(Dollars in Thousands)

MECHANISM	FY 2014 Actual		FY 2015 Enacted		FY 2016 President's Budget		FY 2016 +/- FY 2015	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	2,347	$1,386,961	2,332	$1,377,960	2,399	$1,390,503	67	$12,543
Administrative Supplements	*(148)*	40,845	*(78)*	22,000	*(78)*	22,000	*(0)*	0
Competing:								
Renewal	166	106,670	194	116,313	255	139,075	61	22,762
New	577	308,277	582	348,940	766	417,226	184	68,285
Supplements	0	0	0	0	0	0	0	0
Subtotal, Competing	743	$414,947	776	$465,254	1,021	$556,301	245	$91,047
Subtotal, RPGs	3,090	$1,842,754	3,108	$1,865,214	3,420	$1,968,804	312	$103,590
SBIR/STTR	139	74,675	143	78,317	188	81,086	45	2,769
Research Project Grants	3,229	$1,917,429	3,251	$1,943,531	3,608	$2,049,890	357	$106,359
Research Centers:								
Specialized/Comprehensive	28	$71,535	23	$62,486	35	$77,067	12	$14,581
Clinical Research	0	0	0	0	0	0	0	0
Biotechnology	0	710	0	0	0	0	0	0
Comparative Medicine	1	2,377	1	2,377	1	1,193	0	-1,184
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	29	$74,622	24	$64,863	36	$78,261	12	$13,398
Other Research:								
Research Careers	485	$73,946	486	$74,114	508	$76,374	22	$2,260
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	68	57,888	68	57,364	64	47,054	-4	-10,310
Biomedical Research Support	0	0	0	0	0	0	0	0
Minority Biomedical Research Support	6	2,256	3	1,169	2	1,262	-1	93
Other	117	41,567	70	49,578	423	60,192	353	10,614
Other Research	676	$175,658	627	$182,225	997	$184,882	370	$2,657
Total Research Grants	3,934	$2,167,708	3,902	$2,190,619	4,641	$2,313,033	739	$122,414
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	210	$10,104	239	$10,755	318	$13,540	79	$2,785
Institutional Awards	1,444	77,078	1,605	85,878	1,619	86,298	14	420
Total Research Training	1,654	$87,182	1,844	$96,633	1,937	$99,837	93	$3,204
Research & Develop. Contracts	202	$417,022	186	$384,139	159	$328,072	-27	-$56,067
(SBIR/STTR) (non-add)	*(13)*	*(9,527)*	*(12)*	*(10,657)*	*(11)*	*(9,552)*	*(-1)*	*(-1,105)*
Intramural Research	531	193,424	531	198,359	531	202,326	0	3,967
Res. Management & Support	396	123,248	401	126,115	401	128,637	0	2,522
Res. Management & Support (SBIR Admin) (non-add)	*(0)*	*(1,461)*	*(0)*	*(538)*	*(0)*	*(0)*	*(0)*	*(-538)*
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, NHLBI	927	$2,988,584	932	$2,995,865	932	$3,071,906	0	$76,041

[1] All items in italics and brackets are non-add entries.

Major Changes in the Fiscal Year 2016 President's Budget Request

Major changes by budget mechanism and/or budget activity detail are briefly described below. Note that there may be overlap between budget mechanisms and activity detail and these highlights will not sum to the total change for the FY 2016 budget request for NHLBI, which is $76.041 million more than the FY 2015 Enacted level, for a total of $3,071.906 million.

Research Project Grants (RPGs) (+$106.359 million; total $2,049.890 million):
NHLBI will fund 1,021 competing RPGs and approximately 2,399 noncompeting RPG awards totaling to $1,968.804 million, in FY 2016. NIH budget policy for RPGs in FY 2016 continues the FY 2012 policy of eliminating inflationary increases for future year commitments. However, adjustments for special needs (such as equipment and added personnel) will continue to be accommodated.

Research Training (+$3.204 million; total $99.837 million):
The Ruth L. Kirschstein NRSA budget reflects a stipend increase for entry level postdoctoral trainees and fellows at 2 percent over FY 2015 Enacted levels. The number of FTTPs are increased by 93 from the FY 2015 level of 1,844.

Precision Medicine Cohort (+$20.504 million; total $20.504 million):
NIH proposes to launch a national research cohort of one million or more Americans – to propel our understanding of health and disease and set the foundation for a new way of doing research through engaged participants and open, responsible data sharing. Participants who voluntarily choose to join this effort will be able to share their genomic data, biological specimens, and behavioral data, and, if they choose, link it to their electronic health records (EHRs), taking advantage of the latest in social media and mobile applications, and with appropriate privacy protections in place. Bona fide researchers from across the country will have access to data voluntarily provided, thereby crowdsourcing rich data to the brightest minds in biomedical research. The cohort will be built largely by linking existing cohorts together taking advantage of infrastructure, data security and expertise already in place. NIH will help to connect these existing cohorts, but the current sponsors of the cohorts will maintain their ownership and management. Research on this scale promises to lead to new prevention strategies, novel therapeutics and medical devices, and improvements in how we prescribe drugs – on an *individual* and *personalized basis*.

Research and Development Contracts (-$56.067 million; total $328.072 million):
There is a shift in the receipt of proposals normally supported under this mechanism to submitting applications in response to Program Announcements and Requests for Funding Announcements for research grants to provide innovative research in the heart, lung, and blood disease areas.

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Summary of Changes

(Dollars in Thousands)

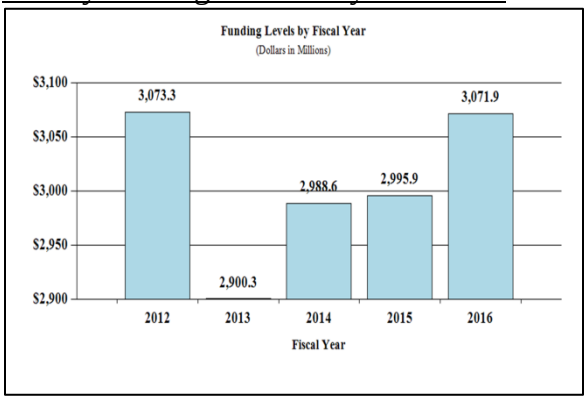
FY 2015 Enacted	$2,995,865
FY 2016 President's Budget	$3,071,906
Net change	$76,041

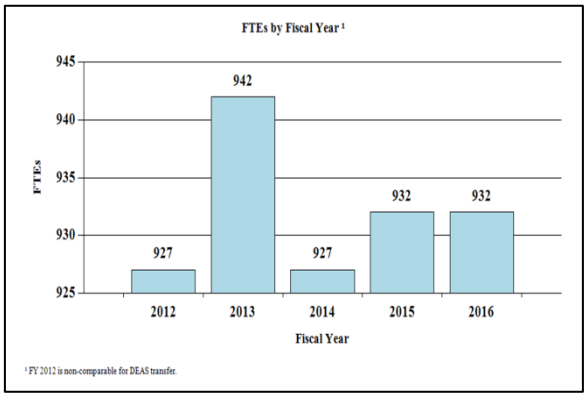
CHANGES	FY 2016 President's Budget FTEs	FY 2016 President's Budget Budget Authority	Change from FY 2015 FTEs	Change from FY 2015 Budget Authority
A. Built-in:				
1. Intramural Research:				
a. Annualization of January 2015 pay increase & benefits		$77,559		$200
b. January FY 2016 pay increase & benefits		77,559		347
c. One more day of pay (n/a for 2015)		77,559		295
d. Differences attributable to change in FTE		77,559		0
e. Payment for centrally furnished services		30,679		748
f. Increased cost of laboratory supplies, materials, other expenses, and non-recurring costs		94,088		1,754
Subtotal				$3,345
2. Research Management and Support:				
a. Annualization of January 2015 pay increase & benefits		$67,682		$175
b. January FY 2016 pay increase & benefits		67,682		307
c. One more day of pay (n/a for 2015)		67,682		267
d. Differences attributable to change in FTE		67,682		0
e. Payment for centrally furnished services		1,600		39
f. Increased cost of laboratory supplies, materials, other expenses, and non-recurring costs		59,356		1,132
Subtotal				$1,920
Subtotal, Built-in				$5,265

CHANGES	FY 2016 President's Budget No.	FY 2016 President's Budget Amount	Change from FY 2015 No.	Change from FY 2015 Amount
B. Program:				
1. Research Project Grants:				
a. Noncompeting	2,399	$1,412,503	67	$12,543
b. Competing	1,021	556,301	245	91,047
c. SBIR/STTR	188	81,086	45	2,769
Subtotal, RPGs	3,608	$2,049,890	357	$106,359
2. Research Centers	36	$78,261	12	$13,398
3. Other Research	997	184,882	370	2,657
4. Research Training	1,937	99,837	93	3,204
5. Research and development contracts	159	328,072	-27	-56,067
Subtotal, Extramural		$2,740,943		$69,552
	FTEs		FTEs	
6. Intramural Research	531	$202,326	0	$622
7. Research Management and Support	401	128,637	0	602
8. Construction		0		0
9. Buildings and Facilities		0		0
Subtotal, Program	932	$3,071,906	0	$70,776
Total changes				$76,041

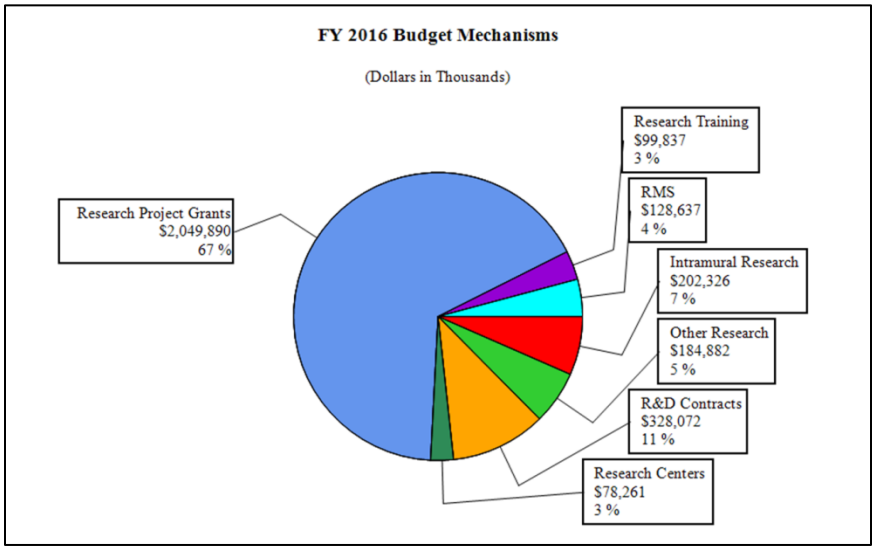
Fiscal Year 2016 Budget Graphs

History of Budget Authority and FTEs:

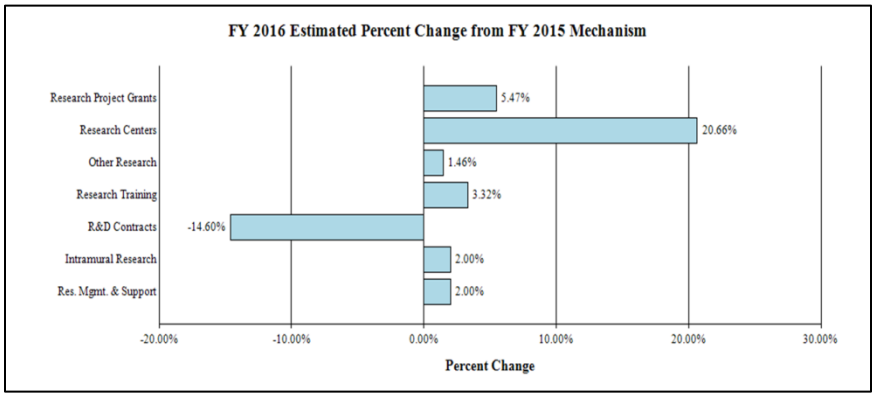




Distribution by Mechanism:



Change by Selected Mechanism:



Budget Authority by Activity[1]
(Dollars in Thousands)

	FY 2014 Actual		FY 2015 Enacted		FY 2016 President's Budget		FY 2016 +/- FY2015	
Extramural Research	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**
Detail								
Heart and Vascular Diseases		$1,709,487		$1,709,154		$1,753,653		$44,499
Lung Diseases		602,491		602,374		618,057		15,683
Blood Diseases and Resources		359,934		359,863		369,233		9,369
Subtotal, Extramural		**$2,671,912**		**$2,671,391**		**$2,740,943**		**$69,552**
Intramural Research	**531**	**$193,424**	**531**	**$198,359**	**531**	**$202,326**	**0**	**$3,967**
Research Management & Support	**396**	**$123,248**	**401**	**$126,115**	**401**	**$128,637**	**0**	**$2,522**
TOTAL	**927**	**$2,988,584**	**932**	**$2,995,865**	**932**	**$3,071,906**	**0**	**$76,041**

[1] Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2015 Amount Authorized	FY 2015 Enacted	2016 Amount Authorized	FY 2016 President's Budget
Research and Investigation	Section 301	42§241	Indefinite	$2,995,865,000	Indefinite	$3,071,906,000
National Heart, Lung, and Blood Institute	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				$2,995,865,000		$3,071,906,000

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
2006	$2,951,270,000	$2,951,270,000	$3,023,381,000	$2,951,270,000
Rescission				($29,513,000)
2007	$2,918,808,000	$2,901,012,000	$2,924,299,000	$2,918,808,000
Rescission				$0
2008	$2,894,341,000	$2,965,775,000	$2,992,197,000	$2,974,900,000
Rescission				($51,972,000)
Supplemental				$15,542,000
2009	$2,924,942,000	$3,025,500,000	$3,006,344,000	$3,015,689,000
Rescission				$0
2010	$3,050,356,000	$3,123,403,000	$3,066,827,000	$3,096,916,000
Rescission				$0
2011	$3,187,516,000		$3,182,524,000	$3,096,916,000
Rescission				($27,192,768)
2012	$3,147,992,000	$3,147,992,000	$3,036,189,000	$3,084,851,000
Rescission				($5,830,368)
2013	$3,076,067,000		$3,085,390,000	$3,079,020,632
Rescission				($6,158,041)
Sequestration				($154,545,663)
2014	$3,098,508,000		$3,077,916,000	$2,988,605,000
Rescission				$0
2015	$2,987,685,000			$2,997,870,000
Rescission				$0
2016	$3,071,906,000			

Justification of Budget Request

National Heart, Lung, and Blood Institute

Authorizing Legislation: Section 301 and title IV of the Public Health Service Act, as amended.
Budget Authority (BA):

	FY 2014 Actual	FY 2015 Enacted	FY 2016 President's Budget	FY 2016 +/- FY 2015
BA	$2,988,584,251	$2,995,865,000	$3,071,906,000	+$76,041,000
FTE	927	932	932	0

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

Director's Overview

For more than 60 years, the National Heart, Lung, and Blood Institute (NHLBI) has led the fight against heart, lung, and blood diseases – the leading causes of death among American men and women. Over this period, steady long-term investments in biomedical research have contributed to a 76 percent decrease in death rates due to coronary heart disease, yet more remains to be done. Chronic heart and lung diseases remain the major causes of hospitalizations and key drivers of growing medical care costs. However, exciting new scientific discoveries and emerging technologies offer great promise for the prevention and treatment of heart and lung diseases. Today's basic science presents unprecedented opportunities to examine the genome, dissect a single cell's molecular circuitry, and image at nano-scale resolution to help us understand the complexity of biological systems, laying the groundwork for breakthroughs that can predict health and pre-empt chronic disease in the near future. Access to widespread electronic health data and advances in big data science and computational biology are accelerating the translation of discovery into health. Together, these multi-level, multi-scale analyses of the complex systems that govern health and disease will ultimately lead to the identification of key interventions capable of bending the curve to improve the longevity and quality of life of for all Americans.

Today's Basic Science for Tomorrow's Breakthroughs

Basic research provides the knowledge needed to create tomorrow's innovative prevention and treatment strategies. When Shinya Yamanaka, the 2012 Nobel Laureate and NHLBI grantee, transformed adult skin cells into induced pluripotent stem cells (iPSCs) with the ability to develop into virtually any cell type in the body, a new paradigm emerged – a patient's own cells could be used to better understand and potentially treat any diseases the patient has. Although heart failure is one of the leading drivers of medical care costs, progress in reducing the burden of this disease has been slowed by the lack of experimental models of human heart failure that can guide new drug development. To further define the molecular basis of heart failure, NHLBI-funded investigators recently generated human heart muscle cells from iPSCs derived from patients with Barth syndrome, a genetic form of heart failure of unknown cause. Using a novel "heart-in-a-dish" human tissue culture model system, the researchers were able to define the molecular pathways that lead to both rare and common forms of heart failure. This proof-of-

concept study demonstrates that modeling diseases using patient-derived cells can enhance our understanding of disease processes and open the doors for new treatment strategies to pre-empt the development of chronic disease.

Translating Discovery into Health – Preventing and Preempting Heart, Lung, Blood, and Sleep (HLBS) Disorders

Emerging experimental approaches such as those of Dr. Yamanaka's are part of a wave of scientific advances in regenerative medicine that present unparalleled opportunities to translate discovery into health. For example, sickle cell disease (SCD) was the first disorder for which a genetic cause was identified nearly 70 years ago, yet a cure for this disease remains out of reach. Bone marrow transplants (BMTs) have been a successful therapy for SCD in children but carry significant risks, particularly that of transplant rejection. Moreover, these risks are prohibitively high for adults with SCD, whose organ systems have sustained cumulative damage over their lifetimes. In a recent breakthrough, NHLBI intramural investigators treated adult patients with a less toxic BMT method, in which roughly half of the bone marrow was replaced with healthy donor stem cells. The procedure successfully reversed SCD in nearly all of the patients. In addition, half of the patients were able to stop taking immunosuppressant drugs, and after years of careful monitoring, none of these patients have experienced transplant rejection, graft-versus-host disease, or many of the debilitating complications of SCD.

These studies demonstrate the relative safety, feasibility, and efficacy of performing BMT in adults with SCD. As NHLBI strives toward an ultimate goal of finding a widely available cure, there is growing excitement about the advent of new gene-editing tools, which excise defective DNA and replace it with healthy DNA sequences. Recent NIH-funded studies in mice and human cells in culture suggest that it may be feasible to develop new BMT protocols with gene-editing technology for patients living with SCD. These pioneering advances provide hope for a not-too-distant future cure of SCD and freedom from its devastating complications.

Population Science and Precision Medicine for Public Health Impact

Fundamental discovery science and its translation into therapeutics and clinical innovation are the foundation of our success in altering the trajectory of high burden diseases in the United States. The NHLBI's large-population cohort studies, such as the Framingham Heart Study (for which there has been over 15,000 participants) and the Women's Health Initiative (with over 161,000 study participants), have been major generators of new knowledge that has informed the molecular basis of disease and identified targets for novel therapies. For example, NHLBI-funded research looking for factors that determine the level of low-density lipoprotein (LDL) – so-called bad cholesterol – led to the discovery of Proprotein convertase subtilisin/kexin type 9 (PCSK-9), a finding researchers translated into a new class of drug therapies to prevent heart attacks. In more recent studies of lipid metabolism, NHLBI-funded investigators have shown that individuals with certain variants in the Apolipoprotein C3 (APOC3) gene exhibit lower triglyceride levels and have a lower risk of having a heart attack. These findings bring us one step closer to precision medicine, in which we can predict who is at risk and foster the development of next-generation drugs that can more effectively prevent the complications of chronic heart disease.

Nurturing Talent and Innovation
Developing the next groundbreaking technique or identifying the next targeted therapy requires the cultivation of a new, diverse cadre of highly talented researchers. NHLBI is committed to the future of the next generation and is working aggressively to increase investment in and the success rates of early-stage investigators (ESIs) and mentored career development (K) awardees. In addition, NHLBI is piloting transitional short-term grants to bridge the chasm between career development (K) awards and research grant (R01) awards and maintaining its substantial commitment to the NIH Loan Repayment Programs to enable scientists with student loan debts to continue to pursue research careers. NHLBI is also focusing efforts in scientific areas in which there are particular gaps in the research workforce, such as blood research. Overall, these efforts are designed to ensure that the next generation of the U.S. biomedical research workforce is poised to sustain our nation's global preeminence in biomedical science.

Summary
NHLBI remains committed to its legacy of success in developing the next generation of scientists and supporting research that addresses the major causes of death among men and women in the United States. Stable long-term research investments hold more promise than ever to elucidate the molecular circuitry of the complex biological systems that sustain health and translate new insights into more precise and effective therapeutic approaches that enhance the lives of all Americans.

Program Descriptions and Accomplishments

Cardiovascular Diseases: Since its founding in June 1948, NHLBI has funded research that has led to a dramatic, 76 percent reduction in death rates from coronary heart disease – a phenomenal return on the Nation's public investment in medical research. This program supports research on the causes, diagnosis, treatment, and prevention of heart and vascular diseases, including atherothrombosis, vascular dementia, coronary artery disease, myocardial infarction and ischemia, heart failure, arrhythmia, sudden cardiac death, congenital heart disease in adults and children, cardiovascular disease complications of diabetes and obesity, and hypertension. The program's efforts span the full spectrum of basic, translational, clinical, epidemiological, behavioral, comparative effectiveness, and health services research.

New opportunities in basic science research are revolutionizing our understanding of heart diseases and enhancing our capacity for precision medicine. For example, until now researchers could only study cardiac function by imaging the entire heart or studying heart cells in a dish. NHLBI-funded researchers, though, recently developed a technique that allows visualization of a single beating heart cell in a live mouse. Relying on this new procedure, researchers will be able to more easily study how individual heart cells behave in their complex natural environment and how their functioning differs in disease states and after treatment with potential therapeutics.

<u>Budget Policy:</u>
The FY 2016 budget estimate for the Heart and Vascular Diseases program is $1,753.653 million, an increase of $44.499 million or 2.6 percent over the FY 2015 Enacted level. In FY 2016, NHLBI will continue support of population based studies investigating cardiovascular disease.

Taking a systems biology approach to understanding health and disease requires understanding disease not only at a cellular level but also at the population level. With this in mind, NHLBI has a longstanding history of supporting large-scale epidemiological studies that have transformed the way the public approaches heart disease, beginning with the Framingham Heart Study, through which scientists learned of the risk factors for heart disease that are now checked in all routine physicals. This research has contributed transformative discoveries to the treatment of heart disease. Researchers also now understand that while cardiovascular disease often strikes in midlife or later, its origins are found much earlier in life, and that the disease is discriminating, revealing itself differently in different populations. Findings such as these pave the way for new interventions to preempt the disease or treat it more effectively.

Population studies have entered an exciting period when advances in assay methods, imaging technologies, and electronic data have created new scientific opportunities. Indeed, new tools have emerged for epidemiology research; for example, researchers can use digital and mobile health applications to ascertain exposure and can rely on electronic medical data sources to sample populations and ascertain outcomes. These tools and others will enable mega-epidemiology studies that analyze outcomes in tens or hundreds of thousands of people to explore complex pathways that predispose individuals to disease. To capitalize on these opportunities, NHLBI established an Advisory Council Working Group on Epidemiology and Population Science to take a strategic look at the current landscape, emerging tools, and future opportunities in population science and make recommendations that will contribute to the Institute's strategic planning process. NHLBI's cohort studies have been tremendously productive and have made great contributions to science, as is evidenced by the significant health and economic benefits from the Women's Health Initiative (see Program Portrait below). Now is the time to look at the potential for a bold vision and new direction for these studies that will allow their proud legacies to continue and grow.

Program Portrait: Women's Health Research

FY 2015 Level: $408.6 million
FY 2016 Level: $409.7 million
Change**:** + $1.1 million

NHLBI has a long history of including women in research, starting with the Framingham Heart Study in 1949 and continuing through many pioneering studies that have greatly contributed to improving women's health and our knowledge about women and heart disease. More than 68 percent of participants in NHLBI-funded cardiovascular trials in FY 2013 were women. This high participation of women is due in part to the fact that NHLBI has invested in studies such as the Women's Health Initiative (WHI) that are dedicated to research on women's health. Excluding the WHI study, nearly half (46 percent) of NHLBI-funded cardiovascular trial participants are women.

WHI is a prime example of how NHLBI-supported science has contributed to women's health. The WHI found – utterly contrary to conventional wisdom – that use of the widely prescribed estrogen/progestin postmenopausal hormone therapy not only failed to protect women from coronary heart disease but also increased their risk of developing invasive breast cancer. In the aftermath of this study, there was a dramatic reduction in the number of women on combined hormone therapy, resulting in fewer cases of cardiovascular disease and breast cancer. A recent in-depth analysis of final data from the WHI Postmenopausal Hormone Therapy Trials found that for each dollar invested in the trial there was a return of $140 in net economic value.[1]

As new knowledge is generated, there is a dynamic to-and-fro between basic research and population science. The landmark findings of WHI have fueled intense study of sex-specific differences in biological processes that may help us understand why the hormone replacement used in the study failed to be cardioprotective as originally postulated. For example, basic research studies discovered that one of the two forms of the estrogen receptor, estrogen receptor-β, and its downstream molecular pathways play an important role in determining the differing cardioprotective responses to therapeutic drugs between male and female mice. These studies have implications for designing new therapies that could be more effective in women with heart disease.

WHI will continue to make significant strides for women and heart disease. Future investigations will examine whether physical activity at levels recommended for older adults will reduce major cardiovascular events (e.g., heart attacks, stroke, and cardiovascular death) in older women and whether a multivitamin and other dietary supplements might have the potential to prevent CVD and cancer in women aged 65 and older.

Lung Diseases: This program supports research on the causes, diagnosis, treatment, and prevention of lung diseases and sleep disorders. Research areas include asthma, chronic obstructive pulmonary disease (COPD), cystic fibrosis, critical care and acute lung injury, developmental biology and pediatric pulmonary diseases, immunology and fibrosis, lung cell and vascular biology, and pulmonary complications of AIDS and tuberculosis. This research portfolio takes a holistic approach, integrating studies at the molecular, cellular, and systems level to understand, prevent, and treat disease.

Emerging technologies are enabling scientists to analyze the inner molecular circuitry of a single cell and trace each adult cell within a complex tissue such as the lung back to its embryonic origin. Recent NHLBI-funded studies have discovered many previously unknown cell markers that allow one to discriminate between the different epithelial cell types in the distal lung in ways that are not possible with a microscope. These analyses also revealed a new progenitor cell type in the alveolar airspaces of the lung. Progenitor cells can become one or more types of cells; although they cannot, like stem cells, become every type of cell. Researchers are exploring ways to direct progenitor cells into becoming particular cell types that doctors might then use for

[1] Roth JA, Etzioni R, Waters TM, et al. Economic return from the Women's Health initiative estrogen plus progestin clinical trial: A modeling study. Ann Intern Med. 2014; 160(9): 594–602.

repairing damaged tissues. The research also uncovered the molecular switches that turn on genetic programs for renewal and repair of the lung after injury. This discovery opens the door to arresting and reversing progressive lung disease by harnessing the intrinsic ability of the lung to repair itself.

Significant progress has been and is continuing to be made in the diagnosis and management of chronic lung diseases, but little progress has been made in lung disease prevention (except for reductions in smoking). While research to improve treatments for lung disease is valuable, prevention will ultimately have the greatest impact in reducing the burden of lung diseases.

Budget Policy:
The FY 2016 budget estimate for the Lung Diseases program is $618.057 million, an increase of $15.683 million or 2.6 percent over the FY 2015 Enacted level.

In FY 2016, NHLBI efforts to prevent lung disease will focus on identifying pre-symptomatic features of lung disease and ways to intervene to prevent lung disease progression. Clinical and molecular advances now allow for the collection of multiple types of data that can inform the trajectory of disease processes and/or age-related changes. To leverage these advances, NHLBI is releasing two new initiatives to use existing data from longitudinal cohorts that have pulmonary-relevant clinical, physiologic, and biological data as well as outcomes that define chronic lung disease(s). This research will identify profiles of the pre-symptomatic stages of incident disease and define and/or validate attributes of resiliency. Concurrently, NHLBI is encouraging investigators to test specific pharmacologic, behavioral, nutritional, or environmental primary prevention interventions for chronic lung diseases in multi-site randomized controlled clinical trials.

Program Portrait: Sleep Research

FY 2015 Level: $ 70.3 million
FY 2016 Level: $ 70.5 million
Change: + $ 0.2 million

Nearly half of all Americans suffer from some sort of sleep disorder, and nearly one-third get fewer than seven hours of sleep per night. Sleep deficiency is associated with up to a twofold increased risk of obesity, diabetes, hypertension, incident cardiovascular disease, stroke, breast cancer, depression, substance abuse, and all-cause mortality. Research supported by the National Center on Sleep Disorders Research, administered within the Lung Diseases program at NHLBI, is now uncovering the molecular links between inadequate sleep and some of these adverse health events. For example, one study in mice demonstrated a correlation between sleep impairment and loss of neurons in a region of the brain that is responsible for controlling alertness. Foundational discoveries at the cellular level are also linking irregular sleep and sleep apnea to changes in the function of the mitochondria, the energy-generating centers within the cell. Perturbations in sleep associated with mitochondrial dysfunction can generate free radicals, which can be toxic to the cell and promote accelerated cell aging and organ dysfunction. Based on these findings, researchers can now test medications that modulate the generation of free radicals to see if these medicines reduce health risks associated with chronic sleep deprivation.

Treatments do exist for some sleep disorders, such as obstructive sleep apnea (OSA), which affects about 15 percent of the general population and significantly impacts cardiovascular health. Positive airway pressure (PAP) is used to compensate for the airway obstruction associated with OSA and is delivered by a minimally invasive device that provides air pressure through a facial appliance; but there are gaps in our knowledge regarding the impact of PAP on cardiovascular risk. In response to the need to better understand the influence of PAP on OSA in patients who are at high risk for cardiovascular disease, NHLBI is funding a randomized controlled trial among patients with transient ischemic attack (TIA, also known as a mini-stroke) and ischemic stroke, comparing the effectiveness of strategies for the diagnosis and treatment of sleep apnea with usual care over 12 months. Data collection has recently been completed, and data analysis is ongoing. Researchers hope to use the results to inform decisions regarding the feasibility of, and potential design options for, conducting larger-scale studies of the treatment of OSA to reduce cardiovascular risk.

Blood Diseases and Resources: This program supports research on the causes, prevention, and treatment of nonmalignant blood diseases, including anemias, such as sickle cell disease and thalassemia; premalignant processes, such as myelodysplasia and myeloproliferative disorders; abnormalities of hemostasis and thrombosis, such as hemophilia; and immune dysfunction.

Basic research in this program area has resulted in scientific breakthroughs that now have implications for many disorders. For example, first discovered in 2004, neutrophil extracellular traps (NETs) are web-like structures released by the white blood cells in the body's immune defense system that trap and kill invading bacteria and other pathogens. NHLBI-funded research has since shown that NETs also play a harmful role in blood clot formation (thrombosis), lung endothelial injury in transfusion-related acute lung injury (TRALI), and blood vessel blockages in sickle cell disease (SCD), which lead to pain crisis and tissue damage. These studies also have preliminary results that suggest that DNase I, a Food and Drug Administration-approved drug, could be an effective treatment for NET-related SCD symptoms, TRALI, and deep vein thrombosis.

The Blood Diseases and Resources program is also responsible for research and research training on the use, safety, efficacy, and availability of blood and blood components for transfusion and cellular therapeutics. One goal of this program is to use adult stem cell technology to produce blood cells in vitro, including hematopoietic stem-cell-derived red blood cells or platelets. This approach holds the promise of generating an abundant number of uniform cells with defined biological properties, free of reactive antigens and infectious agents. Given the current state of

the science and cellular engineering, it is already possible to derive blood cells in sufficient numbers for clinical applications, and stem cell-derived red blood cells have been safely tested in humans. What is now required is to advance remaining aspects of basic and translational research by, for example, discovering additional differentiation pathways, improving the tools and technologies supporting production of high-quality cells in sufficient number, and reducing costs to enable clinical-grade manufacture in a feasible, cost-effective manner. Once these blood products become available, we will be able to avoid current intermittent shortages of blood products, a problem that could occur in national emergencies. Engineered cells could also deliver drugs or biologic factors to treat diseases, including inherited or acquired deficiencies. For example, cells for pharmaceutical use could be transfused to patients with sickle cell disease, for whom compatible red blood cells cannot be easily identified. Many such patients would benefit from personalized platelets or red blood cells even if these products are more costly than the currently available blood products.

Budget Policy:
The FY 2016 budget estimate for the Blood Diseases and Resources program is $369.233 million, an increase of $9.369 million or 2.6 percent over the FY 2015 Enacted level. The program plans for FY 2016 include continued support of initiatives that will address effectiveness and toxicities of red blood cell transfusion; along with the increase in safety, efficacy, and availability of blood and its components for transfusion and cellular therapies.

Program Portrait: Lowering the Cost and Improving the Value of Clinical Trials

FY 2015 Level: $ 2.2 million
FY 2016 Level: $ 5.8 million
Change: +$ 3.6 million

The traditional approach to designing and implementing clinical trials includes in-depth testing and evaluation, which can be costly; narrowly targeted participants for inclusion, which can unintentionally limit broad generalizability of the research findings; and well-controlled delivery settings or infrastructure that cannot be easily reproduced in most standard clinical practices. The development of electronic health records and patient registries now allows for more efficient research practices and more useful trial results. NHLBI, along with other NIH Institutes, is funding the Low-Cost, Pragmatic, Patient-Centered Randomized Controlled Intervention Trials Initiative to take advantage of these tools to inexpensively identify, recruit, and enroll appropriate patients as well as to monitor study results and determine trial outcomes. In addition, funded studies will take place in real-world settings (primary care practices, hospitals, integrated health systems), include a broad representation of patients who have the condition under study, and have clinical endpoints or measures that are relevant to patients and clinicians, such as morbidity, hospitalizations, and quality of life (as opposed to surrogate endpoints such as cholesterol levels, etc.). Clinical research being funded through the initiative includes a study testing cognitive behavior therapy approaches to treating insomnia and a study comparing paramedic airway management treatments for cardiopulmonary arrest. In a separate but related initiative, NHLBI is funding pragmatic clinical trials relating to chronic pulmonary diseases, including pulmonary hypertension, chronic obstructive pulmonary disease (COPD), and obstructive sleep apnea. Like the studies in the other initiative, these trials will achieve greater inclusiveness, rely on electronic medical records to lower costs, take place in real world settings, and establish findings that doctors can easily apply to relevant patients. With these initiatives, NHLBI will be promoting a new paradigm for clinical trials that will lead to cost savings and wider implementation of clinical study findings.

Intramural Research: The Division of Intramural Research (DIR) program conducts basic, translational, clinical, and population research in heart, vascular, lung, blood, sleep, and kidney diseases. This program has made numerous high-impact fundamental discoveries that lay the foundation for many of tomorrow's medical breakthroughs.

Basic researchers in DIR, for example, have developed new technologies that stand to transform how we study RNA biology. The ability to visualize proteins by tagging them with green fluorescent protein (GFP) revolutionized the way we study proteins and eventually led to a Nobel prize. By taking a similar approach to RNA instead of proteins, Dr. Ferré-D'Amaré and colleagues in DIR have now elucidated the structure of an RNA mimic of GFP called Spinach. Knowing this structure will lead to the molecular engineering of more fluorescent RNAs, which can have broad applications in studying RNA biology and RNA-specific disease mechanisms.

On the clinical front, studies conducted by DIR investigators at the NIH Clinical Center led to FDA approval of Eltrombopag for the treatment of Severe Aplastic Anemia (SAA) patients who did not respond to prior immunosuppressive treatment. SAA is a blood disorder in which the bone marrow fails to make enough red blood cells, white blood cells, and platelets. DIR investigators made the surprising and provocative observation that Eltrombopag works by helping to induce proliferation and differentiation of bone marrow stem cells and demonstrating that it has efficacy in increasing production of blood cells in patients with SAA who are refractory to conventional approaches. Indeed several patients that had failed standard therapies and were dependent on chronic transfusions no longer needed transfusions after receiving Eltrombopag therapy. These studies paved the way for FDA approval of Eltrombopag for SAA, which fills a critical treatment gap for this rare but serious blood disorder in those who have failed current treatment options.

Budget Policy:
The FY 2016 President's Budget estimate for the Intramural Research program is $202.326 million, an increase of $3.967 million, or 2.0 percent above the FY 2015 Enacted level.

Research Management and Support (RMS): RMS activities provide administrative, budgetary, logistical, and scientific support in the review, awarding, and monitoring of research grants, training awards, and research and development contracts. RMS activities also include strategic planning, trans-NHLBI coordination, and evaluation of the Institute's programs, as well as regulatory compliance, international coordination, interactions with other Federal agencies and Congress, and dissemination of research findings to the public.

As part of an effort to more efficiently and effectively translate evidence-based interventions developed from research supported throughout the Institute into better patient outcomes, NHLBI recently established the Center for Translational Research and Implementation Science (CTRIS). The mission of CTRIS is to support research to identify and address barriers to translation. CTRIS also takes steps to ensure that clinicians are informed about the latest evidence for treating heart, lung, blood, and sleep diseases. Indeed, this kind of implementation science research may inform other areas of the NHLBI portfolio as well. For example, if this research finds that certain treatments are not used because of the frequency with which they need to be administered, that finding may lead to new research to develop similar treatments with longer-lasting effects.

In 2014, CTRIS coordinated the release of the first systematic evidence-informed report to assist clinicians in preventing and treating the many conditions affecting those living with sickle cell disease. The Evidence-Based Management of Sickle Cell Disease: Expert Panel Report (EPR) provides a clinical resource for primary care providers, nurses, specialists, emergency care personnel, and other members of the health care community, many of whom have limited experience treating people with this condition. EPR recommended the expanded use of currently underutilized treatments for sickle cell disease and its severe health effects. In concert with the release of the EPR and to celebrate Sickle Cell Awareness Month, NHLBI continued to raise public awareness about sickle cell disease through media outreach, articles for the public, and social media.

Budget Policy:
The FY 2016 President's Budget estimate for Research Management and Support is $128.637 million, an increase of $2.522 million, or 2.0 percent above the FY 2015 Enacted level.

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Budget Authority by Object Class[1]
(Dollars in Thousands)

		FY 2015 Enacted	FY 2016 President's Budget	FY 2016 +/- FY 2015
Total compensable work years:				
	Full-time employment	932	932	0
	Full-time equivalent of overtime and holiday hours	1	1	0
	Average ES salary	$165	$165	$0
	Average GM/GS grade	12.2	12.2	0.0
	Average GM/GS salary	$104	$105	$1
	Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$0	$0	$0
	Average salary of ungraded positions	$130	$132	$1
	OBJECT CLASSES	**FY 2015 Enacted**	**FY 2016 President's Budget**	**FY 2016 +/- FY 2015**
	Personnel Compensation			
11.1	Full-Time Permanent	$65,896	$67,269	$1,373
11.3	Other Than Full-Time Permanent	32,631	33,290	659
11.5	Other Personnel Compensation	3,971	4,053	82
11.7	Military Personnel	813	829	17
11.8	Special Personnel Services Payments	8,496	8,667	170
11.9	**Subtotal Personnel Compensation**	**$111,807**	**$114,108**	**$2,301**
12.1	Civilian Personnel Benefits	$30,032	$30,535	$503
12.2	Military Personnel Benefits	585	597	12
13.0	Benefits to Former Personnel	0	0	0
	Subtotal Pay Costs	**$142,424**	**$145,240**	**$2,816**
21.0	Travel & Transportation of Persons	$2,504	$2,544	$40
22.0	Transportation of Things	227	230	4
23.1	Rental Payments to GSA	0	0	0
23.2	Rental Payments to Others	0	0	0
23.3	Communications, Utilities & Misc. Charges	1,049	1,066	17
24.0	Printing & Reproduction	31	32	0
25.1	Consulting Services	$799	$800	$0
25.2	Other Services	46,630	47,376	746
25.3	Purchase of goods and services from government accounts	286,136	291,716	5,581
25.4	Operation & Maintenance of Facilities	$969	$969	$0
25.5	R&D Contracts	199,882	140,037	-59,845
25.6	Medical Care	1,106	1,134	28
25.7	Operation & Maintenance of Equipment	15,498	15,636	138
25.8	Subsistence & Support of Persons	0	0	0
25.0	**Subtotal Other Contractual Services**	**$551,021**	**$497,669**	**-$53,352**
26.0	Supplies & Materials	$14,113	$14,338	$225
31.0	Equipment	12,743	12,915	173
32.0	Land and Structures	0	0	0
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	2,271,752	2,397,870	126,118
42.0	Insurance Claims & Indemnities	0	0	0
43.0	Interest & Dividends	1	1	0
44.0	Refunds	0	0	0
	Subtotal Non-Pay Costs	**$2,853,441**	**$2,926,666**	**$73,225**
	Total Budget Authority by Object Class	**$2,995,865**	**$3,071,906**	**$76,041**

[1] Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Salaries and Expenses
(Dollars in Thousands)

OBJECT CLASSES	FY 2015 Enacted	FY 2016 President's Budget	FY 2016 +/- FY 2015
Personnel Compensation			
Full-Time Permanent (11.1)	$65,896	$67,269	$1,373
Other Than Full-Time Permanent (11.3)	32,631	33,290	659
Other Personnel Compensation (11.5)	3,971	4,053	82
Military Personnel (11.7)	813	829	17
Special Personnel Services Payments (11.8)	8,496	8,667	170
Subtotal Personnel Compensation (11.9)	**$111,807**	**$114,108**	**$2,301**
Civilian Personnel Benefits (12.1)	$30,032	$30,535	$503
Military Personnel Benefits (12.2)	585	597	12
Benefits to Former Personnel (13.0)	0	0	0
Subtotal Pay Costs	**$142,424**	**$145,240**	**$2,816**
Travel & Transportation of Persons (21.0)	$2,504	$2,544	$40
Transportation of Things (22.0)	227	230	4
Rental Payments to Others (23.2)	0	0	0
Communications, Utilities & Misc. Charges (23.3)	1,049	1,066	17
Printing & Reproduction (24.0)	31	32	0
Other Contractual Services:			
Consultant Services (25.1)	28	29	0
Other Services (25.2)	46,630	47,376	746
Purchases from government accounts (25.3)	134,385	137,537	3,153
Operation & Maintenance of Facilities (25.4)	969	969	0
Operation & Maintenance of Equipment (25.7)	15,498	15,636	138
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**$197,510**	**$201,548**	**$4,037**
Supplies & Materials (26.0)	$14,113	$14,338	$225
Subtotal Non-Pay Costs	**$215,435**	**$219,758**	**$4,323**
Total Administrative Costs	**$357,859**	**$364,998**	**$7,139**

Detail of Full-Time Equivalent Employment (FTE)

OFFICE/DIVISION	FY 2014 Actual			FY 2015 Est.			FY 2016 Est.		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Office of the Director									
Direct:	141	3	144	143	3	146	143	3	146
Reimbursable:	12	-	12	12	-	12	12	-	12
Total:	153	3	156	155	3	158	155	3	158
Division of Blood Diseases and Resources									
Direct:	26	-	26	26	-	26	26	-	26
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	26	-	26	26	-	26	26	-	26
Division of Cardiovascular Sciences									
Direct:	132	1	133	132	1	133	132	1	133
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	132	1	133	132	1	133	132	1	133
Division of Lung Diseases									
Direct:	32	-	32	32	-	32	32	-	32
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	32	-	32	32	-	32	32	-	32
Division of Extramural Research Activities									
Direct:	108	-	108	108	-	108	108	-	108
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	108	-	108	108	-	108	108	-	108
Direct:	7	-	7	9	1	10	9	1	10
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	7	-	7	9	1	10	9	1	10
Division of Intramural Research									
Direct:	427	4	431	427	4	431	427	4	431
Reimbursable:	33	1	34	33	1	34	33	1	34
Total:	460	5	465	460	5	465	460	5	465
Total	918	9	927	922	10	932	922	10	932
Includes FTEs whose payroll obligations are supported by 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
2012	12.5
2013	12.4
2014	12.2
2015	12.2
2016	12.2

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Detail of Positions[1]

GRADE	FY 2014 Actual	FY 2015 Enacted	FY 2016 President's Budget
Total, ES Positions	2	2	2
Total, ES Salary	329,949	329,949	329,949
GM/GS-15	87	87	87
GM/GS-14	151	154	154
GM/GS-13	187	188	188
GS-12	81	81	81
GS-11	46	46	46
GS-10	0	0	0
GS-9	42	42	42
GS-8	23	23	23
GS-7	26	26	26
GS-6	9	9	9
GS-5	6	6	6
GS-4	2	2	2
GS-3	2	2	2
GS-2	0	0	0
GS-1	0	0	0
Subtotal	662	666	666
Grades established by Act of July 1, 1944 (42 U.S.C. 207)	0	0	0
Assistant Surgeon General	1	1	1
Director Grade	4	5	5
Senior Grade	2	2	2
Full Grade	2	2	2
Senior Assistant Grade	0	0	0
Assistant Grade	0	0	0
Subtotal	9	10	10
Ungraded	254	254	254
Total permanent positions	670	675	675
Total positions, end of year	948	953	953
Total full-time equivalent (FTE) employment, end of year	927	932	932
Average ES salary	164,974	164,974	164,974
Average GM/GS grade	12.2	12.2	12.2
Average GM/GS salary	102,613	103,639	104,676

[1] Includes FTEs whose payroll obligations are supported by the NIH Common Fund.