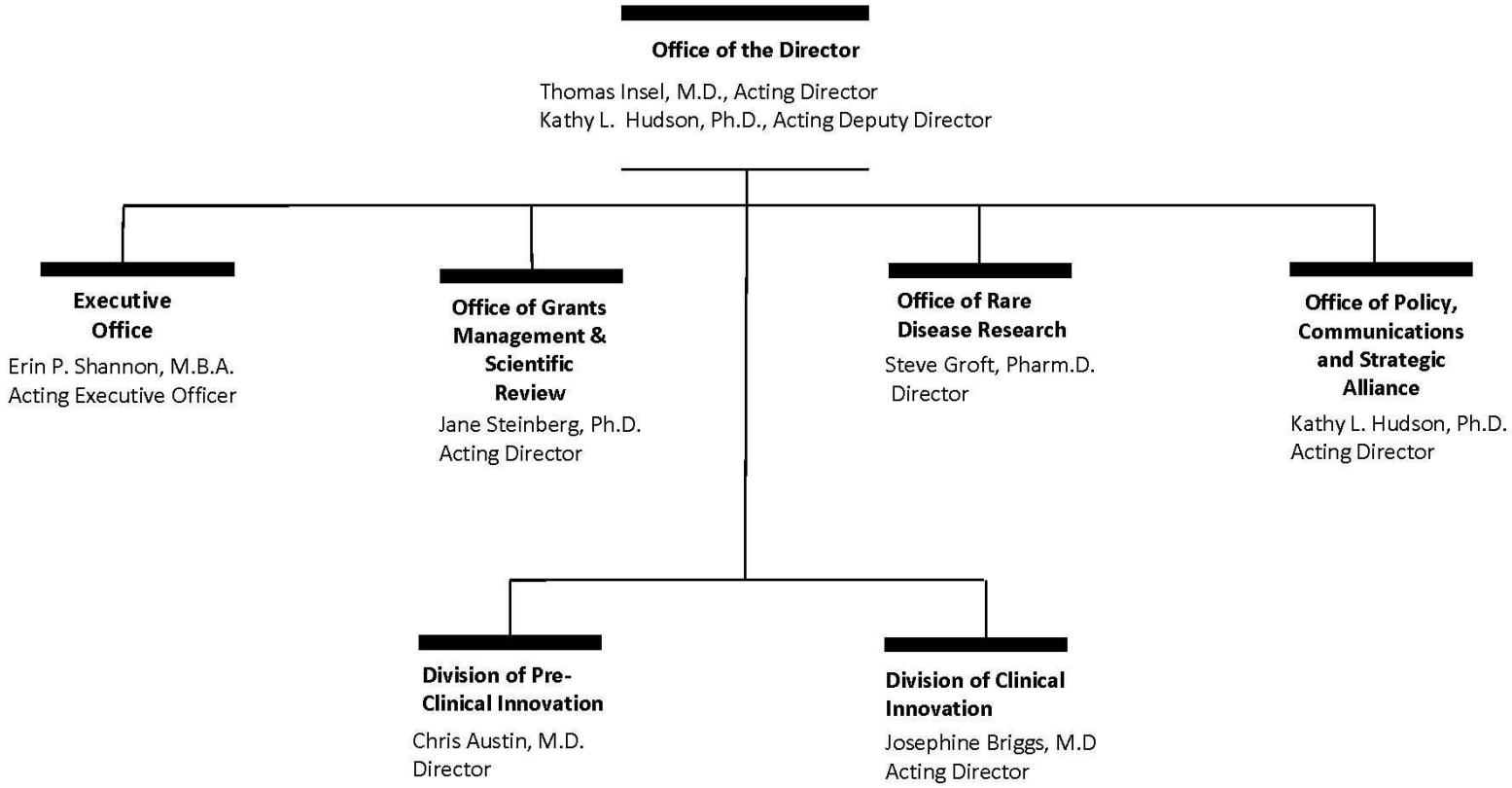
DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Center for Advancing Translational Sciences (NCATS)

National Center for Advancing Translational Sciences



NATIONAL INSTITUTES OF HEALTH

National Center for Advancing Translational Sciences

For carrying out section 301 and title IV of the PHS Act with respect to translational sciences, **[**$576,456,000**]** *$639,033,000*: *Provided*, That up to [$10,000,000] *$50,000,000* shall be available to implement section 402C of the PHS Act, relating to the Cures Acceleration Network [:*Provided further*, That funds appropriated may be used to support the reorganization and activities required to eliminate the National Center for Research Resources: *Provided further*, That the Director of the NIH shall ensure that, of all funds made available to Institute, Center and Office of the Director accounts within "Department of Health and Human Services, National Institutes of Health", at least $487,767,000 is provided to the Clinical and Translational Sciences Awards program]. (*Department of Health and Human Services Appropriations Act, 2012*.)

NATIONAL INSTITUTES OF HEALTH
National Center for Advancing Translational Sciences

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

Source of Funding	FY 2011 Actual	FY 2012 Enacted	FY 2013 PB
Appropriation	0	576,456	639,033
Type 1 Diabetes	0	0	0
Rescission	0	(1,090)	0
Supplemental	0	0	0
Subtotal, adjusted appropriation	0	575,366	639,033
Real transfer under Secretary's transfer authority	0	(164)	0
Comparative Transfers for NCATS reorganization	530,671		0
Comparative Transfers to NCATS for Therapeutics and Rare and Neglected Diseases (TRND)	24,000	0	0
Comparative Transfers to NLM for NCBI and Public Access	(1,079)	(489)	0
Subtotal, adjusted budget authority	553,592	574,713	639,033
Unobligated balance, start of year	0	0	0
Unobligated balance, end of year	0	0	0
Subtotal, adjusted budget authority	553,592	574,713	639,033
Unobligated balance lapsing	0	0	0
Total obligations	553,592	574,713	639,033

[1] Excludes the following amounts for reimbursable activities carried out by this account:
FY 2011 - $72,400 FY 2012 - $42,401 FY 2013 - $24,406

NATIONAL INSTITUTES OF HEALTH

National Center for Advancing Translational 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	0	$37	0	$0	23	$5,326	23	$5,326
Administrative Supplements	*2*	343	*0*	0	*0*	0	*0*	0
Competing:								
Renewal	0	0	0	0	0	0	0	0
New	0	60	23	5,380	86	19,697	63	14,317
Supplements	0	0	0	0	0	0	0	0
Subtotal, Competing	0	$60	23	$5,380	86	$19,697	63	$14,317
Subtotal, RPGs	0	$440	23	$5,380	109	$25,023	86	$19,643
SBIR/STTR	14	$5,154	43	$15,346	47	$17,331	4	$1,985
Research Project Grants	14	$5,594	66	$20,726	156	$42,354	90	$21,628
Research Centers								
Specialized/Comprehensive	0	$9,844	17	$9,930	17	$9,850	0	($80)
Clinical Research	62	430,117	59	406,028	62	406,586	3	558
Biotechnology	0	49	0	0	0	0	0	0
Comparative Medicine	0	196	0	0	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	62	$440,206	76	$415,958	79	$416,436	3	$478
Other Research								
Research Careers	54	$32,197	72	$43,026	72	$42,575	0	($451)
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	0	50	0	0	0	0	0	0
Biomedical Research Support	0	0	0	0	0	0	0	0
Minority Biomedical Research Support	0	0	0	0	0	0	0	0
Other	12	1,123	24	300	24	300	0	0
Other Research	66	$33,370	96	$43,326	96	$42,875	0	($451)
Total Research Grants	142	$479,170	238	$480,010	331	$501,665	93	$21,655
Research Training	FTTPs		FTTPs		FTTPs			
Individual Awards	0	$0	0	$0	0	$0	0	$0
Institutional Awards	0	0	193	13,842	193	13,842	0	0
Total Research Training	0	$0	193	$13,842	193	$13,842	0	$0
Research & Development Contracts	93	$22,078	94	$22,639	128	$48,514	34	$25,875
SBIR/STTR	*0*	*$0*	*0*	*$0*	*0*	*$0*	*0*	*$0*
	FTEs		FTEs		FTEs		FTEs	
Intramural Research	25	$24,000	25	$23,955	25	$40,745	0	$16,790
Research Management and Support	80	28,344	80	34,267	79	34,267	(1)	0
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, NCATS	105	$553,592	105	$574,713	104	$639,033	(1)	$64,320

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 activity 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 budget request for NCATS; the request is $64.320 million more than the FY 2012 Enacted level, for a total of $693.033 million.

Cures Acceleration Network (CAN): (+$39.643 million; total $49.624 million): CAN will fund initiatives designed to address scientific and technical challenges that impede translational research, including support for the Integrated Microsystems for Drug Screening Initiative (which will no longer receive funds from the Common Fund) drug rescue and repurposing, target validation, and others.

Research Project Grants (RPGs; +$19.643 million; total $25.023 million): In FY 2013, NCATS will award an additional 63 competing RPGs over the FY 2012 Enacted level. Investigator-initiated ideas will play a significant role in the mission of NCATS. Additionally, NCATS will support 47 SBIR/STTR awards at a total cost of $17.331 million, which is an increase of $1.985 million over FY 2012. 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.

Reengineering Translational Sciences (+$14.985 million; total $30.331 million): In FY 2013, NCATS will begin direct funding of components of the Molecular Libraries Program (MLP), specially the NIH Chemical Genomics Center.

Clinical and Translational Science Activities (+1.108 million; total $462.503 million in NCATS): The CTSAs are a national consortium designed to transform research and training environments to enhance clinical and translational research. The CTSA program is comprised of research centers, research career awards, and research training through linked grant awards.

Intramural Research (+$16.790 million; total $40.745 million): The FY 2013 budget includes an increase in funding for Intramural Research in NCATS , reflecting a change in funding source for the NIH Chemical Genomics Center (NCGC) under the Molecular Libraries Program. This Center had been funded by the Common Fund and now will be funded through a direct appropriation.

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National Center for Advancing Translational Sciences
Summary of Changes
(Dollars in Thousands)

FY 2012 Enacted			**$574,713**
FY 2013 President's Budget			**$639,033**
Net change			**$64,320**
	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		$2,077		$0
b. January FY 2013 pay increase & benefits		2,077		6
c. One more day of pay		2,077		8
d. Annualization of PY net hires		2,077		0
e. Payment for centrally furnished services		0		0
f. Increased cost of laboratory supplies, materials, other expenses, and non-recurring costs		38,668		0
Subtotal				$14
2. Research Management and Support:				
a. Annualization of January 2012 pay increase & benefits		$13,181		$2
b. January FY 2013 pay increase & benefits		13,181		44
c. One more day of pay		13,181		51
d. Annualization of PY net hires		13,181		0
e. Payment for centrally furnished services		1,242		0
f. Increased cost of laboratory supplies, materials, other expenses, and non-recurring costs		19,844		0
Subtotal				$97
Subtotal, Built-in				$111

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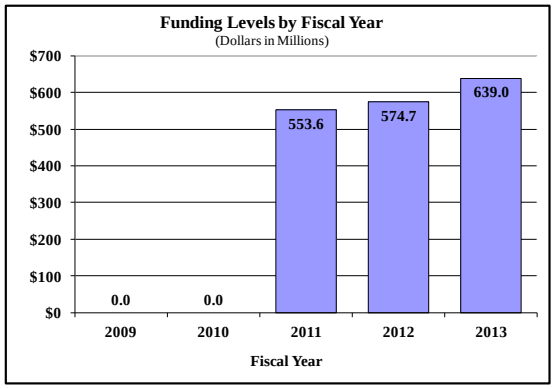
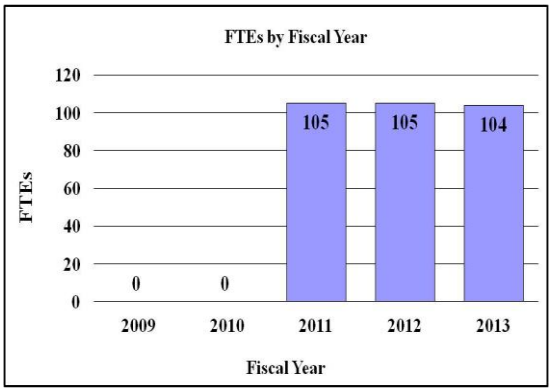
Summary of Changes--continued

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	23	$5,326	23	$5,326
b. Competing	86	19,697	63	14,317
c. SBIR/STTR	47	17,331	4	1,985
Total	156	$42,354	90	$21,628
2. Research Centers	79	$416,436	3	$478
3. Other Research	96	42,875	0	(451)
4. Research Training	193	13,842	0	0
5. Research and development contracts	128	48,514	34	25,875
Subtotal, Extramural		$564,021		$47,530
	FTEs		FTEs	
6. Intramural Research	25	$40,745	0	$16,776
7. Research Management and Support	79	34,267	(1)	(97)
8. Construction		0		0
9. Buildings and Facilities		0		0
Subtotal, program	104	$639,033	(1)	$64,209
Total changes				$64,320

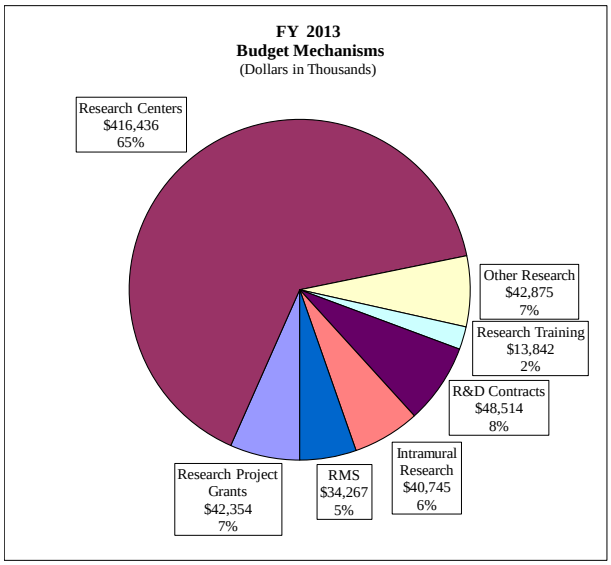
Fiscal Year 2013 Budget Graphs

History of Budget Authority and FTEs:

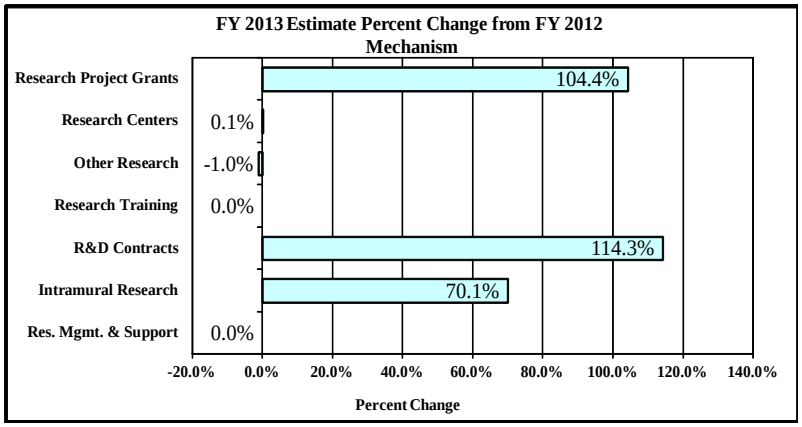




Distribution by Mechanism:



Change by Selected Mechanism:



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National Center for Advancing Translational Sciences

Budget Authority by Activity

(Dollars in Thousands)

	FY 2011 Actual		FY 2012 Enacted		FY 2013 PB		Change vs. FY 2012 Enacted	
Research	**FTEs**	**Amount**	**FTEs**	**Amount**	**FTEs**	**Amount**	**FTEs**	**Amount**
Detail:								
Clinical and Translational Science Activities (CTSA)		**$460,566**		**$461,395**		**$462,503**		**1,108**
CTSA - NIH-wide (non-add)				*486,845*		*486,845*		***0***
Rare Disease Research and Therapeutics	**25**	**34,599**	**25**	**34,565**	**25**	**38,275**		**3,710**
Office for Rare Diseases Research		10,599		10,610		10,530		(80)
Therapeutics for Rare and Neglected Diseases -		24,000		23,955		27,745		3,790
Reengineering Translational Sciences		**5,154**		**15,346**		**30,331**		**14,985**
Cures Acceleration Network		**0**		**9,981**		**49,624**		**39,643**
Translational Research Resources		**24,929**		**19,159**		**24,033**		**4,874**
Subtotal, Research	**25**	**$525,248**	**25**	**$540,446**	**25**	**$604,766**		**$64,320**
Intramural Research (non-add)	*25*	***$24,000***	*25*	***$23,955***	*25*	***$40,745***	**0**	***$16,790***
Research Management & Support	**80**	**$28,344**	**80**	**$34,267**	**79**	**$34,267**	**(1)**	**$0**
TOTAL	**105**	**$553,592**	**105**	**$574,713**	**104**	**$639,033**	**(1)**	**$64,320**

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.
3. Provided by P.L. 112-74, post rescission.

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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	$574,713,000	Indefinite	$639,033,000
National Center for Advancing Translational Sciences	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				$574,713,000		$639,033,000

NATIONAL INSTITUTES OF HEALTH
National Center for Advancing Translational Sciences

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
2004	$0	$0	$0	$0
Rescission				$0
2005	$0	$0	$0	$0
Rescission				$0
2006	$0	$0	$0	$0
Rescission				$0
2007	$0	$0	$0	$0
Rescission				$0
2008	$0	$0	$0	$0
Rescission				$0
Supplemental				$0
2009	$0	$0	$0	$0
Rescission				$0
2010	$0	$0	$0	$0
Rescission				$0
2011	$0		$0	$0
Rescission				$0
2012	$0	$0	$582,326,000	$576,456,000
Rescission				($1,089,502)
2013	$639,033,000			

Justification of Budget Request

National Center for Advancing Translational Sciences

Authorizing Legislation: Section 301 and title IV of the Public Health Service Act, as amended and section 402C of the PHS Act, relating to the Cures Acceleration Network.

Budget Authority (BA):

	FY 2011 Actual	FY 2012 Enacted	FY 2013 President's Budget	FY 2013 +/- FY 2012
BA	$553,592,000	$574,713,000	$639,033,000	+64,320,000
FTE	105	105	104	-1

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

Director's Overview

The process of developing new diagnostics and therapeutics is a complex, costly, and risk-laden endeavor, evidenced by the less than one percent of compounds initially tested actually making it into the patient's medicine cabinet. Recognizing that the process for translating scientific discoveries into new diagnostics and therapeutics is ripe for evidence-based improvements, the National Center for Advancing Translational Sciences (NCATS) was established in FY 2012 to support rigorous scientific research designed to reengineer elements of the development pipeline. Specifically, the mission of NCATS is to catalyze the generation of innovative methods and technologies that enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions. Research projects focus on addressing scientific and technical challenges to reduce, remove, or bypass significant bottlenecks across the continuum of translation. NCATS also encourages results, both positive and negative, to be shared in an open and collaborative environment.

By focusing on developing new tools and methods for developing diagnostics and therapeutics, as opposed to developing therapeutics themselves, NCATS will make it easier for others to bring safer and more effective medical products to market in less time. In this way, NCATS complements, and does not compete with, the work of the private sector, and that of the other NIH Institutes and Centers. The need for NCATS to play both a complementary and catalytic role was also emphasized in its authorizing legislation. For this reason, NCATS has assembled an oversight structure consisting of diverse representation, including those from disease advocacy organizations and private equity firms, along with renowned scholars in translational science and regulatory review. In addition to a national advisory council, NCATS has also established the Cures Acceleration Network (CAN) Board to to provide expert advice on the utilization of

resources and authorities. NCATS will continue these oversight activities in FY 2013 and focus on achieving the aims below.

Using Advances in Science to Overcome Pipeline Barriers. NCATS facilitates the development and utilization of cutting edge technologies to improve how basic discoveries are put into practice. In doing so, NCATS capitalizes on significant scientific progress in fields such as genomics, proteomics, biochemistry, pharmacology, clinical research, biostatistics, and computational biology, as recent advances in these areas have opened an unprecedented window of opportunity for realizing the promise of fundamental research. For example, the application of genomic research and high throughput technologies has resulted in a deluge of new potential drug targets, which can serve as candidates for promising pilot projects to exploit bold new ideas and methods. The Therapeutics for Rare and Neglected Diseases (TRND) program has already taken advantage of these advances. Capitalizing on a novel collaborative partnership model, TRND has rapidly moved two investigational compounds into early clinical trials in the last year for relapsed Chronic Lymphocytic Leukemia (CLL) and for Sickle Cell Disease.

Testing Pipeline Innovations with Promising Research Projects. In addition to developing new methods and resources to accelerate therapeutic and diagnostics development, NCATS is supporting research that provides evidence that these new innovative approaches streamline the research pipeline. For instance, the preparation, submission, and review of clinical protocols can be a time-consuming process, ultimately resulting in a delay in determining the potential success of a new treatment. Through the support of a Clinical and Translational Sciences Awards (CTSA), the University of Wisconsin formed an Institutional Review Board (IRB) Consortium with the Medical College of Wisconsin, the Marshfield Clinic, and Aurora Health Care to rely upon the review of a single IRB for selected multi-site collaborative studies. As of September, 2010, each of the sites had served as reviewer for the others and each of the sites had been willing to defer about 50 percent of its reviews to the other sites. The development of reciprocal IRBs within the CTSA program, as evidenced here, can significantly accelerate the conduct of clinical trials across the nation.

Cultivating Strong Partnerships. To make significant inroads in catalyzing new advances in translational science, NCATS works to establish effective collaborations across disciplines and sectors to tap into the diverse expertise and resources across scientific fields. Several exciting collaborations are underway; for example, NIH convened a group of senior leaders and experts from the pharmaceutical industry, government, academia, and the non-profit sector to explore new opportunities for forging NIH-industry partnerships. One area--drug rescue and repurposing--has been broadly accepted as a valuable approach to speed the development of new drugs while reducing costs associated with duplicative efforts. The first meeting of this group, held in April 2011, focused on cultivating a better understanding of the landscape of rescue and repurposing research, exploring opportunities for new NIH-industry partnerships, and identifying core elements of a framework agreement for rescue and repurposing agreements. NCATS is uniquely positioned to serve as a matchmaker for accelerating this type of research.

Increasing Collaboration with Food and Drug Administration (FDA). NCATS also works closely with the FDA to promote and strengthen the discipline of regulatory science - the development and use of new tools, standards, and approaches to develop products and evaluate product safety, efficacy, and quality. Collaborations so far have enabled (1) researchers at the Washington University School of Medicine in St. Louis to characterize how nanoparticles interact with a host immune response system – a key step in the development of nanotherapeutics; and (2) researchers at Harvard University to advance the design and function of a "heart on a chip" device. NCATS will participate in the management of the current effort in Regulatory Science funded via the Common Fund in FY 2012, and launch new initiatives to collaborate with FDA.

Supporting an Innovative and Collaborative Training Program. NCATS fosters the training of clinicians and researchers in an environment of innovation and collaboration, encouraging the next generation of leaders in translational sciences. Not only does NCATS strengthen the workforce in fields such as clinical pharmacology, but it also trains investigators to integrate knowledge from increasingly inter-related fields when approaching complex and interdisciplinary problems. With the creation of NCATS, NIH will promote novel training mechanisms, such as a drug development apprenticeship for early-stage investigators, and explore cross-training of physicians and scientists between industry, academia, and government labs.

In summary, NCATS accomplishes its mission by conducting and supporting research to develop enhanced methodologies and approaches in translational science that can be used by other NIH Institutes and Centers, academia, industry, and other sectors. Moreover, as NCATS advances our understanding of scientific targets and pathways, new avenues for scientific inquiry are stimulated and pursued; ultimately reaffirming the NIH's commitment to investing in basic science research.

Overall Budget Policy

NCATS's highest priority is to advance the discipline of translational research by catalyzing the development of innovative methods and technologies that accelerate the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions. The NCATS FY 2013 budget will support infrastructure and resources for clinical and translational science efforts nationwide as well as innovative research projects addressing scientific and technical challenges to reduce, remove, or bypass significant bottlenecks across the continuum of translation. Nearly all NCATS investments are highly leveraged, either through a recipient institution, other NIH institutes, or public-private partnerships. NCATS will continue collaborations with the NIH Common Fund, and several exciting projects will be transferred into NCATS from the Office of the Director, such as the intramural portion of the Molecular Libraries. With the increase in funding for CAN, NCATS will be able to support cutting-edge technologies in the areas of microsystems, target validation, and drug rescue and repurposing.

Program Descriptions and Accomplishments

NCATS unifies key programs under one focused mission: catalyzing new synergies in translational research. Programs funded by NCATS are aligned within the following five areas:

(1) Clinical and Translational Sciences Activities

Reengineering the clinical research enterprise is a priority of both NCATS and the Clinical and Translational Sciences Awards program discussed in detail below.

- *NIH Clinical and Translational Sciences Awards (CTSA).* As a national consortium, the CTSA sites share a common vision to improve human health by transforming research and training environments to enhance the efficiency and quality of clinical and translational research. In addition to conducting preclinical research, CTSA institutions support first-in-human trials for clinical candidates across the spectrum of rare and common diseases in appropriate patient subpopulations; develop and test innovative trial designs; support post marketing clinical research; and are a natural home for community outreach, training, and education. Given the expertise and resources of the CTSA program, investigators at these sites are exceptionally well positioned to undertake collaborative approaches when tackling complex, interdisciplinary health challenges - including research on new and more effective methods for therapeutics and diagnostics development. For example, a diverse team of experts at the Weill Cornell Medical College Clinical and Translational Science Center developed fluorescent nanoparticles that are capable of safely illuminating specific types of cancer cells to provide more accurate imaging. This new technology would potentially equip clinicians and researchers with the ability to locate tumors with greater precision, more accurately detect diseased lymph nodes, and control drug distribution for more effective, targeted therapeutic interventions. Currently, this scientific breakthrough is being studied in cases of melanoma to assess the safe distribution and excretion of the nanoparticles.

  In FY 2013, the CTSA program will continue to develop and provide infrastructure and resources for diverse aspects of translational research, from biomarker discovery to community research. These resources and infrastructure will improve the efficiency of clinical trials funded by other NIH Institutes. NCATS will also strengthen the role of the CTSA program's Coordinating Center to amplify its role as a hub for communication across the nation's academic health centers and accelerate the adoption of best practices for clinical and translational research. By coordinating with the other NIH Institutes and Centers, NCATS will enable the CTSAs to support and enhance the mission of the entire NIH. For example, in 2011, the National Institute for Neurological Disease and Stroke (NINDS) made the strategic decision to leverage the CTSA infrastructure in order to advance translational research in neurological disorders by setting up NeuroNext, a clinical research network that would execute early phase, biomarker-informed clinical trials. NeuroNext includes a clinical coordinating center and a data management center, both of which are at CTSA sites. NeuroNext trials will be executed at 25 research sites across the nation; 21 of which are located within CTSAs. NCATS looks forward to continued

partnership with the NINDS to bring new therapies to persons suffering from the large number of neurological disorders.

Program Portrait: Review of the Clinical and Translational Sciences Awards

FY 2012 Level for CTSAs: $461.395 million
FY 2013 Level for CTSAs: $462.503 million
Difference: $1.108 million

Launched in FY 2006, the CTSA program has supported awards to help institutions nationwide create an academic home for clinical and translational science. The program's transition into NCATS in FY 2012 provided an opportunity for NIH to consider how to maximize the success of the CTSA program. As such, NIH Director Francis Collins convened a working group to recommend a strategy for ensuring that the CTSAs most effectively contribute to the mission of NCATS.

The group's analysis of the CTSA program reinforced the role of the CTSAs in providing infrastructure in support of the full spectrum of translational research. This function has prompted many academic health centers to align clinical research programs into a unified program – ultimately leveraging resources and elevating the profile of clinical research. Components common to all CTSAs are coordinated programs in training early-stage clinical investigators; faculty and support staff for patient research in inpatient (and sometimes outpatient) settings; biostatistics and bioethics consultation; and pilot funding for specific research projects, community outreach, and bioinformatics. Beyond the maintenance of core infrastructure, the working group found that the CTSAs also serve as hubs of innovation, and as the program has evolved, many institutions have also begun to develop their own unique and innovative technologies and capabilities. Given that the program is relatively new, the working group stated that each CTSA still struggles with achieving an optimal balance between supporting local institutional needs and creating a national network of information, resources, and expertise.

To continue the progress made in these areas, NCATS will require the CTSAs to maintain essential core components that are critical to the conduct of the entire spectrum translational science in FY 2013. In addition, NCATS will continue to explore new strategies for affording each CTSA the flexibility to develop innovative approaches to translational research, while encouraging each to contribute to a whole that is greater than the sum of its parts. This objective will be achieved, in part, by evaluating each institutional award based upon its performance and strengthening the role of the CTSA Coordinating Center in CTSA activities.

Budget Policy: The FY 2013 President's Budget request is $462.503 million, an increase of $1.108 million or 0.24 percent, over the FY 2012 Enacted level.

(2) Rare Diseases Research and Therapeutics

Research in this category is aimed at accelerating the treatment of rare diseases, either by testing pipeline innovations that result in new therapeutics or by facilitating interactions among key stakeholders that assist in overcoming significant hurdles. Of the known 6,000 rare diseases, we currently have effective treatments for fewer than 250. This area of research fills critical gaps in the field of translation, as research in rare diseases often garners little interest by the private sector. Indeed, NCATS ensures that none of its projects are redundant or duplicative with efforts in industry. This category includes:

- *Therapeutics for Rare and Neglected Diseases (TRND) program.* TRND is specifically intended to stimulate drug discovery and development research collaborations between the NIH and academic scientists, non-profit organizations, and pharmaceutical and biotechnology companies working on rare and neglected

illnesses. The TRND program provides an opportunity to partner with and gain access to rare and neglected disease drug development capabilities, expertise, and clinical/regulatory resources in a *collaborative* environment with the goal of moving promising therapeutics into human clinical trials. Since its initiation in September 2009, TRND has:(1) had two Investigational New Drug (IND) applications approved by FDA and initiated early stage clinical trials on two drugs – auranofin for chronic lymphocytic leukemia and Aes-103 for sickle cell disease (2) built a portfolio of collaborative small molecule and biologics projects with academic, biotechnology company, and foundation partners; (3) implemented two innovative platform technologies; (4) initiated its first natural history study; (5) established a close collaboration with the FDA on regulatory issues; and (6) recruited top scientists from public and private sectors in all disciplines of preclinical and early clinical development.

Program Portrait: University of Kansas, The Leukemia & Lymphoma Society, and TRND Collaboration: A Clinical Trial for Chronic Lymphocytic Leukemia (CLL) Patients

FY 2012 Level for TRND:	$23.955 million
FY 2013 Level for TRND:	$27.745 million
Difference:	$3.790 million

As part of an aggressive effort to speed the delivery of treatments to patients, TRND is partnering with the Leukemia Lymphoma Society (LLS)--a non-profit patient advocacy group--and the University of Kansas Cancer Center (KUCC) to find new uses for approved drugs. This collaborative effort has resulted in the initiation of a clinical trial targeting a rare form of adult leukemia using a drug first approved to treat arthritis more than 25 years ago. The trial is one key piece of a larger collaboration between KU, LLS, and TRND to accelerate discovery and development of safe, effective and affordable cancer treatments.

Initiation of this project was stimulated by a seminal discovery at the NIH Chemical Genomics Center (NCGC) regarding the finding that an anti-arthritis drug, auranofin, induced specific cell death in a rare form of Chronic Lymphocytic Leukemia (CLL) cells obtained from patients. Through this highly innovative collaboration, the project advanced forward in record time; the turn-around time was less than 24 months from discovery of the anti-cancer activity at NCGC, signing the Cooperative Research and Development Agreement, approval of the IND application by FDA, and dosing of the first patient at KU. The TRND goal is to complete initial assessment of safety and efficacy via human clinical trial studies within two years, at which time an industry partner will be engaged to bring the drug to market for this new indication.

- *Office of Rare Diseases Research (ORDR).* ORDR serves as a hub for stimulating and coordinating research on rare diseases at the NIH and collaborates with a host of other entities – including other NIH Institutes and Centers – to accelerate translational research and translation-related activities. ORDR's largest investment is in the Rare Diseases Clinical Research Network (RDCRN), which is made up of 19 distinctive consortia, consisting of 140 participating research institutions in 30 states across the nation and in other countries. These consortia members work in concert to improve the availability of rare disease information, treatment, clinical studies, and general awareness for both patients and the medical community. The RDCRN also aims to provide up-to-date information for patients and to assist in connecting patients with advocacy groups, expert doctors, and clinical research opportunities. The consortia focus on a wide range of more than 150 diseases,

including mitochondrial diseases, spinocerebellar ataxias, rare kidney stone diseases and kidney failure, and primary immune deficiencies, and include several clinical trials that test promising repurposed drugs.

Program Portrait: Global Rare Diseases Patient Registry and Data Repository (GRDR)

FY 2012 Level for GRDR: $0.500 million
FY 2013 Level for GRDR: $0.500 million
Difference: $0 million

In FY 2011, ORDR, in collaboration with PatientCrossroads, the Children's Hospital of Philadelphia, and Medscape, launched a two-year pilot project to establish the Global Rare Diseases Patient Registry and Data Repository (GRDR). The GRDR will work with patient organizations to collect de-identified patient clinical information for research on rare diseases. During the original pilot project, 12 patient groups without a registry and 12 patient groups with existing patient registries assisted in testing aspects of registry functions. In addition, ORDR worked towards developing a web based template and infrastructure to assist patient organizations in establishing their own rare disease-specific registries.

To facilitate the aggregation of de-identified patient clinical information in a standardized manner, ORDR established a national committee to develop a set of minimal Common Data Elements (CDEs) for use by any patient registry. This set of CDEs has been accepted and adopted by numerous patient advocacy groups and professional organizations within and outside of the US for collection of patient information. ORDR has also developed a template for informed consent for participation in patient registry. To accelerate research and better facilitate the understanding of the underlying pathogenesis of rare diseases, the registry will have the capability to link patients' data and medical information with biospecimens thereby interfacing with the ORDR Human Biospecimen Repository. In FY 2013, ORDR will move this effort forward beyond the pilot project phase.

ORDR also cosponsors the Undiagnosed Diseases Program, which has received approximately 5,800 inquiries, reviewed more than 2000 sets of medical records, and accepted 500 patients into protocols within its first 3.5 years of existence. Other ongoing collaborative ORDR programs include the Bench-to-Bedside (B2B), which funds 12 rare diseases research projects per year. ORDR continues its collaboration with the National Human Genome Research Institute in supporting the Genetic and Rare Diseases Information Center (GARD) which provides comprehensive information on rare and/or genetic diseases in English and Spanish to patients, their families, healthcare providers, researchers, and the public. In addition, ORDR co-funded a number of workshops to explore research opportunities or respond to urgent research needs on a wide range of topics important to rare diseases including lysosomal storage diseases and inborn errors of metabolism such as phenylketonuria (PKU), genetic diseases of children, emerging infectious diseases, lymphangioleiomyomatosis (LAM), Joubert syndrome, end-of-life and palliative care, an ORDR/TRND/FDA natural history study workshop to advance translational science, Hermansky-Pudlak syndrome, childhood ataxias, myotonic dystrophy, and EU-USA research collaborations on rare diseases.

Budget Policy: The FY 2013 President's Budget request is $38.275 million, an increase of $3.710 million or 10.73 percent, over the FY 2012 Enacted level. This increase reflects increases in collaborations that NCATS will be doing with other NIH Institutes and Centers, including the NIH Clinical Center. Included in this request are $27.745 million for the TRND program and $10.53 million for ORDR.

(3) Reengineering Translational Sciences

Essential to the NCATS mission is the development of new and innovative approaches to conducting research across the therapeutic development pipeline. In order to achieve these aims, NCATS either directly supports or administratively manages the following initiatives/programs:

- *Molecular Libraries and Imaging Program (MLP).* Originally implemented through the NIH Common Fund, the MLP has been successful in the development of chemical probes for basic and translational research and in the establishment of a database of chemical information that is accessed by over 100,000 users each day. Many of the probes developed have been, or are being, modified for use in the clinic, resulting in patent applications, licenses to pharmaceutical companies, and new therapeutic strategies. NCATS manages the support for small molecule screening through three components funded jointly by NCATS and the NIH Common Fund: (1) the NIH Chemical Genomics Center (NCGC), which provides state of the art high throughput screening capabilities, medicinal chemistry expertise that enables initial "hits" to be modified to become therapeutic lead compounds, capability to screen compounds in diverse types of cellular assays, and the ability to screen RNA and proteins in addition to small molecules; (2) the Small Molecule Repository, which is a one-of-a-kind resource in size, diversity of compounds, the extent to which the compounds have been characterized and the data made public, and quality control measures; and (3) the Cheminformatics, which assists in making data more user-friendly for a wider community and integrating the data with other types of cellular pathway information.

	FY 2012			**FY 2013**		
	Common Fund	NCATS	Total	Common Fund	NCATS	Total
NIH Chemical Genomics Center (NCGC)	$13,000	$0	$13,000	$0	$13,000	$13,000
Small Molecule Repository	6,000	0	6,000	6,000	0	6,000
Cheminformatics Center	5,400	0	5,400	5,400	0	5,400
Total	**24,400**	**0**	**24,400**	**11,400**	**13,000**	**24,400**

- *Bridging Interventional Development Gaps (BrIDGs).* Therapeutic approaches that involve high risk ideas or therapies for uncommon disorders are especially vulnerable to attrition during clinical development - especially those unsuccessful in attracting private sector investment. In these situations, the BrIDGs program can assist in filling in the gaps and reduce some of the common barriers hindering progress in these areas. Notably, BrIDGs is not a grant program, but rather, it makes critical resources available for developing new therapeutic agents. These resources support activities such as generating bulk supplies of the drug candidate or testing the stability or toxic effects of a potential therapeutic. The program also facilitates interactions

between investigators and the FDA during planning and preparation for IND submission. The government's investment in this program has yielded substantial benefits; to date, this program has supported several new INDs, some of which have been licensed for commercialization.

Budget Policy: The FY 2013 President's Budget request is $30.331 million, an increase of $14.985 million or 97.65 percent, over the FY 2012 Enacted level. This increase reflects the shifting of the intramural component of Molecular Libraries (formerly funded by the NIH Common Fund) and the additional emphasis NCATS will have on the Small Business Innovation Research and Small Business Technology Transfer programs. The increase also reflects the increase proportion of research funding that is set-aside for Small Business Innovation Research.

(4) Cures Acceleration Network Activities

CAN was authorized to advance the development of "high need cures" and reduce significant barriers between research discovery and clinical trials. To achieve these objectives, CAN provides the NIH with new flexibilities in its funding authorities. Under CAN, NIH may make large grant awards of up to $15 million per fiscal year, partnership awards that require 1:3 matching funds; and flexible research awards that allow projects to be actively and aggressively managed by using mechanisms similar to those used by the Defense Advanced Research Projects Agency (DARPA). CAN investments will be guided by the CAN Board which will meet four times in FY 2013. In FY 2013, CAN will support the following activities:

- *Integrated Microsystems for Drug Screening Initiative (IMDS).* Current models used for testing potential new drugs and vaccines are often poor predictors of safety and efficacy in humans. For this reason, NCATS is coordinating its efforts with DARPA and the FDA to develop a chip composed of diverse human cells and tissues organized in such a way that it mimics how cells and tissues in humans interact. The chip can be tested with compounds known to be either safe or toxic in humans, in order to identify those signals that are most reliable in predicting safety. Tissues harboring specific diseases could also be placed on this chip to accelerate understanding of disease processes and to test whether various drug candidates alter or overcome those disease mechanisms. NCATS will continue to collaborate with the NIH Common Fund (which is supporting this activity in FY 2012), FDA, and DARPA to build a prototype of this chip over the next few years with the goal that NCATS would then be able to support studies to demonstrate the chip's utility. If successful, this chip has the potential to make drug safety and efficacy assessments more accurate and earlier in the translational pipeline.

Program Portrait: Heart-Lung Micromachine for Safety and Efficacy Testing

FY 2012 Level for IMDS: $0.0 million (NCATS); $14.350 million (Common Fund)
FY 2013 Level for IMDS: $13.894 million (NCATS)
Difference: $0.456 million

One of the major problems slowing development and regulatory approval of new and safer medical products is the lack of experimental *in vitro* model systems that can replace costly and time-consuming animal studies by predicting drug efficacy, bioavailability and toxicity in humans. Although considerable advances have been made in the development of cell culture models, these methods fail to reconstitute structural and mechanical features of whole living organs and integrated multi-organ system physiology that are central to their function.

Breakthroughs in the laboratories of researchers at Harvard Medical School have made it possible to engineer biomimetic microsystems technologies that use living human cells cultured within three-dimensional microfluidic systems to replicate the complex physiological functions and mechanical microenvironment of the breathing lung and beating heart. The long-term goal of this project is to integrate these 'organ-on-chip' microdevices to produce a Heart-Lung Micromachine that can provide quantitative real-time measures of the efficacy, bioavailability, and safety of aerosol-based drugs, nanotherapeutics, and other medical products on integrated lung and heart function.

The specific aims of this proposal include: 1) to demonstrate the ability of the breathing lung-on-a-chip device to measure pulmonary absorption, efficacy, and toxicity of aerosol-based drugs and nanotherapeutics; 2) to demonstrate the ability of the beating heart microdevice to detect cardiotoxicity by measuring changes in cardiac cell contractility, electrical conduction, and tissue inflammation; and 3) to create an integrated heart-lung microsystem technology that can assess the effects of drugs and nanotherapeutics delivered to the lung by aerosol on cardiac function and toxicity *in vitro*.

In these studies, researchers will demonstrate proof-of-principle for a new biomimetic microsystem technology that can analyze efficacy and bioavailability, as well as detect adverse toxicities, associated with use of therapeutic agents before entering clinical trials. If successful, these organ-on-chip microdevices could greatly shorten the timeline and reduce costs associated with development of aerosolized drugs, nanotherapies, and other medical products, as well as inform regulatory decision-making in the future.

- *Target Validation.* Current industry processes for determining whether there is enough evidence that modulation of a drug target will have the desired therapeutic effect, known as target validation, lacks sufficient accuracy and reproducibility. For this reason, NCATS has launched a target validation initiative to develop a more strategic and harmonized approach that reduces duplication of effort and incorporates critical genetic and phenotypic information made available from the wealth of new sequencing data being obtained from the public sector. In FY 2013, NCATS will collaborate with industry to develop a precompetitive consortium capable of providing both a repository and an analytic platform (containing genomic, phenotypic, and bioinformatic information on potential drug targets) for target validation efforts. NCATS will also continue to support pilot projects that aim to discover more systematic and predictable approaches to validating potential new targets. Funding for this effort is a critical step in the process of improving the process of drug development with a goal of bringing more safe and effective therapies from the bench to the bedside.

- *Drug Rescue and Repurposing Initiative.* Repositioning drugs that have not been approved (drug rescue) and drugs that are already approved (drug repurposing) has been broadly accepted as a valuable mechanism to develop therapeutic approaches for new indications more efficiently, more rapidly, and at a lower cost than de novo development required of novel compounds. As industry holds many of the assets and data required for efficient rescue and repurposing, NCATS is working with industry to provide a mechanism for academic investigators and small businesses to apply for NIH funding to conduct research on new indications using compounds from industry provided drug collections. NCATS is also developing a comprehensive database of approved and investigational drugs (the NIH Center for Translational Therapeutics (NCTT) Pharmaceutical Collection) and working with the FDA to advance opportunities in this promising area. Continued funding of this program in FY 2013 will contribute to the NIH effort of decreasing the time, cost, and attrition rate in therapeutic development, to bring more promising new therapies to the public.

Budget Policy: The FY 2013 President's Budget request is $49.624 million, an increase of $39.643 million or 397.18 percent, over the FY 2012 Enacted level, which was the first year of CAN funding. Funding for this program will be used to support the Integrated Microsystems for Drug Screening Initiative, which will no longer receive funds from the Common Fund. Funds will also be increased to support other CAN directed programs, including those described above.

(5) Translational Research Resources

(TRR) program funds specialized support programs and initiatives that provide support to NIH researchers. Additionally, the TRR program manages and administers a portion of the NIH Extramural Loan Repayment Program (LRP). The overall purpose of the LRP is the recruitment and retention of highly qualified health professionals as research investigators.

Budget Policy: The FY 2013 President's Budget request for the Translational Research Resources program is $24.033 million, an increase of $4.874 million or 25.4 percent, over the FY 2012 Enacted level. This level will provide NCATS increased share of trans-NIH programs and initiatives that support the entire spectrum of biomedical research.

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Budget Authority by Object
(Dollars in Thousands)

	FY 2012 Enacted	FY 2013 PB	Increase or Decrease
Total compensable workyears:			
Full-time employment	105	104	(1)
Full-time equivalent of overtime and holiday hours	0	0	0
Average ES salary (*in dollars*)	$174,688	$175,561	$873
Average GM/GS grade	12.5	12.5	0.0
Average GM/GS salary (*in dollars)*	$107,285	$107,821	$536
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207) *(in dollars)*	$111,717	$115,738	$4,021
Average salary of ungraded positions (*in dollars*)	135,170	135,683	513

	OBJECT CLASSES	FY 2012 Enacted	FY 2013 PB	Increase or Decrease
	Personnel Compensation:			
11.1	Full-time permanent	$9,565	$9,536	($29)
11.3	Other than full-time permanent	1,595	1,602	7
11.5	Other personnel compensation	71	71	0
11.7	Military personnel	456	462	6
11.8	Special personnel services payments	303	305	2
	Total, Personnel Compensation	**$11,990**	**$11,976**	**($14)**
12.0	Personnel benefits	$3,025	$2,989	($36)
12.2	Military personnel benefits	294	293	(1)
13.0	Benefits for former personnel	0	0	0
	Subtotal, Pay Costs	**$15,309**	**$15,258**	**($51)**
21.0	Travel and transportation of persons	$393	$334	($59)
22.0	Transportation of things	67	67	0
23.1	Rental payments to GSA	110	110	0
23.2	Rental payments to others	5	5	0
23.3	Communications, utilities and miscellaneous charges	158	158	0
24.0	Printing and reproduction	86	86	0
25.1	Consulting services	10,584	24,439	13,855
25.2	Other services	17,004	21,512	4,508
25.3	Purchase of goods and services from government accounts	26,507	34,417	7,910
25.4	Operation and maintenance of facilities	275	275	0
25.5	Research and development contracts	3,861	19,363	15,502
25.6	Medical care	0	0	0
25.7	Operation and maintenance of equipment	235	235	0
25.8	Subsistence and support of persons	0	0	0
25.0	**Subtotal, Other Contractual Services**	**$58,466**	**$100,241**	**$41,775**
26.0	Supplies and materials	$1,990	$2,990	$1,000
31.0	Equipment	4,277	4,277	0
32.0	Land and structures	0	0	0
33.0	Investments and loans	0	0	0
41.0	Grants, subsidies and contributions	493,852	515,507	21,655
42.0	Insurance claims and indemnities	0	0	0
43.0	Interest and dividends	0	0	0
44.0	Refunds	0	0	0
	Subtotal, Non-Pay Costs	**$559,404**	**$623,775**	**$64,371**
	Total Budget Authority by Object	**$574,713**	**$639,033**	**$64,320**

Includes FTEs which are reimbursed from the NIH Common Fund.

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Salaries and Expenses
(Dollars in Thousands)

OBJECT CLASSES	FY 2012 Enacted	FY 2013 PB	Increase or Decrease
Personnel Compensation:			
Full-time permanent (11.1)	$9,565	$9,536	($29)
Other than full-time permanent (11.3)	1,595	1,602	7
Other personnel compensation (11.5)	71	71	0
Military personnel (11.7)	456	462	6
Special personnel services payments (11.8)	303	305	2
Total Personnel Compensation (11.9)	**$11,990**	**$11,976**	**($14)**
Civilian personnel benefits (12.1)	$3,025	$2,989	($36)
Military personnel benefits (12.2)	294	293	(1)
Benefits to former personnel (13.0)	0	0	0
Subtotal, Pay Costs	**$15,309**	**$15,258**	**($51)**
Travel (21.0)	$393	$334	($59)
Transportation of things (22.0)	67	67	0
Rental payments to others (23.2)	5	5	0
Communications, utilities and miscellaneous charges (23.3)	158	158	0
Printing and reproduction (24.0)	86	86	0
Other Contractual Services:			
Advisory and assistance services (25.1)	10,584	24,439	13,855
Other services (25.2)	17,004	21,512	4,508
Purchases from government accounts (25.3)	10,463	12,463	2,000
Operation and maintenance of facilities (25.4)	275	275	0
Operation and maintenance of equipment (25.7)	235	235	0
Subsistence and support of persons (25.8)	0	0	0
Subtotal Other Contractual Services	**$38,561**	**$58,924**	**$20,363**
Supplies and materials (26.0)	$1,990	$2,990	$1,000
Subtotal, Non-Pay Costs	$41,260	$62,564	$21,304
Total, Administrative Costs	**$56,569**	**$77,822**	**$21,253**

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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
Immediate Office of the Director	4	0	4	4	0	4	4	0	4
Executive Office	15	0	15	15	0	15	15	0	15
Office of Grants Management and Scientific Review	27	0	27	27	0	27	27	0	27
Office of Rare Disease Research	6	0	6	6	0	6	6	0	6
Office of Policy, Communication and Strategic Alliances	9	0	9	9	0	9	9	0	9
Division of Clinical Innovation	12	3	15	12	3	15	12	3	15
Division of Pre-Clinical Innovation	29	0	29	29	0	29	28	0	28
Total	102	3	105	102	3	105	101	3	104
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
2011	12.5
2012	12.5
2013	12.5

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Detail of Positions

GRADE	FY 2011 Actual	FY 2012 Enacted	FY 2013 PB
Total, ES Positions	0	1	1
Total, ES Salary	174,688	174,688	175,561
GM/GS-15	15	15	15
GM/GS-14	25	25	24
GM/GS-13	24	24	24
GS-12	5	5	5
GS-11	2	2	2
GS-10	2	2	2
GS-9	2	2	2
GS-8	4	4	4
GS-7	5	5	5
GS-6	1	1	1
GS-5	0	0	0
GS-4	1	1	1
GS-3	1	1	1
GS-2	0	0	0
GS-1	0	0	0
Subtotal	87	87	86
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	0	0	0
Director Grade	3	3	3
Senior Grade	0	0	0
Full Grade	0	0	0
Senior Assistant Grade	0	0	0
Assistant Grade	0	0	0
Subtotal	3	3	3
Ungraded	56	56	56
Total permanent positions	88	88	87
Total positions, end of year	147	147	146
Total full-time equivalent (FTE) employment, end of year	105	105	104
Average ES salary	174,688	174,688	175,561
Average GM/GS grade	12.5	12.5	12.5
Average GM/GS salary	107,285	107,285	107,821

Includes FTEs which are reimbursed from the NIH Common Fund.