DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Center for Advancing Translational Sciences (NCATS)

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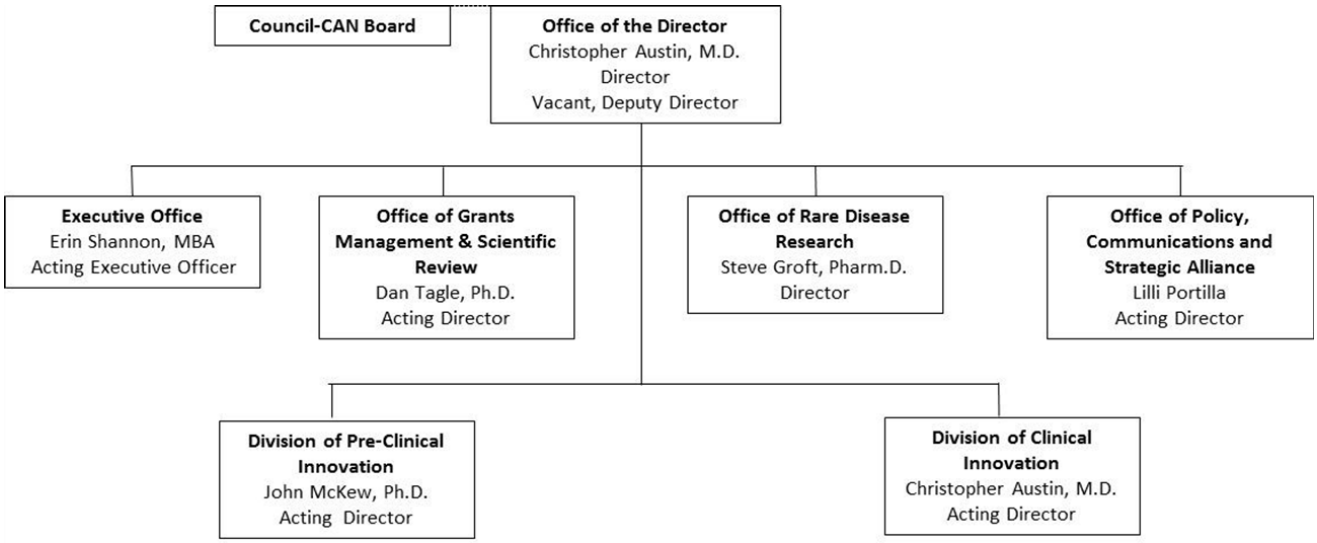
National Center for Advancing Translational Sciences



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National Center for Advancing Translational Sciences

For carrying out section 301 and title IV of the PHS Act with respect to translational sciences, $665,688,000: Provided, That up to $50,000,000 shall be available to implement section 480 of the PHS Act, relating to the Cures Acceleration Network.

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National Center for Advancing Translational Sciences

Amounts Available for Obligation[1]

(Dollars in Thousands)

Source of Funding	FY 2012 Actual	FY 2013 CR	FY 2014 PB
Appropriation	576,456	578,888	665,688
Rescission	(1,090)	0	0
Subtotal, adjusted appropriation	575,366	578,888	665,688
Secretary's Transfer for Alzheimer's disease (AD)	(379)	0	0
Secretary's Transfer for AIDS authorized by PL 112-74, Section 206	(164)	0	0
Comparative Transfers to NLM for NCBI and Public Access	(526)	(681)	0
Subtotal, adjusted budget authority	574,297	578,207	665,688
Unobligated balance, start of year	0		0
Unobligated balance, end of year		0	0
Subtotal, adjusted budget authority	574,297	578,207	665,688
Unobligated balance lapsing	(260)	0	0
T otal obligations	574,037	578,207	665,688

[1] Excludes the following amounts for reimbursable activities carried out by this account:
FY 2012 - $35,004 FY 2013 - $35,007 FY 2014 - $10,755

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National Center for Advancing Translational Sciences

Budget Mechanism – Total [1]
(Dollars in Thousands)

MECHANISM	FY 2012 Actual		FY 2013 CR		FY 2014 PB		Change vs. FY 2012	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Grants								
Research Projects								
Noncompeting	0	$776	0	$7,090	0	$3,018	0	$2,243
Administrative Supplements	*(1)*	39	*(1)*	39	*(1)*	39	*(0)*	0
Competing:								
Renewal	0	68	0	0	0	0	0	-68
New	0	7,073	0	3,174	14	29,245	14	22,172
Supplements	0	0	0	0	0	0	0	0
Subtotal, Competing	0	$7,140	0	$3,174	14	$29,245	14	$22,105
Subtotal, RPGs	0	$7,955	0	$10,302	14	$32,302	14	$24,347
SBIR/STTR	49	15,241	49	15,774	59	18,614	10	3,372
Research Project Grants	49	$23,197	49	$26,076	73	$50,916	24	$27,720
Research Centers								
Specialized/Comprehensive	5	15,523	5	15,523	5	15,523	0	0
Clinical Research	64	396,313	64	396,313	64	397,421	0	1,108
Biotechnology	0	0	0	0	0	0	0	0
Comparative Medicine	0	192	0	192	0	192	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	69	$412,027	69	$412,027	69	$413,135	0	$1,108
Other Research								
Research Careers	70	48,667	70	48,667	70	48,667	0	0
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	0	0	0	0	0	0	0	0
Biomedical Research Support	0	0	0	0	0	0	0	0
Minority Biomedical Research Support	0	0	0	0	0	0	0	0
Other	10	2,294	10	2,794	18	18,905	8	16,611
Other Research	80	$50,961	80	$51,461	88	$67,572	8	$16,611
Total Research Grants	198	$486,185	198	$489,565	230	$531,623	32	$45,439
Ruth L. Kirschstein Training Awards	FTTPs		FTTPs		FTTPs		FTTPs	
Individual	0	0	0	0	0	0	0	0
Institutional	260	11,229	260	11,229	260	11,229	0	0
Total Research Training	260	$11,229	260	$11,229	260	$11,229	0	$0
Research & Development Contracts	158	22,582	156	23,113	158	32,407	0	9,825
SBIR/STTR (non-add)	*(4)*	*(33)*	*(0)*	*(0)*	*(0)*	*(0)*	*-(4)*	*-(33)*
	FTEs		FTEs		FTEs		FTEs	
Intramural Research	25	23,955	32	23,955	32	55,745	7	31,790
Research Management and Support	93	30,346	90	30,346	90	34,684	-3	4,338
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, NCATS	118	$574,297	122	$578,207	122	$665,688	4	$91,391

[1] All items in italics and brackets are "non-adds."

Major Changes in the Fiscal Year 2014 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 2014 budget request for NCATS, which is $91.4 million more than FY 2012 level, for a total of $665.7 million.

Cures Acceleration Network (CAN): (+$40.111 million; total $50.00 million): CAN will fund initiatives designed to address scientific and technical challenges that impede translational research, including support for the Tissue Chips for Drug Screening Initiative, the Discovering New Therapeutic Uses for Existing Molecules Program, and others. Common Fund support of these programs will end in FY 2014 and they will be funded through the NCATS direct appropriation.

Research Project Grants (RPGs): (+$27.720 million; total $50.916 million): In FY 2014, NCATS will award an additional 14 competing RPGs over the FY 2012 Actual level. Investigator-initiated ideas will play a significant role in the mission of NCATS. Additionally, NCATS will support 59 SBIR/STTR awards at a total cost of $18.6 million, which is an increase of $3.4 million over FY 2012. NIH budget policy for RPGs in FY 2014, continues 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.

Reengineering Translational Sciences (+$31.340 million; total $46.614 million): In FY 2014, NCATS will begin direct funding the Bridging Interventional Development Gaps (BrIDGs) program as well as components of the Molecular Libraries Program (MLP), such as the Chemical Genomics Center (NCGC), a chemical informatics platform called the BioAssay Research Database (BARD), and the Small Molecule Repository. These programs have been previously supported by the Common Fund.

Clinical and Translational Science Activities (+1.108 million; total $462.503 million): 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 (+$31.790 million; total $55.745 million): The FY 2014 budget includes an increase in funding for Intramural Research in NCATS, reflecting a change in funding source for the NCGC, BARD and the Small Molecule Repository under the Molecular Libraries program as well as the BrIDGs program. These programs had been funded by the Common Fund and now will be funded through NCATS direct appropriation.

NATIONAL INSTITUTES OF HEALTH
National Center for Advancing Translational Sciences

Summary of Changes

(Dollars in Thousands)

FY 2012 Actual				**$574,297**
FY 2014 President's Budget				**$665,688**
Net change				**$91,391**
	2014 President's Budget		**Change from FY 2012**	
CHANGES	**FTEs**	**Budget Authority**	**FTEs**	**Budget Authority**
A. Built-in:				
1. Intramural Research:				
a. Annualization of March 2013 pay increase & benefits		$5,761		$14
b. January FY 2014 pay increase & benefits		5,761		41
c. One more day of pay		5,761		21
d. Differences attributable to change in FTE		5,761		0
e. Payment for centrally furnished services		1,122		2
f. Increased cost of laboratory supplies, materials, other expenses, and non-recurring costs		48,862		24
Subtotal				$102
2. Research Management and Support:				
a. Annualization of March 2013 pay increase & benefits		$12,785		$30
b. January FY 2014 pay increase & benefits		12,785		83
c. One more day of pay		12,785		42
d. Differences attributable to change in FTE		12,785		0
e. Payment for centrally furnished services		1,647		30
f. Increased cost of laboratory supplies, materials, other expenses, and non-recurring costs		20,252		1
Subtotal				$187
Subtotal, Built-in				$289

NATIONAL INSTITUTES OF HEALTH
National Center for Advancing Translational Sciences

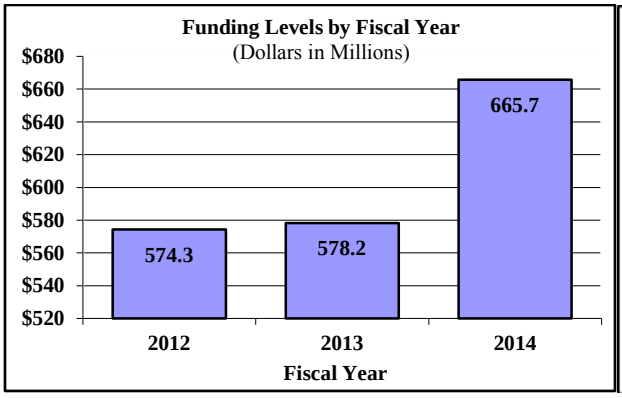
Summary of Changes – Continued

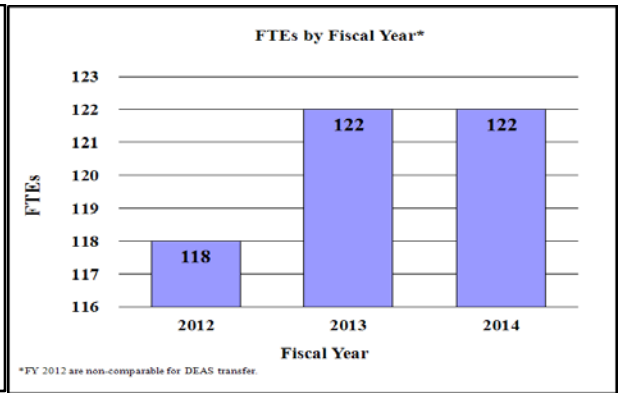
CHANGES	2014 President's Budget		Change from FY 2012	
	No.	Amount	No.	Amount
B. Program:				
1. Research Project Grants:				
a. Noncompeting	0	$3,057	0	$2,243
b. Competing	14	29,245	14	22,105
c. SBIR/STTR	59	18,614	10	3,372
Total	73	$50,916	24	$27,720
2. Research Centers	69	$413,135	0	$1,108
3. Other Research	88	67,572	8	16,611
4. Research Training	260	11,229	1	0
5. Research and development contracts	158	32,407	0	9,825
Subtotal, Extramural		$575,259		$55,264
	FTEs		FTEs	
6. Intramural Research	32	$55,745	7	$31,688
7. Research Management and Support	90	34,684	-3	4,151
8. Construction		0		0
9. Buildings and Facilities		0		0
Subtotal, program	122	$665,688	4	$91,103
Total changes				$91,391

NATIONAL INSTITUTES OF HEALTH
National Center for Advancing Translational Sciences

Fiscal Year 2014 Budget Graphs

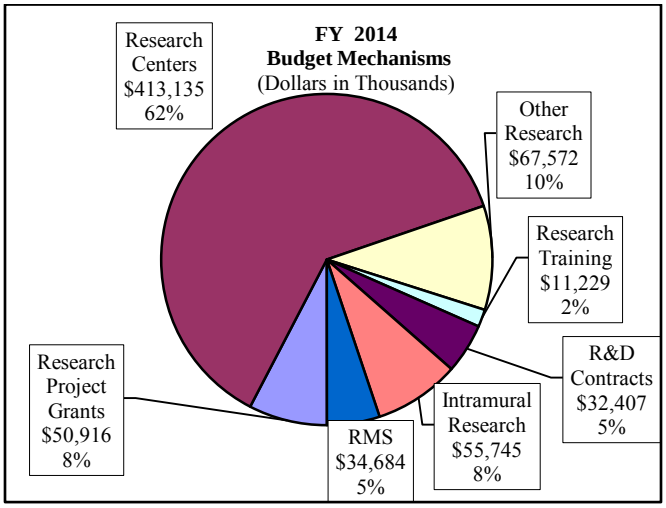
History of Budget Authority and FTEs*



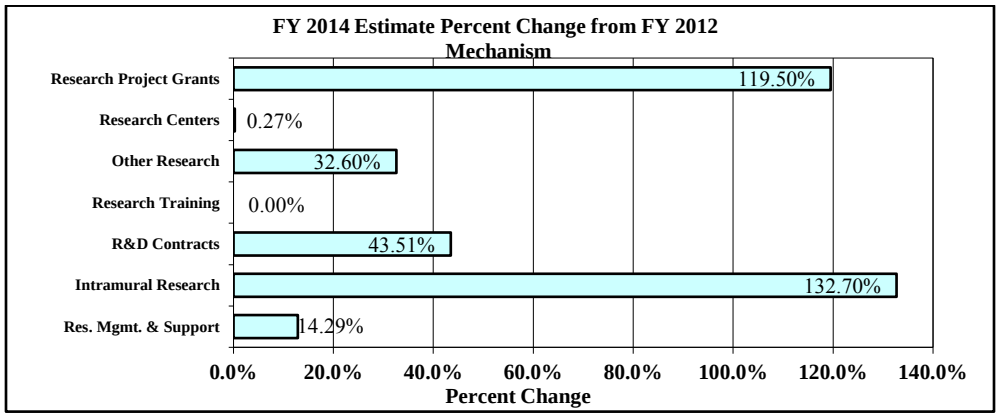


* NCATS was created in FY 2012.

Distribution by Mechanism:



Change by Selected Mechanism:



NATIONAL INSTITUTES OF HEALTH
National Center for Advancing Translational Sciences

Budget Authority by Activity[1,2]
(Dollars in Thousands)

	FY 2012 Actual		FY 2013 CR		FY 2014 PB		Change vs. FY 2012	
Research:	**FTEs**	**Amount**	**FTEs**	**Amount**	**FTEs**	**Amount**	**FTEs**	**Amount**
Detail:								
Clinical and Translational Science Activities		**$461,395**		**$461,395**		**$462,503**		**$1,108**
Rare Disease Research and Therapeutics		**38,665**		**38,680**		**42,455**		**3,790**
Therapeutics for Rare and Neglected Diseases (non-add)		*23,955*		*23,970*		*27,745*		*3,790*
Office for Rare Diseases Research (non-add)		*14,710*		*14,710*		*14,710*		*0*
Reengineering Translational Sciences		**15,274**		**15,774**		**46,614**		**$31,340**
Cures Acceleration Network		**9,889**		**11,889**		**50,000**		**$40,111**
Translational Research Resources		**18,728**		**20,123**		**29,432**		**$10,704**
Subtotal, Research		$543,951		$547,861		$631,004		$87,053
Intramural Research (non-add)	***25***	***$23,955***	***32***	***$23,955***	***32***	***$55,745***	***7***	***$31,790***
Research Management & Support	**93**	**$30,346**	**90**	**$30,346**	**90**	**$34,684**	**-3**	**$4,338**
TOTAL	**118**	**$574,297**	**122**	**$578,207**	**122**	**$665,688**	**4**	**$91,391**

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

NATIONAL INSTITUTES OF HEALTH
National Center for Advancing Translational Sciences

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2013 Amount Authorized	FY 2013 CR	2014 Amount Authorized	FY 2014 PB
Research and Investigation	Section 301	42§241	Indefinite	$578,207,000	Indefinite	$665,688,000
National Center for Advancing Translational Sciences	Section 480	42§281	Indefinite		Indefinite	
Total, Budget Authority				$578,207,000		$665,688,000

NATIONAL INSTITUTES OF HEALTH
National Center for Advancing Translational Sciences

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
2005	-	-	-	-
Rescission				-
2006	-	-	-	-
Rescission				-
2007	-	-	-	-
Rescission				-
2008	-	-	-	-
Rescission				-
2009	-	-	-	-
Rescission				-
Supplemental				-
2010	-	-	-	-
Rescission				-
2011	-	-	-	-
Rescission				-
2012	$721,601,000	-	$582,326,000	$576,456,000
Rescission				($1,089,502)
2013	$639,033,000	-	$631,346,000	-
Rescission				-
2014	$665,688,000	-	-	-

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 480 of the PHS Act, relating to the Cures Acceleration Network.

Budget Authority (BA):

	FY 2012 Actual	FY 2013 CR	FY 2014 President's Budget	FY 2014 +/- FY 2012
BA	$574,297,581	$578,207,000	$665,688,000	+91,390,419
FTE	118	122	122	+4

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

Director's Overview

NCATS was established on December 23, 2011, with the mission to catalyze innovations aimed at enhancing the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions. By improving the process of translation, NCATS enables scientists in both the public and private sectors to develop drugs, devices, and diagnostics more efficiently for any number of diseases, ultimately accelerating the pace at which they are delivered to the patients who need them. There have been dramatic advances in our understanding of the molecular pathogenesis of disease in recent years, and by pairing this knowledge with advances in technology and with expert partners, NCATS is on its way to transforming the translational research process into an efficient and collaborative enterprise. By focusing on commonalities across diseases and organ systems, NCATS complements the work of other NIH institutes and centers as well as that of its pharmaceutical, foundation, and advocacy partners.

NCATS has become a hub of innovation for translational sciences. The Center has launched several major research initiatives, cultivated promising strategic partnerships, and established a presence at the NIH and in the community. The milestones include: guiding an evolution of the national network of clinical and translational research institutions; overseeing an innovative grant program to create new tools for predicting drug toxicity in partnership with the Defense Advanced Research Project Agency (DARPA) and the Food and Drug Administration (FDA); and developing a breakthrough partnership program with eight pharmaceutical companies to find new uses for existing drugs. NCATS has also named a permanent Director and held the first meetings of the NCATS Advisory Council and Cures Acceleration Network Review Board.

NCATS supports the development, demonstration, and dissemination of a broad range of technologies, tools, and resources that facilitate collaborative pre-clinical testing and first-in-human clinical trial implementation. For example, NCATS' Matrix Screening Platform is a

transformative technology that identifies combinations of drugs to treat diseases resistant to single drugs which is particularly important for treatment-resistant cancers. Since this testing is done in a high-speed fully automated robotic format, hundreds or even thousands of drug combinations can be tested in a single day to determine which are best able to kill the cancer cells while minimizing toxic side effects. This approach is now being expanded to other diseases. NCATS has also made major strides by creating the NCATS Pharmaceutical Collection (NPC) and database of every drug approved for human use to enable repurposing via high-throughput screening and applying the NPC to multiple rare diseases, with two repurposed drugs already having entered clinical trials.

NCATS supports several important initiatives aimed at increasing the ability to predict whether a drug will be toxic in humans, as unanticipated toxicity is one of the biggest reasons drugs fail in the development process or are withdrawn after approval. The Tox21 Program, through a collaboration with the Environmental Protection Agency (EPA), the National Institute for Environmental Health Sciences (NIEHS), and the FDA, is testing over 10,000 drugs and environmental chemicals for hundreds of activities relevant to toxicity, with all data being made publically available. Researchers have used this information to develop multiple tools for predicting how chemicals might adversely affect human health and the environment. In addition, the NCATS Tissue Chip for Drug Screening program, a collaboration with DARPA and FDA, supports a novel effort to develop transparent microchips that model the structure and function of living organ tissues. If successful, these organ tissue models will enable researchers to test toxicity and predict more accurately how effective potential drugs would be in humans in a faster, more accurate, and more cost-effective way.

Through its Clinical and Translational Science Awards (CTSA), NCATS supports institutions across the country in their efforts to improve the quality, validity, generalizability, and efficiency of clinical and translational research. The Research Electronic Data Capture (REDCap) system, a freely available powerful enterprise electronic data capture tool that is easy for investigators to use, provides capability for conducting clinical research studies quickly and securely. Integrated clinical data repositories at CTSA institutions and policy agreements that allow searches across multiple institutional repositories facilitate clinical trial recruitment and hypothesis generation. These tools are helping amalgamate CTSA institutions into a national network for observational and interventional trials. Many CTSAs institutions are publishing information about their researchers and resources as linked open data so expertise can be easily discovered and linked to scientific data.

The CTSA programs at institutions across the country partner with NIH supported investigators, foundations, and companies to facilitate translational research studies. For example, building on NIH supported research, 10 CTSA-supported institutions provided resources and partnered with the Cystic Fibrosis Foundation and Vertex Pharmaceuticals to develop the first targeted therapy to treat children with a rare type of this deadly disease. The collaboration enabled the group to conduct multiple clinical trials and obtain FDA approval for the treatment. The drug, called Kalydeco, is the first cystic fibrosis treatment that targets the disease's underlying cause rather than its symptoms.

In order for NCATS to meet its mission, the biomedical workforce must be sufficient in size and equipped with the requisite knowledge and skills for advancing the relatively new discipline of translational science. The CTSA program supports a dedicated clinical and translational research training pipeline to ensure that our nation has the trained research team members needed to move basic research findings into the clinic. Over 4,100 researchers have been trained so far. These CTSA training programs incorporate nationally endorsed core competencies required for translational researchers, including the principles and application of translational science, collaborative team science, project management, and entrepreneurship. Training competencies focused on therapeutic development are currently being developed.

NCATS is committed to increasing its support for accelerating the bench-to-bedside process. Some challenges for FY 2014 include enhancing the ability to predict successful new approaches to treatment, diagnostics and prevention; increasing data sharing among research scientists; creating incentives for the publication of clinical trials results; and expanding the synergy between NCATS-supported and disease-specific investigators and projects.

In FY 2014, NCATS proposes to greatly expand its successful drug repurposing initiative to encompass up to 100 rare diseases which currently have no treatment. Specifically, the program would support collaborations with external investigators to accomplish rare disease assay development, NPC screening of the assay, and testing of selected identified drugs in animal models of the disease to allow selection of a clinical trial candidate(s). In addition, NCATS proposes to obtain, through acquisition, additional quantities of drugs currently in the NPC collection and its continued expansion of drugs currently in clinical trials. NCATS' Matrix Screening Platform would also be applied to these assays/projects when appropriate. Importantly, after appropriate delay for publication and IP filing, all screening data would be placed in the publically available NPC browser for the community to mine.

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 2014 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. Several exciting projects that have been previously funded by the NIH Common Fund, will be directly funded by NCATS. These programs include the intramural portion of the Molecular Libraries as well as components of the CAN program.

Program Descriptions and Accomplishments

(1) Clinical and Translational Science Activities

NCATS' CTSA program focuses on enhancing the quality and efficiency of the full spectrum of translational research by cultivating a national network of institutions focused on transforming the research and training environment. Institutional CTSA awards are the centerpiece of the program, creating academic homes for translational sciences, providing research resources needed by local and national research communities, and supporting the training of clinical and translational scientists. There are currently 61 sites, located in 30 states and the District of Columbia. The sites together comprise the CTSA Consortium, which leverages the collective resources of its members by sharing best practices and collaboration.

CTSA support also includes infrastructure and resources for clinical research, including all phases of clinical trials. However, specific support for clinical trials through pilot projects and within training programs is limited by NCATS authorization to trials only through the end of phase IIA. Examples of critical clinical research resources include streamlining the IRB process, addressing recruitment issues for clinical trials, and forming interdisciplinary collaborations to address emerging scientific opportunities.

Begun in FY2006, the CTSA program focused initially on re-engineering existing capabilities at academic institutions and developing new resources in the areas of clinical and translational research training, community outreach, and informatics. NCATS has solicited input for building on and enhancing the program from the public with a Request for Information (RFI), from NIH leaders with a NIH Working Group, and from CTSA principal investigators. In addition, the NIH has commissioned the Institute of Medicine (IOM) to assemble an ad hoc expert committee to evaluate the CTSA program. Committee members are reviewing existing evaluations, seeking stakeholder input and public input through public workshops, and other means. In June 2013, the IOM committee will release a report with recommendations.

The CTSA program aims to transform translational research across the nation by:

- Facilitating collaboration among basic, pre-clinical, and clinical scientists;
- Providing a foundation of shared practices and resources that improve quality, efficiency, and reduce costs of clinical research, including multi-site trials;
- Building on institutional strengths and facilitating nimble partnerships with healthcare providers, foundations, industry, and patient communities; and
- Strengthening the clinical research workforce through rigorous training and engaging patient and provider communities in the research process.

Through the CTSA consortium, investigators at CTSA-supported institutions work together to better address national health issues. By focusing on data-sharing, regulatory hurdles, patient recruitment, communication, and other key function areas of research, the consortium strives to dramatically increase the efficiency and effectiveness of the clinical and translational research process.

In FY 2014, the CTSA program expects to:

- Continue to provide infrastructure support for the full spectrum of translational research
- Encourage consortial activities that improve nationally the quality and efficiency of clinical research at lower cost
- Enhance engagement with NIH ICs and patient communities
- Encourage consortial and community engagement projects through possible solicitations

Budget Policy: The FY 2014 President's Budget request is $462.503 million, an increase of $1.108 million or 0.2 percent above the FY 2012 Actual level.

(2) Rare Diseases Research and Therapeutics

- *The Therapeutics for Rare and Neglected Disease (TRND) Program*

The goal of the TRND program is to encourage and speed the development of new treatments for rare and neglected diseases by stimulating research collaborations among NIH and academic scientists, nonprofit organizations, and pharmaceutical and biotechnology companies. The TRND program operates by forming public-private partnerships, which leverage the unique strengths and capabilities of each party, and develops new technologies and collaborative models to improve the efficiency of therapeutic development.

The TRND program was initiated in May 2009, originally establishing infrastructure and funding six pilot projects through FY 2010. TRND now has a portfolio of 14 active projects targeting drug development for some of the most devastating diseases afflicting either small populations in the US or large populations in the developing world. Three projects, targeting Sickle Cell Disease, Hereditary Inclusion Body Myopathy, and Chronic Lymphocytic Leukemia, have already yielded successful Investigational New Drug (IND) applications to the Food and Drug Administration, and are currently in first-in-human clinical trials. Two additional projects are on schedule for IND submission in FY 2013.

In addition to meeting its project-specific goals, TRND continues to develop novel technologies and collaborations that improve the efficiency of the translational process. For example, two projects are developing novel platform technologies that can be used to develop therapeutics to treat a variety of other human disorders. In addition, TRND is a founding partner in the Learning Collaborative (TLC), a collaboration between the University of Kansas Institute for Advancing Medical Innovation, the Leukemia and Lymphoma Society, and TRND to develop novel collaborative structures to speed the development of new drugs for blood cancers.

In response to a Congressional request, TRND prepared an annual report that identified the number of projects started each year, cost per project, and the outcome of each project. The report was submitted to the Committees on Appropriation in September 2012.

- *Office of Rare Disease Research (ORDR)*

In the United States, a disease is considered to be rare if it affects fewer than 200,000 Americans. There are almost 7,000 rare diseases, affecting an estimated 25 million Americans and their families. Rare diseases are frequently characterized by severe and progressive chronic illness, disability, and premature death; a large percentage of rare diseases are genetic and affect children. Over 95% of rare diseases have inadequate or no treatment. Few drug companies conduct research into rare diseases since it is difficult to recover the costs of developing treatments for relatively small, geographically dispersed populations. ORDR supports a number of programs and activities to address these needs.

- *The Rare Diseases Clinical Research Network (RDCRN)*

The RDCRN is an innovative international clinical studies network led by ORDR in collaboration with eight other NIH institutes. The RDCRN consists of 17 separate consortia that are working with 90 patient advocacy groups and currently studies 200 rare diseases in natural history and clinical studies at 167 clinical centers. 56 of the enrolling clinical centers are located internationally. Since August 2009, 10 studies have completed accrual and are in the final analysis phase. A total of 11,624 participants have been enrolled since the start of the second grant cycle. From August 2009 to September 24, 2012, the network activated 67 multi-site clinical research studies and 130 new investigators have been trained through the RDCRN training program. 77 clinical studies are actively accruing.

- *The Genetic and Rare Diseases Information Center (GARD)*

GARD was established in 2002 by ORDR and the National Human Genome Research Institute (NHGRI) to help people find useful information about genetic and rare diseases in English and Spanish. GARD helps patients and their families to find information on a genetic or rare disease in a number of ways: On the GARD Web site, by e-mail or Web inquiry, by telephone or by mail, or TTY. Each month, there are approximately 185,000 visits to the GARD Web pages. GARD has received 77% of inquiries from the United States and 13% from international sources. Inquiries have been received for more than 5,400 separate diseases.

- *Global Rare Diseases Patient Registry (GRDR) and Rare Diseases-HUB for Biospecimens (RD-HUB)*

The GRDR aims to enable aggregation of de-identified patient data from various rare disease registries, using standardized vocabulary, Common Data Elements (CDEs), and controlled libraries of disease questions. The aggregated data will be made available to investigators to facilitate research within and across rare diseases. ORDR has developed a set of CDEs to assist <u>any</u> patient advocacy group to establish a patient registry and a template for informed consent for participating patients. A key for any disease research is a source of bio-specimens, which are materials taken from the human body (e.g. tissue, blood plasma, urine) that are stored for research purposes. A portal to locate bio-repositories for rare diseases such as the RD-HUB will help identify needed specimens for researchers

Program Portrait: The Therapeutics for Rare and Neglected Disease (TRND) Program: Potential Treatment for Sickle Cell Disease Project

FY 2012 Level: $23.96 Million
FY 2014 Level: $27.75 Million
Change: +$3.79 Million

Sickle cell disease (SCD) is a recessive, genetic blood disorder affecting red blood cells. Red blood cells contain hemoglobin, a protein that helps the cells carry oxygen through the body. Patients with SCD have an abnormal form of hemoglobin that causes the red blood cells to take on a rigid, sickle shape. These rigid cells can block small blood vessels, causing decreased blood flow, inflammation, pain, and strokes. This can result in significant and permanent damage to tissues and can be fatal. SCD presents in childhood and affects millions of people worldwide. In the United States, SCD affects approximately 80,000 patients, and occurs in one of every 500 African-American births.

The novel compound Aes-103 is the first drug candidate to directly target the underlying molecular cause of SCD, the abnormal hemoglobin protein. This project seeks to develop Aes-103 as an effective treatment for both adults and children with SCD. In less than a year of signing the collaborative agreement between TRND and AesRx, all pre-clinical toxicology, chemistry, manufacturing and controls, and regulatory studies necessary to support an Investigational New Drug (IND) application with FDA were completed, and the IND was filed. Aes-103 was moved into Phase I clinical trials in both healthy volunteers and SCD patients. TRND has established a project team that includes TRND staff, AesRx, and a leading sickle cell clinical researcher from the National Heart, Lung, and Blood Institute (NHLBI). After TRND became involved with this project, AesRx was able to obtain a Massachusetts Life Science Accelerator Grant, which provided support for additional studies necessary to complete clinical development of Aes-103.

Budget Policy: The FY 2014 President's Budget request is $42.455 million, an increase of $3.790 million, or 9.8 percent above the FY 2012 Actual 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 is $27.745 million for the TRND program and $14.710 million for the ORDR.

(3) Re-engineering Translational Sciences

- *Bridging Interventional Development Gaps*

The Bridging Interventional Development Gaps (BrIDGs) program makes available, on a competitive basis, certain critical resources needed for the development of new therapeutic agents. Investigators do not receive grant funds through this program. Instead, successful applicants receive access to NIH contractors who are experts in conducting preclinical studies, which are necessary for any compound to be considered for future trials in humans. In general, synthesis, formulation, pharmacokinetic, and toxicology services in support of investigator-held Investigational New Drug (IND) applications to the FDA are available.
This program has been successful in demonstrating the power of data to derisk therapeutics development. BrIDGs has completed 19 projects since its inception, 12 of these have successfully filed INDs or clinical trials agreements and 8 projects are in clinical development currently. During or after involvement with the BrIDGs program five therapeutics have been licensed from the principle investigator, providing additional funding to support further development of these treatments.

- *The NIH Molecular Libraries Probe Production Centers Network (MLPCN)*

The MLPCN is a network of national laboratories, whose aim is to generate novel small molecule probes by performing high throughput screening, secondary screens, and medicinal chemistry. The assays for these probes are sourced from the scientific community. The NIH Chemical Genomics Center (NCGC) is one of the centers in the MLPCN. Through this program, extramural and intramural biomedical researchers gain access to the collaborative assay development, large-scale small molecule screening, informatics, and medicinal chemistry necessary to identify chemical probes which are used both to validate new drug targets and to initiate new drug development programs. All of the NCGC's projects are highly collaborative and interactive. The NCGC's portfolio currently consists of over 200 collaborations with external scientists throughout the U.S. in every area of biology and disease, with projects spanning from rare and neglected diseases to basic research in study of novel proteins. NCATS scientists also develop new technologies for high-throughput assay development and screening, informatics and modeling, and analytical and medicinal chemistry, to increase the efficiency of the probe development process.

In FY 2012, as part of the MLPCN, the NCGC began developing a chemical informatics (cheminformatics) platform called the BioAssay Research Database (BARD). When completed in FY 2013, BARD will allow researchers around the world to access and ask research questions using the chemical and biological data produced over the ten years of the NIH Molecular Libraries Program. This will be the world's largest collection of information on the pharmaceutical and biological activities of chemical compounds, and will be invaluable for the research community, public and private, in their translational programs. Given the importance of this resource for advancing translational science, NCATS plans to continue the development of BARD as an open-source platform, and maintain and continuously improve it with new data deposited from the research community.

The Molecular Libraries Small Molecule Repository (MLSMR) is a chemical library containing 350,000+ small molecule compounds. The MLSMR was created as part of the MLPCN program, and is a gold-standard collection of diverse and analytically verified compounds which is the product of ten years of NIH effort. The collection has been tested in over 500 diverse assays as part of the Molecular Libraries program, all the data from which are in BARD, making these by far the best studied chemicals in the world, and therefore an unmatched resource for translational discovery. NCATS intends to continue support of this large compound library, in order to acquire, purify, manage and disseminate the compounds to researchers throughout the country to empower their translational science.

Program Portrait: Toxicology in the 21st Century

FY 2012 Level: $5.0 Million
FY 2014 Level: $5.0 Million
Change: +$0.0 Million

The Toxicology in the 21st Century (Tox21) program, a cross-agency collaboration involving the NIH (NIEHS and NCATS), EPA, and FDA, is aimed at developing better ways to assess the potential toxicity of drugs and environmental chemicals. To accomplish this goal, Tox21 is testing 10,000 different chemicals for their ability to disrupt biological processes that may lead to adverse health effects. A major part of Tox21 is the robotic screening and informatics platform at NCATS that uses fast, completely automated robotic screening to test thousands of chemicals each day for toxic effects on cells. Computational analysis of the effects of the thousands of chemicals in hundreds of different cell types and biological pathways is allowing Tox21 to create predictive algorithms that will be used to refine, and ultimately replace, animal testing. This promises to revolutionize both hazard assessment of environmental chemicals, and development of new drugs, since unpredicted drug toxicity is one of the primary reasons programs to develop new drugs fail.

- *The Small Business Innovation Research and Small Business Technology Transfer Programs*

The Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs are resources for small businesses to further expand upon the NCATS' mission of catalyzing "the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions." Since the main goal of the SBIR/STTR programs is to develop and commercialize novel technologies and products, NCATS' goal is to develop specialized SBIR/STTR funding announcements and contract topics that will assist in the in the development of innovative tools, technologies, and intervention platforms that would support the creation of novel therapeutics and/or diagnostics. NCATS has convened an internal work group with representation from across all its divisions to determine how this unique program can be used more effective and efficiently.

Budget Policy: The FY 2014 President's Budget request is $46.614 million, an increase of $31.340 million, or 205.2 percent above the FY 2012 Actual level. This increase reflects direct funding of the MLPCN which was formerly funded by the NIH Common Fund. The increase also reflects the increased proportion of research funding that is statutorily set-aside for Small Business Innovation Research.

(4) Cures Acceleration Network: An Innovation in Scientific Discovery Support

The Cures Acceleration Network (CAN) was authorized by Congress to advance the development of high need cures and reduce significant barriers between research discovery and clinical trials. To achieve these objectives, CAN provides NCATS with new flexibilities in its funding authorities. Under CAN, NCATS 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 using the special funding mechanism called other transactions authority (OTA), which allows

projects to be actively and aggressively managed by using mechanisms similar to those used by the Defense Advanced Research Projects Agency (DARPA) at the U.S. Department of Defense.

At the request of Congress, NCATS contracted with the Institute of Medicine to explore the authorities provided through the Cures Acceleration Network. On June 4-5, 2012, the IOM Forum on Drug Discovery, Development, and Translation held a workshop which discussed approaches and strategies to accelerating translational science using the authorities provided through CAN, including flexible research authority and matching grant authority. The workshop also discussed promising models for public-private collaborations that could be strengthened or facilitated by activities under CAN and identified barriers and potential solutions to facilitate coordination of activities under CAN with the FDA regulatory review process and timelines. The workshop summary was delivered to the CAN Review Board and will help guide NCATS as it works to accelerate the development of treatments and cures.

- *Tissue Chips for Drug Screening*

To help streamline the therapeutic development pipeline, NCATS, in collaboration with the DARPA and the FDA, is leading an initiative to improve the process for predicting whether drugs will be safe in humans. This initiative, which marks the first interagency collaboration launched by NCATS, aims to develop 3-D human tissue "chips" (i.e., microfluidic systems) that accurately model the structure and function of human organs, such as the lung, liver, and heart. Once developed, researchers can use these models to predict whether a candidate drug, vaccine or biologic agent is safe or toxic in humans in a faster and more cost-effective way than current methods.

While individual organ chips are already being used in some areas, this project intends to dramatically improve upon existing test measures – cell cultures, human and animal testing – and overcome the limits of individual organ chips by combining organs on a single chip, to emulate the entire human body, in addition to designing software that can control and analyze different functions.

- *Discovering New Therapeutic Uses for Existing Molecules: Rescuing and Repurposing Drugs*

Developing a brand-new drug takes an enormous amount of time, money, and effort, mainly because of bottlenecks in the drug discovery process. To help combat these challenges, NCATS launched the Discovering New Therapeutic Uses for Existing Molecules program. It is a collaborative pilot program designed to develop partnerships between pharmaceutical companies and the biomedical research community to advance therapeutic development. This innovative program matches researchers with a selection of molecular compounds from industry to test ideas for new therapeutic uses, with the ultimate goal of identifying promising new treatments for patients. NCATS has collaborated with eight companies, including Abbott, AstraZeneca, Bristol-Myers Squibb Company, Eli Lilly and Company, GlaxoSmithKline, Janssen Pharmaceutical Research & Development, L.L.C., Pfizer, and Sanofi. Collectively, these companies have made 58 of these compounds available for the pilot program. The compounds have undergone significant research and development by industry, including safety testing in

humans, providing a strong starting point for scientists and permitting the process to move more rapidly. Through the Therapeutics Discovery program, NCATS is re-engineering the way the various sectors collaborate. Not only does the program seek to match novel scientific ideas to existing compounds, but it also provides template agreements, reducing the negotiation time that could otherwise delay the research.

Budget Policy: The FY 2014 President's Budget request is $50.0 million, an increase of $40.111 million, or 405.6 percent above the FY 2012 Actual level, which was the first year of CAN funding. Funding for this program will be used to support the Tissue Chip for Drug Screening initiative and the Discovering New Therapeutics for Existing Molecules program, formerly funded by the NIH Common Fund. Funds will also be increased to support other CAN directed programs, including those described above.

(5) Translational Research Resources (TRR)

The TRR program funds specialized support programs and initiatives that provide support to NIH researchers. Additionally, TRR manages and administers NCATS portion of the NIH Extramural Loan Repayment Program (LRP). Through repayment of their student loans, health care professionals are better positioned to further their research careers. NCATS is especially interested in supporting activities that improve the quality, validity, generalizability, and efficiency of clinical and translational research. The overall purpose of the LRP is the recruitment and retention of highly qualified health professionals as research investigators.

Budget Policy: The FY 2014 President's Budget estimate is $29.432 million, an increase of $10.704 million, or 57.2 percent above the FY 2012 Actual level. This level will provide for NCATS increased share of trans-NIH programs and initiatives that support the entire spectrum of biomedical research.

(6) Research Management and Support

The NCATS RMS activities provide administrative, budgetary, logistical, and scientific support in the review, award, and monitoring of research grants, training awards, and research and development contracts.

Budget Policy: In FY 2014, NCATS's request provides $34.684 million for RMS, an increase of $4.338 million or 14.3 percent from the FY 2012 level. These resources will be used to support the above activities, and to promote sound stewardship of our resources.

NATIONAL INSTITUTES OF HEALTH
National Center for Advancing Translational Sciences

Budget Authority by Object Class
(Dollars in Thousands)

	FY 2012 Actual	FY 2014 PB	Increase or Decrease
Total compensable workyears:			
Full-time employment	118	122	4
Full-time equivalent of overtime and holiday hours	0	0	0
Average ES salary (in whole dollars)	$0	$155,500	$155,500
Average GM/GS grade	12.8	12.6	(0.2)
Average GM/GS salary (in whole dollars)	$110,930	$108,760	($2,170)
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207) (in whole dollars)	$128,621	$130,807	$2,186
Average salary of ungraded positions (in whole dollars)	$146,358	$149,285	$2,927

	OBJECT CLASSES	FY 2012 Actual	FY 2014 PB	Increase or Decrease
	Personnel Compensation:			
11.1	Full-time permanent	$7,890	$8,777	$887
11.3	Other than full-time permanent	2,903	6,409	3,506
11.5	Other personnel compensation	287	363	76
11.7	Military personnel	288	331	43
11.8	Special personnel services payments	516	1,296	780
	Total, Personnel Compensation	**$11,883**	**$17,176**	**$5,293**
12.0	Personnel benefits	$2,968	$3,874	$906
12.2	Military personnel benefits	357	404	47
13.0	Benefits for former personnel	0	0	0
	Subtotal, Pay Costs	**$15,209**	**$21,454**	**$6,245**
21.0	Travel and transportation of persons	$291	$291	($0)
22.0	Transportation of things	70	70	(0)
23.1	Rental payments to GSA	9	9	0
23.2	Rental payments to others	1	1	(0)
23.3	Communications, utilities and miscellaneous charges	226	226	0
24.0	Printing and reproduction	10	11	1
25.1	Consulting services	1,130	1,482	352
25.2	Other services	24,970	25,041	71
25.3	Purchase of goods and services from government accounts	28,477	39,866	11,389
25.4	Operation and maintenance of facilities	303	303	0
25.5	Research and development contracts	3,794	28,489	24,695
25.6	Medical care	202	202	0
25.7	Operation and maintenance of equipment	134	134	(0)
25.8	Subsistence and support of persons	0	0	0
25.0	**Subtotal, Other Contractual Services**	**$59,010**	**$95,517**	**$36,507**
26.0	Supplies and materials	$1,319	$1,319	$0
31.0	Equipment	738	3,938	3,200
32.0	Land and structures	0	0	0
33.0	Investments and loans	0	0	0
41.0	Grants, subsidies and contributions	497,413	542,852	45,439
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	**$559,088**	**$644,234**	**$85,146**
	Total Budget Authority by Object Class	**$574,297**	**$665,688**	**$91,391**

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

NATIONAL INSTITUTES OF HEALTH
National Center for Advancing Translational Sciences

Salaries and Expenses
(Dollars in Thousands)

OBJECT CLASSES	FY 2012 Actual	FY 2014 PB	Increase or Decrease
Personnel Compensation:			
Full-time permanent (11.1)	$7,890	$8,777	$887
Other than full-time permanent (11.3)	2,903	6,409	3,506
Other personnel compensation (11.5)	287	363	76
Military personnel (11.7)	288	331	43
Special personnel services payments (11.8)	516	1,296	780
Total Personnel Compensation (11.9)	**$11,884**	**$17,176**	**$5,292**
Civilian personnel benefits (12.1)	$2,968	$3,874	$906
Military personnel benefits (12.2)	357	404	47
Benefits to former personnel (13.0)	0	0	0
Subtotal, Pay Costs	**$15,209**	**$21,454**	**$6,245**
Travel (21.0)	$291	$291	$0
Transportation of things (22.0)	70	70	0
Rental payments to others (23.2)	1	1	0
Communications, utilities and miscellaneous charges (23.3)	226	226	0
Printing and reproduction (24.0)	10	11	1
Other Contractual Services:			
Advisory and assistance services (25.1)	1,130	1,482	352
Other services (25.2)	24,970	25,041	71
Purchases from government accounts (25.3)	10,338	15,815	5,477
Operation and maintenance of facilities (25.4)	303	303	0
Operation and maintenance of equipment (25.7)	134	134	0
Subsistence and support of persons (25.8)	0	0	0
Subtotal Other Contractual Services	**$36,875**	**$42,775**	**$5,900**
Supplies and materials (26.0)	$1,310	$1,310	$0
Subtotal, Non-Pay Costs	$38,783	$44,684	$5,901
Total, Administrative Costs	**$53,992**	**$66,138**	**$12,146**

NATIONAL INSTITUTES OF HEALTH
National Center for Advancing Translational Sciences

Details of Full-Time Equivalent Employment (FTEs)

OFFICE/DIVISION	FY 2012 Actual			FY 2013 CR			FY 2014 PB		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Office of the Director									
Direct:	4	-	4	4	-	4	4	-	4
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	4	-	4	4	-	4	4	-	4
Executive Office									
Direct:	19	-	19	19	-	19	19	-	19
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	19	-	19	19	-	19	19	-	19
Office of Grants Management and Scientific Review									
Direct:	13	-	13	17	-	17	27	-	27
Reimbursable:	19	-	19	19	-	19	9	-	9
Total:	32	-	32	36	-	36	36	-	36
Office of Rare Diseases Research									
Direct:	7	-	7	7	-	7	7	-	7
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	7	-	7	7	-	7	7	-	7
Office of Policy, Communications and Strategic Alliances									
Direct:	10	-	10	10	-	10	10	-	10
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	10	-	10	10	-	10	10	-	10
Division of Pre-Clinical Innovation									
Direct:	26	-	26	26	-	26	27	-	27
Reimbursable:	6	-	6	6	-	6	5	-	5
Total:	32	-	32	32	-	32	32	-	32
Division of Clinical Innovation									
Direct:	12	2	14	12	2	14	12	2	14
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	12	2	14	12	2	14	12	2	14
Total	116	2	118	120	2	122	120	2	122
Includes FTEs whose payroll obligations are supported by the NIH Common Fund. FTEs supported by funds from Cooperative Research and Development Agreements.									

FISCAL YEAR	Average GS Grade
2012	12.8
2013	12.6
2014	12.6

NATIONAL INSTITUTES OF HEALTH
National Center for Advancing Translational Sciences

Detail of Positions

GRADE	FY 2012 Actual	FY 2013 CR	FY 2014 PB
Total, ES Positions	0	1	2
Total, ES Salary	$0	$155,500	$311,000
GM/GS-15	20	19	18
GM/GS-14	26	26	26
GM/GS-13	26	26	26
GS-12	3	4	4
GS-11	2	2	2
GS-10	1	1	1
GS-9	5	5	5
GS-8	2	3	3
GS-7	3	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	91	94	93
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	0	0	0
Director Grade	1	1	1
Senior Grade	1	1	1
Full Grade	0	0	0
Senior Assistant Grade	0	0	0
Assistant Grade	0	0	0
Subtotal	2	2	2
Ungraded	47	47	47
Total permanent positions	93	97	97
Total positions, end of year	140	144	144
Total full-time equiv (FTE) at YE	118	122	122
Average ES salary	$0	$155,500	$155,500
Average GM/GS grade	12.8	12.6	12.6
Average GM/GS salary	$110,930	$108,760	$108,760

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