

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Common Fund

FY 2011 Budget	Page No.
Common Fund Mechanism Table.....	2
Common Fund by Initiative Table.....	3
Justification Narrative.....	4

NATIONAL INSTITUTES OF HEALTH

Common Fund

(Dollars in Thousands)

Budget Mechanism - Total

MECHANISM	FY 2009 Actual		FY 2009 Recovery Act Actual		FY 2010 Recovery Act Estimated		FY 2010 Enacted		FY 2011 PB		Change	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Grants:												
Research Projects:												
Noncompeting	157	\$81,671	0	\$0	26	\$32,788	214	\$114,233	257	\$145,110	43	\$30,877
Administrative supplements	(58)	6,007	(6)	1,756	(1)	25	(29)	3,000	(29)	3,000	0	0
Competing:												
Renewal	4	4,097	0	0	0	0	0	0	0	0	0	0
New	221	173,407	47	60,865	14	30,978	222	178,946	224	184,449	2	5,503
Supplements	0	0	1	201	0	0	0	0	0	0	0	0
Subtotal, competing	225	177,504	48	61,066	14	30,978	222	178,946	224	184,449	2	5,503
Subtotal, RPGs	382	265,182	48	62,822	40	63,791	436	296,179	481	332,559	45	36,380
SBIR/STTR	0	0	0	0	0	0	0	0	0	0	0	0
Subtotal, RPGs	382	265,182	48	62,822	40	63,791	436	296,179	481	332,559	45	36,380
Research Centers:												
Specialized/comprehensive	38	129,884	3	5,471	2	4,753	36	115,822	37	119,297	1	3,475
Clinical research	9	6,786	0	0	0	0	9	6,603	9	6,801	0	198
Biotechnology	18	6,667	0	0	0	0	21	7,556	22	7,783	1	227
Comparative medicine	0	0	0	0	0	0	0	0	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0	0	0	0	0
Subtotal, Centers	65	143,337	3	5,471	2	4,753	66	129,981	68	133,881	2	3,900
Other Research:												
Research careers	48	49,580	0	0	0	0	28	25,382	11	10,191	(17)	-15,191
Cancer education	0	0	0	0	0	0	0	0	0	0	0	0
Cooperative clinical research	0	0	0	0	0	0	0	0	0	0	0	0
Biomedical research support	0	0	0	0	0	0	0	0	0	0	0	0
Minority biomedical research support	0	0	0	0	0	0	0	0	0	0	0	0
Other	19	26,066	0	0	0	0	11	20,703	14	26,182	3	5,479
Subtotal, Other Research	67	75,646	0	0	0	0	39	46,085	25	36,373	(14)	-9,712
Total Research Grants	514	484,165	51	68,293	42	68,544	541	472,245	574	502,813	33	30,568
Research Training:	<u>FTEs</u>		<u>FTEs</u>		<u>FTEs</u>		<u>FTEs</u>		<u>FTEs</u>			
Individual awards	0	0	0	0	0	0	0	0	0	0	0	0
Institutional awards	405	14,046	0	0	0	0	328	13,224	236	9,907	(92)	-3,317
Total, Training	405	14,046	0	0	0	0	328	13,224	236	9,907	(92)	-3,317
Research & development contracts (SBIR/STTR)	0	10,219	0	0	0	0	0	25,419	0	14,419	0	-11,000
	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Intramural research	<u>FTEs</u>		<u>FTEs</u>		<u>FTEs</u>		<u>FTEs</u>		<u>FTEs</u>		<u>FTEs</u>	
Intramural research	0	21,478	0	0	0	0	0	21,800	0	22,498	0	698
Research management and support	0	11,225	0	0	0	0	0	11,421	0	11,992	0	571
Construction	0	0	0	0	0	0	0	0	0	0	0	0
Buildings and Facilities	0	0	0	0	0	0	0	0	0	0	0	0
Total, Common Fund	0	541,133	0	68,293	0	68,544	0	544,109	0	561,629	0	17,520

**NATIONAL INSTITUTES OF HEALTH
Common Fund by Initiative**
(Dollars in Thousands)

Title of Initiative	FY 2009 Actual (B.A.)	FY 2010 Enacted	FY 2011 PB	Change
Molecular Libraries and Imaging				
Creation of NIH Bioactive Small Molecule Library & Screening	\$86,667	\$80,200	\$80,700	\$500
Cheminformatics	4,100	4,100	3,900	-200
Technology Development	17,870	22,000	18,000	-4,000
Development of High-Specificity/High-Sensitivity Imaging	0	0	0	0
Imaging Probe Database	700	700	500	-200
Core Synthesis Facility to Produce Imaging Probes	3,000	0	0	0
Subtotal, Molecular Libraries and Imaging	112,337	107,000	103,100	-3,900
Building Blocks, Biological Pathways and Networks				
National Technology Centers & Metabolomics Development	11,851	11,600	10,281	-1,319
Metabolomics Technology Development	0	0	0	0
Subtotal, Building Blocks, Biological Pathways and Networks	11,851	11,600	10,281	-1,319
Structural Biology				
Membrane Protein Production	10,698	10,000	8,000	-2,000
Bioinformatics and Computational Biology				
National Centers for Biomedical Computing	26,578	24,500	19,700	-4,800
Nanomedicine				
Nanomedicine Development Centers	25,000	25,000	16,000	-9,000
Human Microbiome				
Sequence a Reference Set of Genomes	16,248	12,523	2,200	-10,323
Demonstration Projects	13,576	8,733	8,093	-640
New Tools and Technologies for Metagenomic Analyses	6,040	10,000	8,000	-2,000
Data Coordination	2,498	2,236	2,118	-118
Resource Repository for Materials & Reagents	400	400	400	0
ELSI Studies Unique to HMP	625	500	500	0
HMP Workshops	0	635	635	0
Subtotal, Human Microbiome	39,387	35,027	21,946	-13,081
Epigenomics				
Mapping Centers	10,040	10,000	10,000	0
Human Health and Disease	4,157	8,000	4,000	-4,000
Data Management Center for the Mapping Centers	3,093	3,000	3,000	0
Technology Development in Epigenetics	3,899	7,000	7,000	0
NIH International Committee on Epigenomics (NICE)	0	0	0	0
Discovery of Novel Epigenetic Marks in Mammalian Cells	3,688	4,000	0	-4,000
Subtotal, Epigenomics	24,877	32,000	24,000	-8,000
Genotype-Tissue Expression (GTEx) Resources				
Genotype-Tissue Expression (GTEx) Resources	0	11,127	2,499	-8,628
Interdisciplinary Research				
Interdisciplinary Research Centers	43,118	39,563	39,563	0
Interdisciplinary Research Training Initiative	1,839	0	0	0
Innovation in Interdisciplinary Technology and Methods	2,939	2,968	0	-2,968
Subtotal, Interdisciplinary Research	47,896	42,531	39,563	-2,968
High-risk Research				
NIH Director's Pioneer Awards	35,404	40,600	40,600	0
NIH Director's New Innovator Awards	99,514	80,000	80,000	0
Transformative R01's	29,074	70,000	75,000	5,000
Subtotal, High-Risk Research	163,992	190,600	195,600	5,000
Public-Private Partnerships				
Public-Private Partnerships	592	0	0	0
Re-engineering the Clinical Research Enterprise				
Clinical Research Policy Analysis and Coordination	1,930	0	0	0
Feasibility of Integrating and Expanding Clinical Research Networks	0	0	0	0
Translational Research Core Services	2,659	8,000	5,000	-3,000
Dynamic Assessment of Patient-Reported Chronic Disease Outcomes	11,069	8,190	8,190	0
Enhance Clinical Research Training via the National Multi-disciplinary CR Career Development Program and CRTP and MSTP Expansions	8,741	1,100	880	-220
Clinical and Translational Science Awards	53,224	25,245	22,703	-2,542
Subtotal, Re-engineering the Clinical Research Enterprise	77,623	42,535	36,773	-5,762
Strategic Planning Funds	302	5,463	5,463	0
Subtotal Common Fund	541,133	537,383	482,925	-54,458
New Initiatives in Common Fund	0	6,726	78,704	71,978
Total Common Fund	541,133	544,109	561,629	17,520

**Office of the Director
Justification
Common Fund**

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

	FY 2009	FY 2010	FY 2011	FY 2011+/- FY 2010
	<u>Appropriation</u>	<u>Appropriation</u>	<u>PB</u>	<u>Decrease</u>
Budget Authority	\$541,133,00	\$544,109,000	\$561,629,000	\$17,520,000
FTE	0	0	0	0

This document provides justification for the Fiscal Year (FY) 2011 activities of the National Institutes of Health Common Fund, including HIV/AIDS activities. Details of the FY 2011 HIV/AIDS activities are in the "Office of AIDS Research (OAR)" Section of the Overview. Details on the Common Fund are located in the Overview, Volume One. Program funds are allocated as follows: Competitive Grants/Cooperative Agreements; Contracts; Direct Federal/Intramural and Other.

The Common Fund received \$136.837 million through the American Recovery and Reinvestment Act, of which \$68.293 million has been obligated in FY 2009, and an additional \$68.544 million will be obligated in FY 2010. These funds are being used to create jobs, stimulate the economy, and accelerate research to further our understanding of the molecular basis of human health and disease, fuel health care reform through by identification of potential drug targets and development of cell-based therapies, and increase the efficacy of K-12 science education in America.

Overview

The NIH Common Fund was codified in the 2006 NIH Reform Act. The Act calls for the Common Fund to support important areas of emerging scientific opportunities, rising public health challenges, or knowledge gaps that deserve special emphasis and would benefit from conducting or supporting additional research that involves collaboration between two or more national research institutes or national centers, or would otherwise benefit from strategic coordination and planning. The Common Fund supports programs that test new ways of fostering innovation, develop tools, data sets, and technologies that will be broadly stimulatory, and develop resources that will enhance research supported by the Institutes and Centers (ICs). These programs are designed to be transiently funded by the Common Fund for 5-10 years, either because the new funding mechanisms have been tested and can be adapted by the ICs, the tools and technologies have been developed and are ready to be deployed through IC-supported research, or the resources have proven themselves useful and can therefore move to

the ICs for continued support, The transient nature of Common Fund programs also allows the Common Fund to continually respond to emerging opportunities and challenges through the development of new programs.

With the first programs funded beginning in FY 2004, Common Fund programs are beginning to revolve. Two programs that were intended to enable NIH as a whole to be better coordinated with other entities have transitioned to the Office of the Director for continued support: the Public Private Partnership Program and the Clinical Research Policy Analysis and Coordination Program. The Interdisciplinary Research training initiative which piloted a novel award type specifically designed to foster interdisciplinary approaches ended in FY 2009, but the NIH Neuroscience Blueprint has adopted the use of this training mechanism. The Interdisciplinary Research Technology Development awards end in FY 2010; the tools developed are expected to be used by IC-funded investigators in a variety of awards, but the tool-development projects themselves are not expected to continue. Similarly, the Discovery of Novel Marks initiative within the Epigenomics Program will end in FY 2010 with data obtained expected to stimulate IC-funded projects from several ICs. Finally, the Imaging Probe Development Center, developed within the Molecular Libraries and Imaging Program, will transition to multi-IC funding within the NIH Intramural Program in FY 2011 since it has proven to be a useful trans-NIH resource.

Several Common Fund programs focus on using emerging technologies in molecular biology to understand human biology and disease. The Human Microbiome Program is developing and applying high throughput genomics and computational approaches to generate a reference set of genomes from the micro-organisms that inhabit various organs of the human body, the so-called human microbiome. These efforts will accelerate our understanding of the relationship between the human Microbiome and health and disease. Similarly, the Epigenomics program is developing reference data pertaining to the human epigenome - the entire set of chemical and structural modifications to DNA that, although not inherited, determine which genes are active in a given cell type. These modifications can have profound effects on health and disease. In yet another example, the Genotype-Tissue Expression (GTEx) project is using high throughput genetic and genomic approaches to develop a set of reference gene expression profiles for specific human tissues that will greatly enhance our ability to characterize the genetic variation that underlies specific diseases.

The use of discoveries in basic science to develop new and better treatments is also a focus of several Common Fund programs. The Molecular Libraries and Imaging program, for example, is feeding the drug development pipeline by identifying small molecules that may serve as targets for new disease therapies. The NIH Rapid Access to Intervention Development (RAID) program is providing public sector researchers and small businesses with much needed resources to speed up the analysis, synthesis and formulation of potentially beneficial molecules. The Clinical and Translational Science Awards (CTSAs) foster clinical research translation and training to effectively shorten the path from science discovery to effective treatments.

Health care reform will be a key topic of strategic planning in 2010. A workshop will be held with leading health economists to articulate research questions that NIH should address pertaining to the impact of health care reform. Projects funded through the High Risk/High Reward initiatives are also relevant to health care reform, as they will enable movement toward personalized medicine. For example, projects are identifying and validating new genetic and molecular markers that may one day be able to predict individual's susceptibility to cancer, the likelihood a cancer will metastasize, and the likelihood the cancer will be resistant to chemotherapy.

The 2010 strategic planning efforts will also consider global health concerns. The NIH is surveying the public and private landscape for pressing needs and opportunities that might not be addressed except through Common Fund support. Issues pertinent to global health are also being addressed through existing Common Fund programs, including Molecular Libraries, and the High Risk/High Reward initiatives. Several projects in the High Risk-High Reward program are employing new approaches to the diagnosis and treatment of challenging and complex global diseases such as malaria, tuberculosis, and HIV/AIDS. New therapeutic treatments and technologies that can be deployed in resource-limited areas and with limited training are being developed. Research to define the underlying host- and strain-specific risk factors for multiple strain tuberculosis and to develop new molecular biomarkers for the diagnosis of tuberculosis based on bacterial burden in animals are being pursued to strengthen our ability to develop better diagnostics and treatments for these devastating illnesses.

Three High Risk/High Reward initiatives launched by the NIH Director through the Common Fund - the Transformative Research Project (TR01) awards, the Pioneer awards, and the New Innovator awards - represent a unique approach to stimulate exceptionally innovative ideas and individuals. These awards are allowing creative investigators to define their own innovative, high-risk, original, and unconventional research topics, and provide adequate resources to pursue them.

Major Changes in the Fiscal Year 2011 Budget Request

Major changes by budget mechanism and/or budget activity detail are briefly described below. Note that there may be overlap between budget mechanism and activity detail; d these highlights will not sum to the total change for the FY 2011 budget request for the NIH Common Fund, which is \$17.520 million more than the FY 2010 Enacted level, for a total of \$561.629 million.

Research Project Grants (+\$36.380 million, total \$332.559 million)

The NIH Common Fund expects to support a total of 481 Research Project Grant (RPG) awards in FY 2011. Noncompeting RPGs will increase by 43 awards and increase by \$30.877 million. Competing RPGs will increase by 2 awards and increase by \$5.503 million. The NIH Budget policy for RPGs in FY 2011 includes a 2.0 percent inflationary increase in noncompeting awards and for the average costs in competing grants.

Research Centers (+\$3.900 million, total \$133.881 million)

The NIH Common Fund plans to support a total of 68 Research Center Awards in FY 2011. The increase in number and amount provides flexibility to the NIH Director in funding new FY 2011 Common Fund initiatives.

Research Careers (-\$15.191 million, total \$10.191 million)

The level of funding provided to the Clinical and Translational Science Awards (CTSAs) continues to transition from the NIH Common Fund to the NCRR. This transition reduces the estimated Common Fund activity in Research Careers.

Other Research, Other (+\$5.479 million, total \$26.182 million)

The requested level of funding allows the Common Fund to maintain use of \$25.000 million in Flexibility Research Authority (FRA) and fund existing FY 2011 commitments. \$16.000 million of the FRA will be used in FY2011 to fund ongoing projects within the Nanomedicine program. In addition, \$9.000 million are requested to use as needed for New Programs to be developed. These funds provide a great deal of flexibility for application and review so will allow the NIH Director to respond rapidly to emerging needs and opportunities.

Institutional Training Awards (-\$3.317 million, total \$9.907 million)

The requested level of funding reflects the FY 2011 estimated Common Fund commitments to ongoing Institutional Training Awards and includes the NIH policy allowing a 6 percent stipend increase for the Ruth L. Kirschstein National Research Service Training Awards.

Research and Development Contracts (-\$11.000 million, total \$14.419 million)

The requested level of funding reflects the expiration of the pilot phase of the Genotype-Tissue Expression (GTEx) initiative.

FY 2011 Justification

Highlights and Progress of the NIH Common Fund Areas

Molecular Libraries and Imaging

The pharmaceutical industry has for years used a process known as high-throughput screening (HTS) to identify new small molecule probes that can be used for drug development and to study biological processes involved in disease. Prior to the launch of the Molecular Libraries and Imaging Program, HTS capabilities were not available to academic researchers. This program provides public sector, biomedical researchers much needed access to HTS approaches to develop small molecule probes. Data about the structure and function of the probes are deposited in a free, online public database called PubChem (<http://pubchem.ncbi.nlm.nih.gov/>), which was designed and implemented by the Molecular Libraries and Imaging program. The program has developed over 100 probes that are revealing new insights into biology and identifying new leads for drug development. In FY 2011, the program investigators will expand the size and diversity of the small molecule probe collection and identify at least 40 new probes from assays provided by the scientific community. The PubChem database will expand from 40 million compounds and 60,000 weekly users.

Budget Policy: The FY 2011 budget estimate of \$103.100 million for this program represents a decrease of \$3.900 million or 3.6 percent less than the FY 2010 Enacted level. A reduction in technology development commitments influences the estimated decrease.

Building Blocks, Pathways, and Networks

The basic building blocks of the human body, from individual genes to entire organs, work together to promote normal development and sustain health. This amazing feature of biological systems is accomplished mainly through ever-changing relationships between the proteins that make up biological pathways. Understanding how these pathways are interconnected and maintained, how they can become disturbed, and what might be done to restore disturbed pathways to their normal functions is key to understanding health and disease. Although scientists can currently study interactions between proteins within cells, their ability to do this is equivalent to taking a snapshot - looking at a single, isolated moment in time. The National Technology Centers for Networks and Pathways (TCNP) program supports the development of new technologies to help researchers view dynamic events, such as protein-protein interactions, in cells to better understand these processes work under normal conditions and in disease. The centers serve as an important overall resource for NIH-supported investigators by promoting collaboration amongst biomedical researchers and speeding the transfer of new technologies to other laboratories.

Budget Policy: The FY 2011 budget estimate of \$10.281 million for this program represents a decrease of \$1.319 million or 11.4 percent less than the FY 2010 Enacted level.

FY 2011 funds will be used for continued development of new technology and dissemination of these research tools at the TCNPs, although it is estimated to be at a reduced level.

Structural Biology

The overall structure and health of a cell are maintained by an important class of proteins called membrane-bound proteins. Understanding how membrane-bound proteins function is key to understanding human biology and how biological processes are altered in disease and can be targeted in treatment. In order to understand better how membrane-bound proteins function, however, one needs to produce sufficient quantities for study in a laboratory setting. This is very difficult and is frequently the main roadblock in any experiment using membrane proteins. The Structural Biology initiatives aim to create new methods and approaches for producing membrane-bound proteins in sufficient quantity and quality for use in research studies. The ability to produce membrane-bound proteins to meet this need has led to major breakthroughs in biological sciences and disease research. In FY 2009, the Structural Biology Centers began a second five-year phase of support through the Common Fund. While the first five years of the program led to major breakthroughs in the ability to produce and analyze membrane proteins, it revealed that this class of proteins is highly variable - methods that work for one protein seem unlikely to work for many. Therefore, the second five years of this program are intended to discover unifying principles so that membrane proteins may be more broadly studied.

Budget Policy: The FY 2011 budget estimate of \$8.000 million for this program represents a decrease of \$2.000 million or 20.0 percent less than the FY 2010 Enacted level. Since this program is maturing and its utility with respect to individual diseases has become apparent, it is anticipated that the NIH Institutes will provide additional support. Funding will be used to continue the ground-breaking work ongoing within the Structural Biology Centers and support a series of investigator-initiated projects aimed at developing innovative methods for membrane protein production. It is expected that such methods will speed the rate of membrane protein structure determination and accelerate research in this field.

Bioinformatics and Computational Biology

In an age where the ability to manage and organize large amounts of varied biomedical data is necessary for research, the need for informatics tools is critical. These tools must be tailored to handle the large amounts of data and use engineering systems that are adapted to handle the type of data that are generated from studies of biological systems. The Bioinformatics and Computational Biology program, which supports the National Centers for Biomedical Computing (NCBCs), was funded beginning in 2003-2004 and has completed its first phase of funding through the Common Fund. The first phase established the utility of a network of integrated centers that collectively address a broad range of biological problems that revolve as the tools are developed. In the second phase of the program, the network of centers will gradually transition to NIH's Institutes and Centers (ICs) support. The Centers will function as core resources for the development of novel software and computational tools that address IC-specific problems.

Budget Policy: The FY 2011 budget estimate of \$19.700 million for this program represents a decrease of \$4.800 million or 19.6 percent less than the FY 2010 Enacted level. The decrease is consistent with the natural transition of NCBC support from the Common Fund to the ICs as described in the original NCBC plan.

Nanomedicine

Nanotechnology, the study and manipulation of molecules less than 100 nanometers in size, holds tremendous promise for use in diagnosing and treating disease. Molecules of this size have unique properties that make them suitable for interacting with and reporting on a number of biological processes involved in disease. Nanotechnology is currently being used to: deliver drugs to specific locations in the body, diagnose disease, and view inside the body through the use of imaging. The Common Fund Nanomedicine program takes things one step further. The goal of this program is to use nanotechnology to understand and manipulate biological processes in a cell for specific medical purposes. For example, nanoscale protein folding machines are being developed for the treatment of diseases such as Alzheimer's and Huntington's, where misfolded proteins are thought to play a role. In FY 2005, a network of eight Nanomedicine Centers at academic institutions across the country was established. The program underwent an extensive review in 2009 to inform the next phase, which will focus on making the nanobiological structures developed in first phase more clinically useful. The second phase of the program will constitute a more focused effort involving a smaller number of highly productive centers.

Budget Policy: The FY 2011 budget estimate of \$16.000 million for this program represents a decrease of \$9.000 million or 36.0 percent less than the FY 2010 Enacted level. It is anticipated that the centers successful in achieving respective milestones toward clinical objectives will receive continued support from both the IC whose mission aligns with the clinical objectives of the Center and the Common Fund. The ICs that contribute to the Centers during this transition phase are expected to continue support for the clinical objectives if needed after the period of Common Fund support ends. The decrease in Common Fund support is offset by an overall increase in NIH support for Nanotechnology. The continued use of Flexible Research Authority (FRA) supports this program in FY 2011.

Human Microbiome Project

Microbes such as bacteria, viruses, and fungi found naturally in the human body outnumber human cells by a factor of 100. Many of the microbes living in our bodies are beneficial whereas others cause disease. Bacteria have been implicated in conditions as diverse as asthma, cancer and obesity; yet the great majority of bacteria and viruses that reside on and in people are unidentified and uncharacterized. The Common Fund Human Microbiome Project was launched in FY 2008 to leverage advances in high throughput genomic technologies to identify and characterize approximately 600 new human microbes and to establish precedence for a definitive, causal link between certain bacteria and disease. The program is focusing on sampling microbes from several different body sites from many different individuals to determine whether there is a common set of microbes, or so-called microbiome, that is shared by all people or

whether each person has a unique microbiome. In FY 2011, the program investigators will focus on sequencing and cataloging of the microbiome samples, establishing links between the microbiome and disease, developing technologies to isolate and identify unknown microbes.

Budget Policy: The FY 2011 budget estimate of \$21.946 million for this program represents a decrease of \$13.081 million or 37.3 percent less than the FY 2010 Enacted level. Plans to complete a vast majority of the sequencing initiative in FY 2010 influence the FY 2011 level of support.

Epigenomics

Epigenetics is an expanding area of science that involves the study of changes in the control of genes activity that do not depend on the gene sequence. Some human diseases, such as cancer, are known to involve epigenetic changes; however, the role of epigenetics in other diseases is largely unknown and is difficult to study because researchers lack the tools to efficiently detect and correlate changes in the epigenome to specific diseases or health conditions. The Common Fund Epigenomics program includes a series of complementary initiatives to generate the research tools, technologies, and infrastructure needed to accelerate our understanding of the role of epigenomics in human health and disease. The Reference Epigenome Mapping Centers are developing comprehensive maps of all epigenetic changes in a specific cell type that can be used to identify epigenomic changes that underlie biology and disease, and may be targeted in new therapeutics. An Epigenomics Data Analysis and Coordination Center is developing standardized datasets from the Mapping Center studies that will be made available to the public. Two other initiatives support projects on Technology Development in Epigenetics and Discovery of Novel Epigenetic Marks in Mammalian Cells. A fourth initiative, the Epigenomics of Human Health and Disease, provides funds for investigators to determine how or whether epigenomic changes correlate with disease.

Budget Policy: The FY 2011 budget estimate of \$24.000 million for this program represents a decrease of \$8.000 million or 25.0 percent less than the FY 2010 Enacted level. The FY 2010 completion of several 2-year projects funded under the Discovery of Novel Epigenetic Marks in Mammalian Cells initiative accounts for the estimated decrease in funding.

Genotype-Tissue Expression (GTEx)

Although genome-wide studies are an effective way to identify specific genes that may be associated with a disease, many diseases involve changes in DNA that lie outside of a specific gene region, making it difficult to study them using this approach. The Genotype-Tissue Expression (GTEx) project provides the scientific community with a much-needed resource with which to study how gene activity is controlled and how DNA variation is associated with human disease. The GTEx project was initiated in FY 2010 as a two-year pilot to test the feasibility of collecting high-quality RNA and DNA from multiple tissues from approximately 160 donors identified through autopsy or organ transplant. If the pilot phase proves successful, the project will be scaled up to involve approximately 1000 donors. The project will also involve consultation and research into

the ethical, legal, and social issues raised by the research, support for new statistical methods, and creation of a database of genetic and clinical data generated by the program and obtained from other sources. The database will allow users to view and download data about possible genomic regions that correlate with human disease while providing a controlled system to ensure privacy about genetic and clinical data. The tissue repository will also serve as a resource for conducting many kinds of follow-up analyses. The program will continue into FY2011.

Budget Policy: The FY 2011 budget estimate of \$2.499 million for this program represents a decrease of \$8.628 million or 77.5 percent less than the FY 2010 Enacted level. Beginning in FY 2010, the pilot phase of the GTEx included a contract that incurs no costs in FY 2011. Support of a small grant program analyzing data generated through the contract continues in FY 2011.

Interdisciplinary Research Consortia

A major focus of the NIH Common Fund is to foster new modes of conducting research. Today, the complexities of the biological problems being examined require a range of expertise. In the past, scientists were trained in one field or technique or they focused on one type of biological system. Current biological problems and questions require that researchers access a range of techniques and expertise. This requires scientists to work with scientists whose area of expertise differs from their own. In FY 2007, the NIH awarded funds to nine Interdisciplinary Research Consortia to explore new ways to integrate different scientific disciplines to address critical health challenges. In parallel, the Interdisciplinary Research program promotes the testing of new models of trans-NIH science management by teams of NIH staff. Common Fund support of this program is currently planned to end after FY 2011, but a review of the program will inform decisions about the ongoing need for a centralized source of funds to encourage this type of research.

Budget Policy: The FY 2011 budget estimate of \$39.563 million for this program represents a decrease of \$2.968 million or 7.0 percent less than the FY 2010 Enacted level. This decrease reflects the continued natural transition of the program from the Common Fund to the ICs.

High-Risk High-Reward Investigator-Initiated Research

Research that aims to transform science is inherently difficult; if it was either obvious or easy, the need for transformation would not exist. A primary goal of the Common Fund is to provide opportunities for investigators to take risks when the potential impact is high, to think outside the box, and to try things that may not fare well in standard peer review, which relies on solid preliminary data to support proposed hypotheses. Although all of the Common Fund programs encourage risk-taking to overcome significant challenges in research, most of them involve designated funds for particular high risk objectives (such as clinical applications of nanobiology) or approaches (such as screening for new drugs or probes in the MLPCN.) However, three initiatives within the Common Fund foster innovation, risk-taking, and transformative research in any area of health research chosen by the investigators: the Pioneer Program, the New Innovator

Program, and the Transformative Research Projects (TR01) program. These initiatives represent complementary approaches to foster innovation and promote transformation.

Budget Policy: The FY 2011 budget estimate of \$195.600 million for this program represents an increase of \$5.000 million or 2.6 percent more than the FY 2010 Enacted level. The estimated increase in FY 2011 funds supports a new cadre of TR01 investigators to explore bold ideas that have the potential to catapult biomedical research and speed the translation of research findings into improved health.

Re-engineering the Clinical Research Enterprise

This program seeks to enhance the efficiency and effectiveness of clinical research. The initiatives within Re-engineering the Clinical Research Enterprise strive to transform the entire system of clinical research in order to fulfill the potential of modern medicine. These initiatives will foster the creation of new partnerships and a higher level of institutional integration in order to improve the working relationships among the numerous entities that are part of the clinical research process.

Translational Research Core Services: NIH Rapid Access to Intervention Development (RAID)

Many promising new therapeutics encounter roadblocks during clinical development. Especially vulnerable are therapeutic approaches that involve high risk ideas or therapies for uncommon disorders that cannot attract private sector investment. Where private sector support for drug development is limited or not available, the NIH Rapid Access to Intervention Development Pilot program (NIH-RAID) can help fill the gap and reduce some of the common barriers that block progress of therapeutic discoveries from the bench to the bedside. The NIH-RAID program is not a grant program. Instead, it makes available critical resources that are needed to develop new therapeutic agents, including ones that can generate bulk amounts of the drug candidate or test its stability or toxic effects. It also provides researchers with access to expertise at the Food and Drug Administration on document preparation and submission.

Budget Policy: The FY 2011 budget estimate of \$5.000 million for this program represents a decrease of \$3.000 million or 37.5 percent less than the FY 2010 Enacted level. The funds provide continued support for ongoing programs and outreach efforts to researchers who may benefit from these resources.

Dynamic Assessment of Patient-Reported Chronic Disease Outcomes: Patient-Reported Outcomes Measurements Information System (PROMIS)

PROMIS is a revolutionary effort to enhance the precision of measures of patient-reported symptoms and function or outcomes. Patient-reported outcomes are essential for proper medical care but are often difficult to collect reliably. The PROMIS program has developed an interactive, computerized testing system that accurately reports patient-reported outcomes by adapting questions to the responses of each individual patient. This standardized measurement tool will increase the comparability of studies while reducing the reporting burden on patients. The initial PROMIS network of seven research sites and one coordinating

center developed questionnaires tailored to a number of symptoms of chronic diseases and conditions including anxiety, pain, and fatigue. In FY 2009, the second phase of the PROMIS program began with an expansion of the network to 14 research sites and three supporting centers to extend the PROMIS system to several new areas with an emphasis on questionnaires tailored to children, minorities, women and the underserved.

Budget Policy: The FY 2011 budget estimate of \$8.190 million for this program is in parallel with the FY 2010 Enacted level for the program. The estimated level of funding allows the PROMIS network of investigators to translate existing questionnaires into other languages, to develop new questionnaires, to test the new questionnaires, and to validate the PROMIS system in a large scale clinical trial focusing primarily on Asian-American and Latin-American cancer patients.

Clinical and Translational Science Awards (CTSAs)

The CTSA program is a unique and bold venture to restructure and improve the clinical research enterprise. The CTSA program is transforming how clinical and translational research and training is conducted by enabling researchers to provide and deliver new treatments more efficiently and quickly to patients. To better address the needs of the clinical research community, the longstanding General Clinical Research Centers program (GCRC), administered by NCRR, was transitioned into the CTSA program. Currently, the CTSA program is administered and funded by both the NIH Common Fund and NCRR. As the program expands, its management and function will transition solely to NCRR.

Budget Policy: The FY 2011 budget estimate of \$22.703 million for this program represents a decrease of \$2.542 million or 10.1 percent less than the FY 2010 Enacted level. The reduced level continues the planned transition of the program solely to NCRR by FY 2012. . The FY 2010 - FY 2011 planned Common Fund support to the CTSA's is \$25.245 million and \$22.703, million. The planned NCRR CTSA support in FY 2010 - FY 2011 is \$457.700 million and \$477.700 million.

NIH Strategic Planning Funds

The core mission of the NIH Common Fund is to foster collaboration, coordination, and strategic planning activities across the NIH. New research opportunities that would benefit from Common Fund support are being envisioned for FY2011. To facilitate these planning efforts, the NIH Director is convening a series of trans-NIH workshops and brainstorming sessions, beginning in FY2010, involving external and internal experts, public and private sector partners, and stakeholders. These planning efforts are being supported through the Common Fund Strategic Planning Funds.

Budget Policy: As in FY 2010, the budget estimate provides \$5.463 million to this program in FY 2011.

New Common Fund Initiatives

The Common Fund is intended to allow the NIH Director to address pressing needs and emerging opportunities in a nimble fashion. Planning for these funds occurs on a continual basis as input is gathered from Strategic Planning Workshops and other sources. Planning for FY 2011 programs is occurring during FY 2010. These programs will address the highest priorities for the NIH Director, spanning the gamut of basic to clinical research. Topics being considered for new Common Fund programs include:

Global Health

- New models for prospective longitudinal cohort studies
- Regulatory science/joint initiative with the FDA
- Opportunities in Science, Technology, Engineering, and Math Education
- Development of novel therapeutics/expansion and redesign of RAID
- Health Economics
- Development of Protein Affinity Reagents
- Participation in an international effort to analyze mouse models
- Translational applications of stem cells
- Partnerships with HMO Research Networks for enhanced clinical research
- Science of Behavior Change
- Global analyses of cellular networks

Additional areas in need of investment will be articulated through a "think tank" strategic planning meeting to be held in early 2010 involving scientific leaders from many areas of health research.

Budget Policy: The budget estimate of \$78.704 million represents an increase of \$71.978 million or 91 percent more than the FY2010 Enacted level. This increase in funds reflects the churn created by the design of the Common Fund to have revolving program areas. As programs end with FY 2010 funds, it has created flexibility for the Director to develop new programs in FY 2011 that address his priorities.

Recovery Act and the Common Fund

Recovery Act Implementation

Recovery Act Funding: \$136.837 million

In FY 2009, the Common Fund received \$136.837 million under the Recovery Act. Of this amount, \$68.293 million was obligated in FY 2009 and \$68.544 million will be obligated in FY 2010.

The Common Fund ARRA funding is being used to support NIH Director's New Innovator awards, the Challenge Grant and Grand Opportunities "GO" Grant programs, additional meritorious grants that could not be paid in fiscal years 2008 and 2009 because of budget limitations, and supplements for existing grants. These programs are intended to stimulate innovation, build research infrastructure that will support trans-NIH activities, purchase new equipment, hire new employees, employ students and teachers to conduct biomedical research over the summer, and greatly accelerate the pace of research in ways that would not have been possible without the additional ARRA support.

The Common Fund ARRA awards address a broad range of research topics, including:

High Throughput Molecular Screening: The Common Fund is using ARRA to further fuel this area of research by supporting a series of projects aimed at developing new screening tests and chemistry resources for use in HTS of small molecules to accelerate drug development.

Stem Cells: ARRA funds are being used to explore basic mechanisms underlying stem cell differentiation and to develop novel cell-based therapies.

Behavioral and Social Sciences: Common Fund ARRA projects aim to strengthen our understanding of the connection between human behavior and health. Support was also provided for projects that will allow patient-reported outcomes of therapies to be used more effectively in clinical trials.

Science, Technology, Engineering, and Math (S.T.E.M.) Education - A signature project for the Common Fund, this series of awards represents a new effort at the NIH to assess efficacy of some existing STEM Ed programs and to prepare for new initiatives that will bolster K-12 science education in the US.