DEPARTMENT OF HEALTH AND HUMAN SERVICES

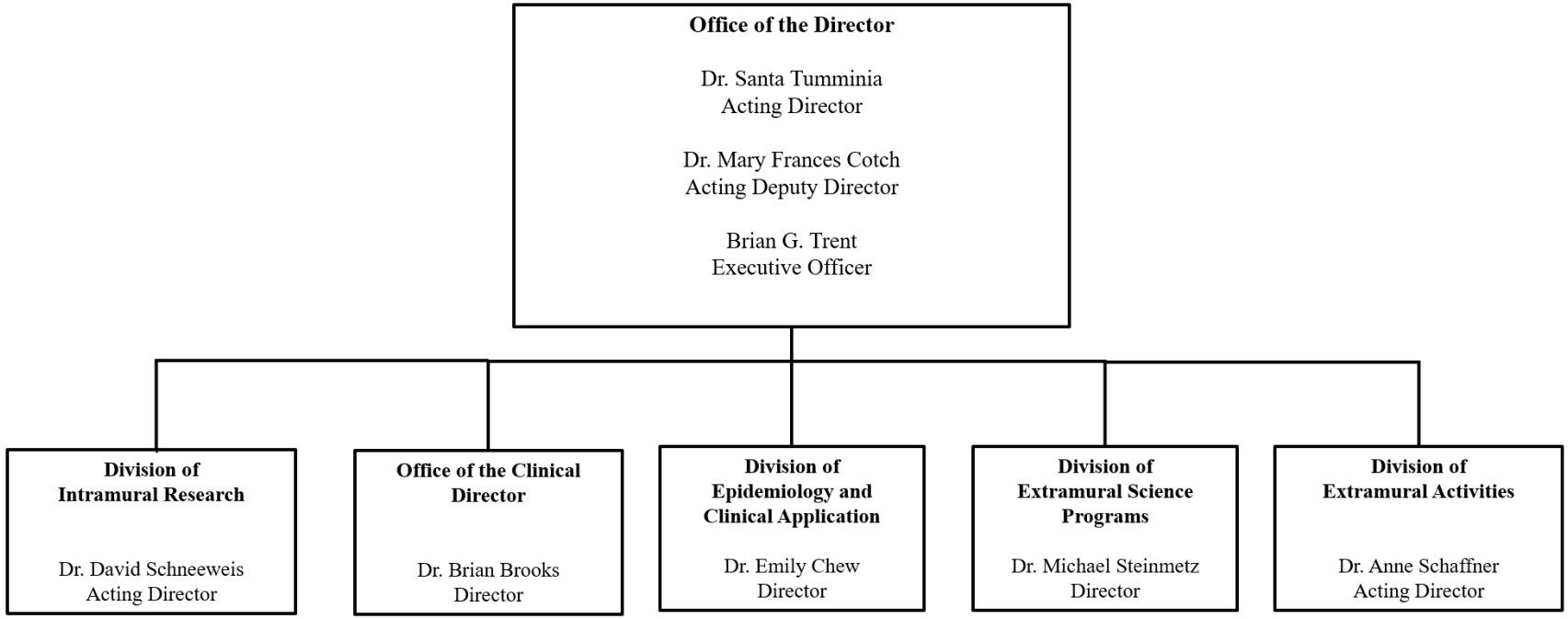
NATIONAL INSTITUTES OF HEALTH

National Eye Institute (NEI)

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Organizational Chart



NATIONAL INSTITUTES OF HEALTH

National Eye Institute

For carrying out section 301 and title IV of the PHS Act with respect to eye diseases and visual disorders, [$824,090,000]*$749,003,000.*

NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Amounts Available for Obligation[1]

(Dollars in Thousands)

Source of Funding	FY 2019 Final	FY 2020 Enacted	FY 2021 President's Budget
Appropriation	$796,536	$824,090	$749,003
Mandatory Appropriation: (non-add)			
Type 1 Diabetes	*(0)*	*(0)*	*(0)*
Other Mandatory financing	*(0)*	*(0)*	*(0)*
Rescission	0	0	0
Sequestration	0	0	0
Secretary's Transfer	-2,736	0	0
Subtotal, adjusted appropriation	$793,800	$824,090	$749,003
OAR HIV/AIDS Transfers	-17	-765	0
HEAL Transfer from NINDS	0	0	0
Subtotal, adjusted budget authority	$793,783	$823,325	$749,003
Unobligated balance, start of year	0	0	0
Unobligated balance, end of year	0	0	0
Subtotal, adjusted budget authority	$793,783	$823,325	$749,003
Unobligated balance lapsing	-16	0	0
Total obligations	$793,767	$823,325	$749,003

[1] Excludes the following amounts (in thousands) for reimbursable activities carried out by this account:
FY 2019 - $19,548 FY 2020 - $25,100 FY 2021 - $21,500

NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Budget Mechanism - Total[1]

(Dollars in Thousands)

MECHANISM	FY 2019 Final		FY 2020 Enacted		FY 2021 President's Budget		FY 2021 +/- FY 2020 Enacted	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	858	$353,857	871	$359,451	810	$334,290	-61	-$25,162
Administrative Supplements	*(56)*	6,651	*(36)*	4,500	*(25)*	3,123	*(-11)*	-1,377
Competing:								
Renewal	81	36,522	104	42,432	93	35,338	-11	-7,094
New	254	100,196	264	107,576	236	89,590	-28	-17,986
Supplements	0	0	0	0	0	0	0	0
Subtotal, Competing	335	$136,718	368	$150,008	329	$124,928	-39	-$25,081
Subtotal, RPGs	1,193	$497,226	1,239	$513,959	1,139	$462,340	-100	-$51,619
SBIR/STTR	50	24,720	55	25,512	50	23,241	-5	-2,271
Research Project Grants	1,243	$521,946	1,294	$539,471	1,189	$485,582	-105	-$53,890
Research Centers:								
Specialized/Comprehensive	42	$27,259	42	$27,259	38	$24,805	-4	-$2,453
Clinical Research	0	0	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0	0	0
Comparative Medicine	0	144	0	144	0	131	0	-13
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	42	$27,402	42	$27,402	38	$24,936	-4	-$2,466
Other Research:								
Research Careers	100	$19,773	104	$20,673	95	$18,812	-9	-$1,861
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	38	35,821	38	39,814	35	36,231	-3	-3,583
Biomedical Research Support	0	0	0	0	0	0	0	0
Minority Biomedical Research Support	0	0	0	0	0	0	0	0
Other	39	16,954	35	16,200	32	14,742	-3	-1,458
Other Research	177	$72,548	177	$76,687	162	$69,785	-15	-$6,902
Total Research Grants	1,462	$621,897	1,513	$643,561	1,389	$580,303	-124	-$63,258
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	99	$4,833	99	$4,972	99	$4,972	0	$0
Institutional Awards	146	6,994	146	7,202	146	7,202	0	0
Total Research Training	245	$11,827	245	$12,174	245	$12,174	0	$0
Research & Develop. Contracts	41	$40,862	41	$43,761	41	$42,771	0	-$990
(SBIR/STTR) (non-add)	*(0)*	*(265)*	*(0)*	*(265)*	*(0)*	*(265)*	*(0)*	*(0)*
Intramural Research	175	89,916	183	93,456	183	84,897	0	-8,559
Res. Management & Support	82	29,281	90	30,373	90	28,858	0	-1,515
Res. Management & Support (SBIR Admin) (non-add)	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, NEI	257	$793,783	273	$823,325	273	$749,003	0	-$74,322

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

Major Changes in the Fiscal Year 2021 President's Budget Request

Major changes by budget mechanism and/or budget detail are briefly described below. Note that there may be overlap between budget mechanisms and activity detail and these highlights will not sum to the total change for the FY 2021 President's Budget. The FY 2021 President's Budget for NEI is $749.0 million, a decrease of $74.3 million from the FY 2020 Enacted level.

Research Project Grants (RPGs) (-$53.9 million; total $485.6 million):
NEI will reduce funding for Non-Competing RPGs by 7.0 percent, which is a $25.2 million decrease from their FY 2020 Enacted level. The number of Competing RPGs is expected to decrease by 10.6 percent, or 39 grants compared to the FY 2020 Enacted level of 368 awards, and the amount to support competing awards will be reduced by $25.1 million from FY 2020, or 16.7 percent. These reductions are distributed across all programmatic areas and basic, translational or clinical research.

Research Centers (-$2.5 million; total $24.9 million):
NEI will reduce funding for Research Centers by 9.0 percent, resulting in 4 fewer awards.

Other Research (-$6.9 million; total $69.8 million):
NEI will reduce funding for Other Research mechanisms by 9.0 percent. Research Careers are expected to decrease by 9.0 percent, or 9 grants compared to the FY 2020 Enacted level of 104 awards. Cooperative Clinical Research is expected to decrease by 9.0 percent resulting in 3 fewer awards.

Intramural Research (-$8.6 million; total $84.9 million):
NEI will reduce funding for Intramural Research by 9.2 percent, which is a $8.6 million decrease from the FY 2020 Enacted level. These reductions are distributed across all programmatic areas and basic, translational or clinical research.

NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Summary of Changes

(Dollars in Thousands)

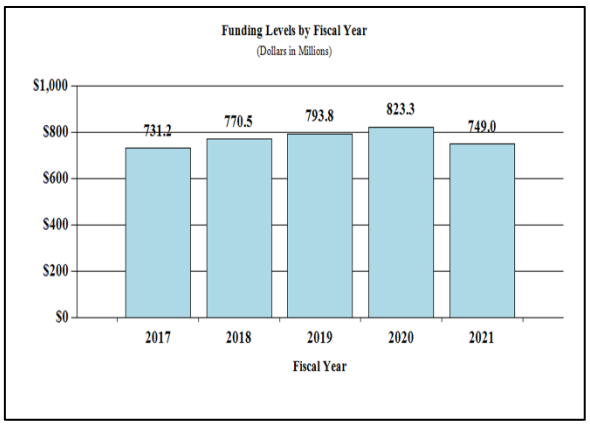
FY 2020 Enacted	$823,325
FY 2021 President's Budget	$749,003
Net change	-$74,322

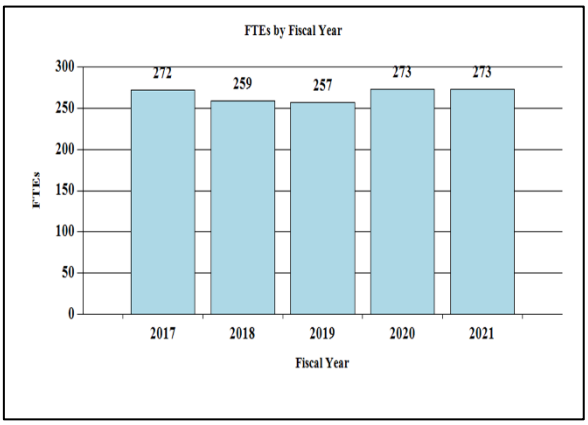
CHANGES	FY 2021 President's Budget FTEs	FY 2021 President's Budget Budget Authority	Change from FY 2020 Enacted FTEs	Change from FY 2020 Enacted Budget Authority
A. Built-in:				
1. Intramural Research:				
a. Annualization of January 2020 pay increase & benefits		$36,887		$242
b. January FY 2021 pay increase & benefits		36,887		546
c. Paid days adjustment		36,887		-139
d. Differences attributable to change in FTE		36,887		0
e. Payment for centrally furnished services		12,497		-2,134
f. Cost of laboratory supplies, materials, other expenses, and non-recurring costs		35,513		467
Subtotal				-$1,017
2. Research Management and Support:				
a. Annualization of January 2020 pay increase & benefits		$16,204		$106
b. January FY 2021 pay increase & benefits		16,204		238
c. Paid days adjustment		16,204		-61
d. Differences attributable to change in FTE		16,204		0
e. Payment for centrally furnished services		3,506		-619
f. Cost of laboratory supplies, materials, other expenses, and non-recurring costs		9,149		102
Subtotal				-$233
Subtotal, Built-in				-$1,250

CHANGES	FY 2021 President's Budget No.	FY 2021 President's Budget Amount	Change from FY 2020 Enacted No.	Change from FY 2020 Enacted Amount
B. Program:				
1. Research Project Grants:				
a. Noncompeting	810	$337,413	-61	-$26,539
b. Competing	329	124,928	-39	-25,081
c. SBIR/STTR	50	23,241	-5	-2,271
Subtotal, RPGs	1,189	$485,582	-105	-$53,890
2. Research Centers	38	$24,936	-4	-$2,466
3. Other Research	162	69,785	-15	-6,902
4. Research Training	245	12,174	0	0
5. Research and development contracts	41	42,771	0	-990
Subtotal, Extramural		$635,248		-$64,248
	FTEs		FTEs	
6. Intramural Research	183	$84,897	0	-$7,542
7. Research Management and Support	90	28,858	0	-1,282
8. Construction		0		0
9. Buildings and Facilities		0		0
Subtotal, Program	273	$749,003	0	-$73,072
Total changes				-$74,322

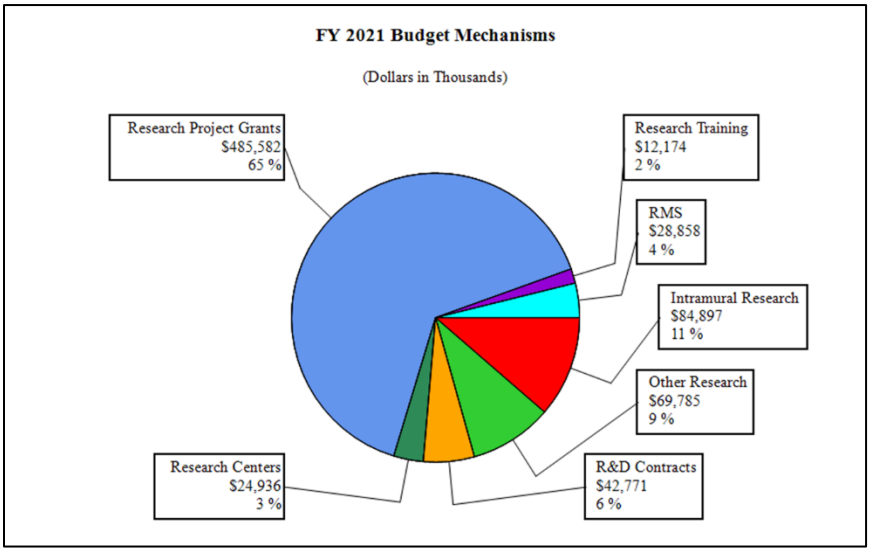
Fiscal Year 2021 Budget Graphs

History of Budget Authority and FTEs:

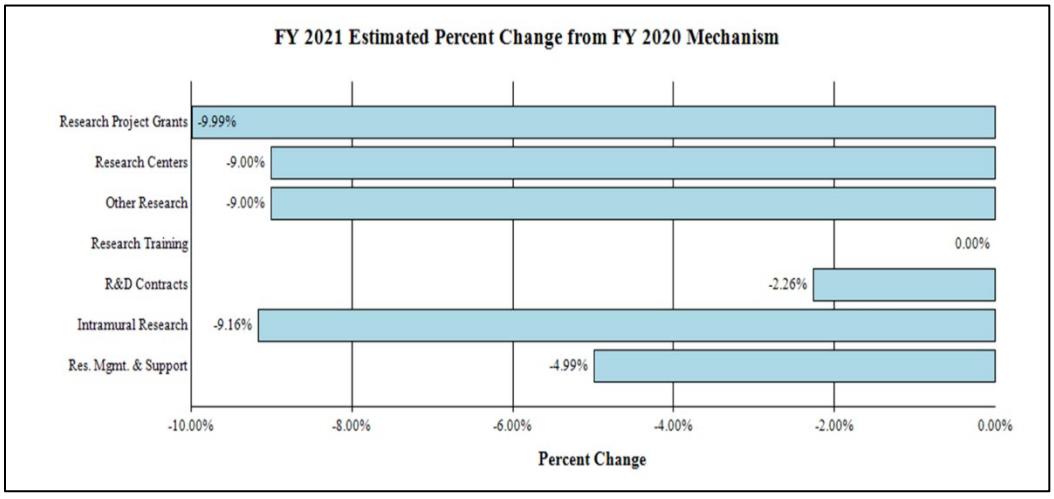




Distribution by Mechanism:



Change by Selected Mechanisms:



NATIONAL INSTITUTES OF HEALTH
National Eye Institute

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

	FY 2019 Final		FY 2020 Enacted		FY 2021 President's Budget		FY 2021 +/- FY2020	
Extramural Research	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**
Detail								
Retinal Diseases Research		$326,836		$338,905		$307,777		-$31,128
Corneal Diseases, Cataract, and Glaucoma Research		218,136		226,191		205,415		-20,775
Sensorimotor Disorders, Visual Processing, and Rehabilitation Research		129,614		134,400		122,055		-12,344
Subtotal, Extramural		**$674,586**		**$699,496**		**$635,248**		**-$64,248**
Intramural Research	**175**	**$89,916**	**183**	**$93,456**	**183**	**$84,897**	**0**	**-$8,559**
Research Management & Support	**82**	**$29,281**	**90**	**$30,373**	**90**	**$28,858**	**0**	**-$1,515**
TOTAL	**257**	**$793,783**	**273**	**$823,325**	**273**	**$749,003**	**0**	**-$74,322**

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

NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2020 Amount Authorized	FY 2020 Enacted	2021 Amount Authorized	FY 2021 President's Budget
Research and Investigation	Section 301	42§241	Indefinite	$823,325,000	Indefinite	$749,003,000
National Eye Institute	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				$823,325,000		$749,003,000

NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
2012	$719,059,000	$719,059,000	$692,938,000	$704,043,000
Rescission				$1,330,641
2013	$693,015,000		$695,115,000	$702,712,359
Rescission				$1,405,425
Sequestration				($35,271,328)
2014	$699,216,000		$701,407,000	$682,077,000
Rescission				$0
2015	$675,168,000			$684,191,000
Rescission				$0
2016	$695,154,000	$698,108,000	$709,549,000	$715,903,000
Rescission				$0
2017[1]	$707,998,000	$735,576,000	$740,826,000	$732,618,000
Rescission				$0
2018	$549,847,000	$743,881,000	$758,552,000	$772,317,000
Rescission				$0
2019	$711,015,000	$781,540,000	$796,955,000	$796,536,000
Rescission				$0
2020	$685,644,000	$835,465,000	$840,163,000	$824,090,000
Rescission				$0
2021	$749,003,000			

[1] Budget Estimate to Congress includes mandatory financing.

Justification of Budget Request

National Eye Institute

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

Budget Authority (BA):

	FY 2019 Final	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 +/- FY 2020
BA	$793,783,000	$823,325,000	$749,003,000	-74,322,000
FTE	257	273	273	0

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

Director's Overview

Eye diseases that lead to blindness, such as age-related macular degeneration (AMD), diabetic retinopathy, and glaucoma, affect millions of Americans of all ages and ethnicities. These and other less common diseases disable productive careers and rob people of their mobility and independence. NEI supports vision research through approximately 1,600 research grants and training awards made to scientists at more than 250 medical centers, hospitals, and universities across 44 states and around the world. NEI also conducts laboratory and patient-oriented research in facilities at NIH.

Treating Vision Loss, Then and Now and Beyond

When looking back 20 years, it may seem like medical advances have transformed vision care at "blinding" speed, but the process of translating discoveries into treatments can take decades. For example, in 1993, NEI researchers discovered *RPE65*, one of several genes that when mutated causes Leber congenital amaurosis (LCA), a severe form of childhood blindness. It took years of research to understand the connection between the gene and disease, to develop gene therapies and to test them in animal models. Ultimately, these efforts resulted in the first Food and Drug Administration (FDA)-approved gene replacement therapy in 2017 in which a normal copy of *RPE65* is introduced to patients. LCA gene replacement demonstrated the proof-of-principle for treating patients with diseases caused by mutated genes, and NEI is funding several other gene therapy studies. The field of gene therapy is once again being transformed, this time by a gene editing technology; instead of introducing a whole new gene, a tool called CRISPR can fix specific gene mutations in the patient's own DNA. Editas Medicine, a pharmaceutical company specializing in gene editing technology, building on the work of NEI researchers, conducts the first-in-human CRISPR trial to help patients with LCA caused by a mutation in another gene, *CEP290*, also discovered by NEI scientists.

The long arc of research has paid off in other areas too. Diabetes patients with retinopathy would often lose vision due to leaky abnormal blood vessels in their retina. In the 1980s, laser surgery targeting these vessels dramatically rescued vision in some patients, but also left scar tissue. Twenty-five years later, research on the formation of these vessels led to effective drug therapies that can reverse lost vision in patients. In 2005, optogenetics emerged as a powerful research tool that uses opsins, the light-sensing proteins discovered through vision research. By incorporating opsin proteins into select neurons in research animals, scientists can use light to switch the neurons on and off to understand how those neurons control behavior. More recently, NEI has invested in optogenetics as a therapy to restore vision in cases where the light-sensitive photoreceptors are gone. NEI scientists have inserted these opsin proteins to introduce light-sensitivity in other retinal neurons in blind mice. The teams have been bioengineering faster and more sensitive opsin activity to restore visual functions. By combining optogenetics with other therapies, the future of genetically restoring vision to the blind looks promising.

Imaging in Four Dimensions and in the Predictable Future

One of the biggest transformations in eye care over the last 20 years has been imaging the tissues within the eye and identifying biomarkers for earlier disease detection. While the transparent eye has allowed doctors to photograph the retina to look at the health of cells, blood vessels and plaque formation, revolutionary tools such as Optical Coherence Tomography (OCT) now provide 3D cross-sectional images of deep layers of tissue, to examine tissue thickness and leaky blood vessels, which informs treatment decisions in real time. This non-invasive imaging technique can also be used to examine blood vessels running through different areas of the eye (OCT- angiography, OCT-A), which has improved diagnosis of vision and neurologic disease. NEI researchers developed handheld portable OCT-A, which now enables accessible eye imaging for infants and bedridden patients, pre-surgery. The use of adaptive optics—an imaging technology that measures and corrects for light distortions in the eye—paired with OCT yields vivid 3D images of individual cells in living patients, which can be tracked at subsequent patient visits as they respond to treatment. Another powerful new imaging technology is three-photon microscopy, capable of producing high-resolution, non-invasive images deep within ocular tissues. Not only has imaging improved outcomes for visual disorders, but recent research demonstrated that markers in the eye can potentially detect Alzheimer's Disease before it can be detected in other parts of the nervous system.

With the future in sight, artificial intelligence (AI) is becoming a more useful tool to analyze images and make diagnoses, and NEI funds basic, translational, and clinical AI research across its portfolio. For example, the NEI Small Business program funds clinical studies developing AI and telemedicine tools that can provide early detection and prompt diagnostics for glaucoma, diabetic retinopathy, and retinopathy of prematurity, a significant cause of blindness for very low birthweight premature infants. In 2018, the FDA approved IDx-DR, an AI diagnostic system partly built on NEI-supported research. IDx-DR analyzes retinal images to screen and detect diabetic retinopathy, an important step in managing a disease that causes vision loss in over 30 million Americans. NEI recently funded a clinical study that tested NGoggle, an easy-to-wear device that can assess vision loss by analyzing signals between the brain and eyes. This portable system based on AI and virtual reality can improve diagnostic testing for glaucoma, one of the leading causes of visual impairment in the United States.

The Cutting Edge of Regenerative Medicine

In 2006, the discovery of induced pluripotent stem cells (iPSCs)— adult cells that have been genetically reprogrammed to a developmental stage such that they can be turned into any cell type in the body— revolutionized the field of biomedical and vision research. This breakthrough opened the door for transformative regenerative medicine therapies. The NEI Audacious Goal Initiative (AGI) pioneers regenerative medicine in the retina to restore vision loss due to injury or degenerative disease. Recent increases in the NEI budget have allowed the AGI to expand research opportunities in regenerative medicine, without sacrificing other NEI priority research areas. The AGI has launched three key research consortia, representing 16 highly collaborative projects and $62 million to image individual cells in the eye as they respond to light, identify factors that control cell regeneration in the visual system, and develop animal models to test regenerative therapies. AGI efforts to expand knowledge around cellular environments in the eye is a vital component in the application of regenerative medicine. For example, scientists are excited about a rare subpopulation of retinal cells that respond to light to regulate the sleep-wake cycle because they have the ability to resistant eye injuries, to survive under many disease conditions, and to regenerate. A recent study discovered that a gene found in these cells called thrombospondin-1 plays a vital part in increasing cell regeneration. Further insights into how these cells regenerate may provide valuable insights on how to reduce vision loss following eye diseases.

The ability to turn stem cells into a retinal pigment epithelium (RPE) layer, a sheet of cells in the back of the eye that supports neighboring light-sensing cells, is the foundation for constructing a complete retina. Researchers at NEI were able to derive iPSCs from patients with advanced age-related macular degeneration (AMD) and convert those stem cells into healthy RPE tissue. The newly developed tissue prevented blindness in animal models and lead to the first-in-human clinical trials using replacement tissue derived from iPSCs. In a separate study, the scientists were also able to incorporate 3-D bioprinting to build a network of capillaries to supply blood to the RPE tissue. NEI collaborates with FUJIFILM Cellular Dynamics, Inc., a cell manufacturing company based on NEI-funded research converting stem cells into retinal neurons, to recreate a retina from stem cells entirely in the laboratory. This goal is to develop 3-D ocular tissue and technologies to treat eyes damaged in traumatic injury, such as those of soldiers impacted by a roadside blast.

Investing in Age-Related Macular Degeneration

Although AMD is the leading cause of vision loss in older Americans, and several genes and pathways have been implicated in its development, therapy options have been limited. NEI has capitalized on recent increased appropriations to develop a multipronged strategy for AMD. NEI established the AMD Pathobiology Working Group in 2016 to leverage new genomic discoveries and discuss new methodologies. The Workgroup published a report in July 2019 that assessed the state of knowledge for AMD pathogenesis and provided recommendations to prioritize future research that will expedite the discovery of targeted therapies. Landmark genomics studies have given us genetic footholds (such as the inflammation control gene CFH) to explore new molecular pathways such as the immune system and cholesterol, as well as environmental risks like smoking. New research from Genome Wide Association Studies on AMD compared populations of people with and without AMD and identified 52 genetic variants within 34 genomic regions that were significantly associated with the disease. The publicly available data

provide a valuable resource for vision scientists to unlock information on disease mechanisms associated with these genes and aid in the development of new treatment strategies. Recent findings from a large-scale genetic screening of mice uncovered important genes that are linked to disease mechanisms that affect the eye and revealed important genetic risks associated with diseases like AMD that can have growing impacts on improving diagnostics.

Today, multiple drug options for the 'wet form' of AMD block VEGF, a growth factor that stimulates abnormal growth of blood vessels that leak into the retina. These drugs have been remarkably effective in preventing vision loss and even restoring lost vision in many patients. By contrast, there are currently no therapies for the 'dry' form of advanced AMD, characterized by the death of photoreceptor cells and underlying RPE cells. Multiple trials for this form of the disease are now underway to replace damaged cells in the back of the eye, such as the NEI trial creating iPSC-derived tissue patches from patients. The Age-Related Eye Disease Studies (AREDS), designed to explore the natural history and risk factors of AMD, demonstrated specific dietary supplements were successful in delaying progression to advanced AMD in roughly one in four patients; detailed imaging and artificial intelligence may hopefully assist doctors in personalizing treatments in the future. In a bold effort to build on the AREDS investment, NEI has partnered with the New York Stem Cell Foundation to facilitate drug discovery and other basic research efforts by creating a database of genetic and clinical information from a cohort of AMD patients along with generating RPE cell lines derived from stem cells from these individuals that will soon be available for the scientific community to use. Separately, a project coinciding with the AMD Ryan Initiative Study, tracking eye health of 200 people with early AMD, will begin to evaluate the effectiveness of a new procedure that measures how the eye adjusts to the dark to help screen and monitor the disease at early to middle stages.

Another new investment in AMD research builds on the very successful Diabetic Retinopathy Clinical Research Retina Network. Originally established in 2004 to partner community clinics with academic research centers for creating a robust diabetic retinopathy research pipeline with efficient infrastructure, the Retina Network has just expanded to cover other retinal conditions, including AMD.

Beyond 2020 Vision

In July 2019, Director Paul Sieving, MD, PhD, announced he was leaving NEI after 18 years. Even as a national search is underway to identify a new director, NEI is launching new research initiatives. To help NEI look toward the future of vision research, the NEI Council endorsed a strategic planning process, with significant scientific and community input. The plan will be organized around cross-cutting areas of emphasis in order to capitalize on scientific opportunities enabled by emerging technologies and research needs. To complement the NEI AGI, which focuses on the back of the eye, the newly launched Anterior Segment Initiative (ASI) will prioritize the front of the eye (cornea, dry eye, pain). In November, NEI issued an ASI Request for Information to solicit ideas from researchers, patients, and other vision stakeholders. Recently, NEI researchers published promising results from clinical trials on DNase, an enzyme-based eye-drop used to treat severe dry eye, a disease that has limited drug therapy options and can seriously compromise vision and quality of life if not properly treated. The same researchers

also conducted the first in-human clinical trial on eye drops made from pooled human antibodies to treat patients with dry eye disease by targeting their immune system.

NEI is leveraging partnerships to explore new areas of research. A new partnership between NEI and the Department of Defense initiated in 2019 allows DoD Vision Research Program grant applicants to get concurrent NIH review, enabling NEI to fund research within its mission from a different pool of applicants, often with a greater engineering focus. The Eyes of Africa Project is an international collaborative of researchers that examines the genetic, economic, societal, and personal effects of vision loss in Africa. African Americans have both an increased prevalence of glaucoma and disproportionately higher rate of vision loss. NEI recently supported studies that identified genes related to glaucoma in populations of African descent. NEI's National Eye Health Education Program (NEHEP) supports population health by educating professionals and the public about the importance of eye health; NEHEP released a new strategic plan in 2019 and will launch a pilot project in 2020 to assess the impact of its outreach to Spanish-speaking audiences.

Overall Budget Policy:
The FY 2021 President's Budget request is $749.0 million, a decrease of $74.3 million or 9.0 percent compared with the FY 2020 Enacted level.

Program Descriptions and Accomplishments

Retinal Diseases Research: The retina is the light-sensitive neural tissue that lines the inside of the eye and sends visual messages through the optic nerve to the brain. Damage to the retina through disease or retinal detachment can lead to severe vision loss. The goals of this program are to increase the understanding of disease mechanisms that cause vision loss and to develop improved methods of prevention, diagnosis, and treatment. To meet these goals, NEI supports research on the cell biology, physiology, neuroscience, and immunology of the retina. Major areas addressed within the Retina Program include:

- **Age-related Macular Degeneration.** A leading cause of vision loss, AMD is a disease that blurs the sharp, central vision required for reading, driving, and face recognition. There are two forms of advanced AMD: geographic atrophy ("dry") AMD, a gradual breakdown of light sensing photoreceptor neurons; and neovascular ("wet") AMD, when abnormal blood vessels grow underneath the retina.
- **Retinopathy.** Diabetic retinopathy is a complication of diabetes in which abnormal blood vessels grow on the surface of the retinal and may swell and leak fluid. Retinopathy of Prematurity is a potentially blinding disorder that affects premature infants with very low birthweight.
- **Retinal monogenic disorders.** Some retinal degenerative diseases are caused by single genetic mutations, including retinitis pigmentosa, Usher syndrome, and ocular albinism.
- **Uveitis.** Inflammatory diseases that produce swelling and destroy eye tissue, sometimes leading to severe vision loss.

Accomplishments: Cells in the retina have been classified by their shape and response to light, but new techniques can measure the level of gene expression in individual cells, demonstrating

an incredible diversity of cells previously unknown. Applying big data analytics to this cell atlas enables comparisons of primate retinal cells to other species like mice, and an understanding of what underlies the sharp central vision unique to primates compared to peripheral vision. NEI researchers generated comprehensive classifications of cells in the primate retina and compared them to those of mice to understand the functions of vision. Between central and peripheral retina, 80 percent of the 65 different cell types were the same, but substantial differences in gene expression may underpin the divergent functions. These findings may improve therapy development for diseases like AMD, which is unique to primates.

A paradigm-changing technology, known as OCT, allows doctors to image cross-sections of the eye in patients to inform treatment decisions. OCT-angiography non-invasively images the tiny retina blood vessels which are often impacted by disease. However existing tabletop OCT systems could not be used for bedridden patients, patients undergoing surgery, or infants and children. For these populations, NEI researchers developed a new handheld OCT device and obtained high resolution images from infants to detect precise abnormalities in the retina. Some blinding diseases, like Retinitis pigmentosa, destroy light detecting photoreceptor cells, while initially preserving other cell types. Current retinal prosthesis therapies, such as the FDA-approved Argus II, electrically stimulate these cells to provide rudimentary vision, but sharp resolution has been limited as non-targeted cells are also stimulated. A recent study found that selective activation of retinal ganglion cells using electrodes resulted in an improved ability to enhance cell resolution—a step closer to improving the quality of artificial vision. Optogenetics is a technology that turns light-sensing proteins, opsins, into switches that can be genetically engineered in other retinal cells to make them responsive to light. Researchers were able to utilize medium-wavelength opsins in mammals to restore vision in dim light, which brings promise for human patients to be able to read and use a video monitor instead of relying on adaptive prosthetics to restore light-sensitivities.

NEI supported two recent clinical trials to compare effectiveness of drug therapies for uveitis. The POINT trial found that the delivery of three corticosteroids therapy options directly into the eye resulted in marked improvements to treat uveitis compared to administering around the eyeball. The FAST trial found that two commonly used drugs with differing price points performed similarly in treating the non-infectious form of uveitis. The cheaper drug was also found to be more effective than the more expensive therapy at treating severe forms of uveitis.

Budget Policy: The FY 2021 Budget request is $307.8 million, a decrease of $31.1 million or 9.2 percent compared with the FY 2020 Enacted level.

Corneal Diseases, Cataract, and Glaucoma Research: Corneal diseases, cataracts, and glaucoma cause more visits to ophthalmologists a year than any other vision disorders. NEI supports research to address these conditions that originate in the front of the eye.

- **Corneal disease research.** Corneal injuries, infections, and diseases can be extremely painful and require immediate medical attention. NEI's corneal research encompasses injuries sustained from recreation and the workplace as well as eye trauma.
- **Cataract research.** Cataracts, a clouding of the lens in the eye that affects vision, are the leading cause of blindness worldwide. NEI researchers investigate strategies to prevent cataract formation and progression through research to understand the physiological basis

of how the lens in the healthy eye remains transparent at the cellular and molecular levels.

- **Glaucoma research.** Glaucoma is a group of blinding diseases that result from damage to the optic nerve, the bundle of fibers that transmit signals from the eyes to the brain. Current therapies focus on reducing excessive fluid pressure in the eye, which causes nerve damage in the most common form of glaucoma.

Accomplishments: Recent outbreaks of Zika virus and other flaviviruses have uncovered a significant need to gain a deeper understanding of viral pathogenesis in the eye. A study following 112 infants prenatally exposed to the Zika virus in Brazil confirmed that over 21 percent of them had eye abnormalities, including a few who were born to mothers infected during the third trimester. Research in this area led to new clinical guidelines for the management of children with congenital Zika infection and helps prioritize future investments to develop reliable diagnostic tests and ocular antiviral therapies for flavivirus infections.

A recent analysis on single fiber cells that develop the eye lens helped uncover the diversity of gene expression in ocular lens cells, which may aid in efforts to restore vision issues caused by cataracts. On the global front, a new NEI grant will allow a team of investigators to study cataracts, uveitis, and other ocular complications that persist in Ebola survivors, including those who have cleared the virus from their system, to help find effective treatment and infection control methods for this complex disease.

NEI basic research on a molecular signaling cascade led to the Food and Drug Administration approval, in 2019, of Rocklatan, once-daily eye drops to treat patients with the most common form of glaucoma. This drug complements existing glaucoma medications and patients taking a combination therapy have benefited from their additive effects on eye pressure.

Budget Policy: The FY 2021 Budget request is $205.4 million, a decrease of $20.8 million or 9.2 percent compared with the FY 2020 Enacted level. While anterior eye diseases affecting the front of the eye, such as corneal diseases and cataracts, can lead to vision loss in patients at any age, NEI places additional priority on research exploring the impact of aging and environmental factors on conditions such as corneal dysfunction, glaucoma, and cataract formation. Front-of-the-eye research also includes ocular pain, ocular infection, inflammation, and immunology.

Sensorimotor Disorders, Visual Processing, and Rehabilitation Research: NEI funds basic and applied brain research, and research on rehabilitation for individuals with low vision. NEI neuroscientists have made remarkable progress in understanding what goes on in the face-processing areas in the brain.

- **Sensorimotor disorders and visual processing research.** Strabismus (misalignment of the eyes) and amblyopia (commonly known as "lazy eye") are common disorders that develop during childhood. Program goals center on gaining a better understanding of the neuromuscular control of gaze and the development of the visual system in children at high risk for these disorders. Neuroscientists working in vision research seek to understand how the brain processes the visual information that floods our eyes, how neural activity is related to visual perception, and how the visual system interacts with cognitive and motor systems. Additional research is directed at trying to open the so-

called “critical period” and thereby allow some recovery of visual function and stereopsis in adult amblyopia subjects.

- **Refractive errors.** Refractive errors, such as nearsightedness, farsightedness, and astigmatism, are commonly correctable with eye glasses or contact lenses in the United States but remain a tremendous economic and personal burden globally. The major goals of this program are to discover the biochemical pathways that govern eye growth and to uncover the risk factors associated with refractive errors.
- **Rehabilitation research.** Low vision is the term used to describe chronic visual conditions that are not correctable by eye glasses or contact lenses. NEI supports rehabilitation research to improve the quality of life for people with visual impairments by helping them maximize the use of remaining vision and by devising improved aids and strategies to assist those without useful vision.

Accomplishments: Twenty years ago, recovery of vision lost due to traumatic brain injury or stroke was not expected. Researchers recently discovered that visual plasticity—the ability to train and rehabilitate vision based on perceptual learning—paired with noninvasive brain stimulation can reduce recovery time and aid in restoring visual function for stroke or brain injury patients, providing insights into more effective blindness rehabilitation interventions.

Budget Policy: The FY 2021 Budget request is $122.1 million, a decrease of $12.3 million or 9.2 percent compared with the FY 2020 Enacted level. NEI conducts pediatric clinical studies for strabismus, amblyopia, and refractive error. Interventions for these conditions, as well as low vision and blindness rehabilitation are most effective when introduced at early stages.

Program Portrait: Vision Processing—From Basic Research to Improving Quality of Life
FY 2020 Level: $51.2 million
FY 2021 Level: $46.6 million
Change: $ 4.6 million

Approximately one third of the human brain is involved in vision processing; much of what we know about brain organization and function is through vision research. A new frontier of remarkable work in this field is creating opportunities for scientists to translate their cutting-edge research into improving quality of life for Americans.

Over the past 20 years, advanced technologies, such as functional magnetic resonance imaging (fMRI), which non-invasively images brain activity based on patterns of blood flow, have allowed investigators to explore the neural mechanisms underlying visual recognition. Recently, researchers used fMRI to shed light on how the human visual system is organized and, on its ability, to develop over time. They discovered that experiences at a young age with unique cartoon characters from Pokémon games created new activations within the visual cortex that resulted in long-lasting brain storage of these images years later. These findings not only provide better insights into how the brain organizes different types of visual information like Pokémon characters, but also highlight the strong and lasting effects of visual plasticity—the brain’s ability to adapt and rewire its connections—during early development, which can inform future research such as work on rehabilitation. Computer models of neural networks have been used to characterize different types visual processing, such as the brain’s ability to quickly recognize an object. A recent study utilized multielectrode recordings of neurons to compare neural activity in primates with computer models for object recognition tasks. They found that recurrent neural network models, those with back-and-forth or feedback connections,

function similarly to the biological circuits and are critical for complex object recognition and challenging tasks. These findings provide a strong premise to guide model development in the future. The trans-NIH Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative is continuing to accelerate the development and application of new technologies in neuroscience and medicine. Nearly 20 percent of BRAIN grantees focus on vision research, and another 20 percent of projects are awarded to current or past NEI grantees. This cross-cutting collaborative allows NEI and the vision research community to integrate their work with other NIH institutes, federal, and non-federal partners to execute novel approaches and discoveries, such as the development of visual prosthetics. The BRAIN Initiative funded the researchers at Second Sight to develop and clinically test a novel visual cortical prosthetic system—the Orion. The prosthetic is currently undergoing clinical trials with the aim to treat patients with blindness caused by certain diseases or traumas. NEI also supports the brain-machine interface (BMI)—a technology used to analyze the transfer of messages across neural circuits—to allow people with spinal cord injuries to move prosthetic limbs via their thought processes. Basic research on the function and interactions of different cortical areas that relate to sight, object recognition, eye movement, decision making, attention, and visual processing allow researchers to develop technologies that can record and use signals that oversee thoughts to activate motor movements. For example, BMI was used to harness a tetraplegic patient's intraparietal cortex—the part of the brain that is involved with eye movement—to play simple melodies on the piano by analyzing her visual and mental intent and translating those signals to move the fingers of a robot arm.

Intramural Research: NEI basic and clinical studies conducted on NIH campus are focused on the cause, prevention, and treatment of eye diseases and vision disorders; cellular and molecular mechanisms of eye development, infectious diseases of the eye; inflammatory and immunological responses; mechanisms of visual perception by the brain; and sensory control of movements.

Accomplishments: A recent intramural NEI study discovered that the innate immune system can have a protective effect in slowing retinal degeneration in retinitis pigmentosa but can worsen symptoms in AMD. These findings point to the complexity of the immune system's ability to have beneficial or harmful effects depending on the disease. It also highlights the need to guide future research in developing therapies that can complement the immune system to treat retinal degeneration.

NEI visual neuroscientists used a novel approach to teach monkeys to recognize arbitrary visual images, which they remembered for months and years. This allowed researchers to explore where and how long-term memories are represented in the brain. The research is part of a larger project that will provide more understanding of how long-term memories are linked to reward-seeking behavior and how that could be used to develop targeted therapeutics for depression.

Budget Policy: The FY 2021 Budget request is $84.9 million, a decrease of $8.6 million or 9.2 percent compared with the FY 2020 Enacted level.

Research Management and Support (RMS): RMS provides support and essential services to research programs and monitors their budgets. Included in this line item is personnel to carry out leadership and management functions, human resource support, training, travel, purchasing, facilities, budget, planning, information technology, and extramural grant award and management. NEI currently oversees more than 1,600 grants and contracts, including research

project grants, core center grants, research career development awards, cooperative clinical research agreements, training grants, and research and development contracts.

Accomplishments: Over the past 20 years, NIH's clinical center has doubled its clinical footprint, from admitting an average of 3,000 admitted patient visits to now approximately 5,000 visits per year and increasing clinical studies from 25 to 45, which include patients with eye disorders and other clinical focus areas. Over the past two years, NEI has recruited four tenure-track Investigators – all women – doubling its number of women investigators from four to eight. Women now account for almost a third of NEI investigators (8 of 25), up substantially from 17 percent before the recent hires. One of the new hires has the prestigious Earl Stadtman designation, two have been selected as prestigious Lasker Research Scholars, and three are part of the new NIH Distinguished Scholars Program.

Budget Policy: The FY 2021 Budget request is $28.9 million, a decrease of $1.5 million or 5.0 percent compared with the FY 2020 Enacted level.

NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Budget Authority by Object Class[1]

(Dollars in Thousands)

		FY 2020 Enacted	FY 2021 President's Budget	FY 2021 +/- FY 2020
Total compensable workyears:				
	Full-time equivalent	273	273	0
	Full-time equivalent of overtime and holiday hours	0	0	0
	Average ES salary	$198	$199	$2
	Average GM/GS grade	12.4	12.4	0.0
	Average GM/GS salary	$115	$116	$1
	Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$108	$112	$3
	Average salary of ungraded positions	$161	$162	$1
	OBJECT CLASSES	**FY 2020 Enacted**	**FY 2021 President's Budget**	**FY 2021 +/- FY 2020**
	Personnel Compensation			
11.1	Full-Time Permanent	21,225	21,309	84
11.3	Other Than Full-Time Permanent	12,020	12,068	47
11.5	Other Personnel Compensation	1,374	1,380	5
11.7	Military Personnel	251	258	7
11.8	Special Personnel Services Payments	5,653	5,675	22
11.9	**Subtotal Personnel Compensation**	**$40,523**	**$40,689**	**$166**
12.1	Civilian Personnel Benefits	11,654	12,105	451
12.2	Military Personnel Benefits	289	297	8
13.0	Benefits to Former Personnel	0	0	0
	Subtotal Pay Costs	**$52,466**	**$53,091**	**$625**
21.0	Travel & Transportation of Persons	1,052	848	-203
22.0	Transportation of Things	116	93	-23
23.1	Rental Payments to GSA	1	1	0
23.2	Rental Payments to Others	10	8	-2
23.3	Communications, Utilities & Misc. Charges	296	241	-55
24.0	Printing & Reproduction	3	3	0
25.1	Consulting Services	93	77	-16
25.2	Other Services	25,116	20,730	-4,386
25.3	Purchase of goods and services from government accounts	63,498	59,232	-4,266
25.4	Operation & Maintenance of Facilities	594	465	-129
25.5	R&D Contracts	13,936	13,433	-503
25.6	Medical Care	325	266	-59
25.7	Operation & Maintenance of Equipment	2,460	1,980	-480
25.8	Subsistence & Support of Persons	12	12	0
25.0	**Subtotal Other Contractual Services**	**$106,035**	**$96,197**	**-$9,838**
26.0	Supplies & Materials	4,278	3,425	-854
31.0	Equipment	3,329	2,614	-714
32.0	Land and Structures	0	0	0
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	655,735	592,477	-63,258
42.0	Insurance Claims & Indemnities	0	0	0
43.0	Interest & Dividends	5	5	0
44.0	Refunds	0	0	0
	Subtotal Non-Pay Costs	**$770,859**	**$695,912**	**-$74,947**
	Total Budget Authority by Object Class	**$823,325**	**$749,003**	**-$74,322**

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

NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Salaries and Expenses
(Dollars in Thousands)

OBJECT CLASSES	FY 2020 Enacted	FY 2021 President's Budget	FY 2021 +/- FY 2020
Personnel Compensation			
Full-Time Permanent (11.1)	$21,225	$21,309	$84
Other Than Full-Time Permanent (11.3)	12,020	12,068	47
Other Personnel Compensation (11.5)	1,374	1,380	5
Military Personnel (11.7)	251	258	7
Special Personnel Services Payments (11.8)	5,653	5,675	22
Subtotal Personnel Compensation (11.9)	**$40,523**	**$40,689**	**$166**
Civilian Personnel Benefits (12.1)	$11,654	$12,105	$451
Military Personnel Benefits (12.2)	289	297	8
Benefits to Former Personnel (13.0)	0	0	0
Subtotal Pay Costs	**$52,466**	**$53,091**	**$625**
Travel & Transportation of Persons (21.0)	$1,052	$848	-$203
Transportation of Things (22.0)	116	93	-23
Rental Payments to Others (23.2)	10	8	-2
Communications, Utilities & Misc. Charges (23.3)	296	241	-55
Printing & Reproduction (24.0)	3	3	0
Other Contractual Services:			
Consultant Services (25.1)	93	77	-16
Other Services (25.2)	25,116	20,730	-4,386
Purchases from government accounts (25.3)	42,644	37,254	-5,390
Operation & Maintenance of Facilities (25.4)	594	465	-129
Operation & Maintenance of Equipment (25.7)	2,460	1,980	-480
Subsistence & Support of Persons (25.8)	12	12	0
Subtotal Other Contractual Services	**$70,919**	**$60,519**	**-$10,400**
Supplies & Materials (26.0)	$4,278	$3,425	-$854
Subtotal Non-Pay Costs	**$76,674**	**$65,137**	**-$11,537**
Total Administrative Costs	**$129,140**	**$118,228**	**-$10,912**

NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Detail of Full-Time Equivalent Employment (FTE)

OFFICE/DIVISION	FY 2019 Final			FY 2020 Enacted			FY 2021 President's Budget		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Division of Epidemiology and Clinical Applications									
Direct:	10	-	10	10	-	10	10	-	10
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	10	-	10	10	-	10	10	-	10
Division of Extramural Activities									
Direct:	15	-	15	15	-	15	15	-	15
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	15	-	15	15	-	15	15	-	15
Division of Extramural Science									
Direct:	16	-	16	16	-	16	16	-	16
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	16	-	16	16	-	16	16	-	16
Division of Intramural Research									
Direct:	130	-	130	144	-	144	144	-	144
Reimbursable:	3	-	3	3	-	3	3	-	3
Total:	133	-	133	147	-	147	147	-	147
Office of the Director									
Direct:	81	2	83	84	1	85	84	1	85
Reimbursable:	-	-	-	-	-	-	-	-	-
Total:	81	2	83	84	1	85	84	1	85
Total	255	2	257	272	1	273	272	1	273
Includes FTEs whose payroll obligations are supported by the NIH Common Fund.									
FTEs supported by funds from Cooperative Research and Development Agreements.	0	0	0	0	0	0	0	0	0

FISCAL YEAR	Average GS Grade
2017	12.4
2018	12.4
2019	12.4
2020	12.4
2021	12.4

NATIONAL INSTITUTES OF HEALTH
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Detail of Positions[1]

GRADE	FY 2019 Final	FY 2020 Enacted	FY 2021 President's Budget
Total, ES Positions	1	1	1
Total, ES Salary	192,254	197,637	199,179
GM/GS-15	36	36	36
GM/GS-14	19	19	19
GM/GS-13	50	50	50
GS-12	35	35	35
GS-11	25	25	25
GS-10	1	1	1
GS-9	9	9	9
GS-8	2	2	2
GS-7	3	3	3
GS-6	3	3	3
GS-5	0	0	0
GS-4	2	2	2
GS-3	1	1	1
GS-2	0	0	0
GS-1	0	0	0
Subtotal	186	186	186
Grades established by Act of July 1, 1944 (42 U.S.C. 207)			
Assistant Surgeon General	0	0	0
Director Grade	0	0	0
Senior Grade	1	1	1
Full Grade	0	0	0
Senior Assistant Grade	0	0	0
Assistant Grade	0	0	0
Subtotal	1	1	1
Ungraded	70	86	86
Total permanent positions	187	187	187
Total positions, end of year	257	273	273
Total full-time equivalent (FTE) employment, end of year	257	273	273
Average ES salary	192,254	197,637	199,179
Average GM/GS grade	12.4	12.4	12.4
Average GM/GS salary	112,045	115,169	116,067

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