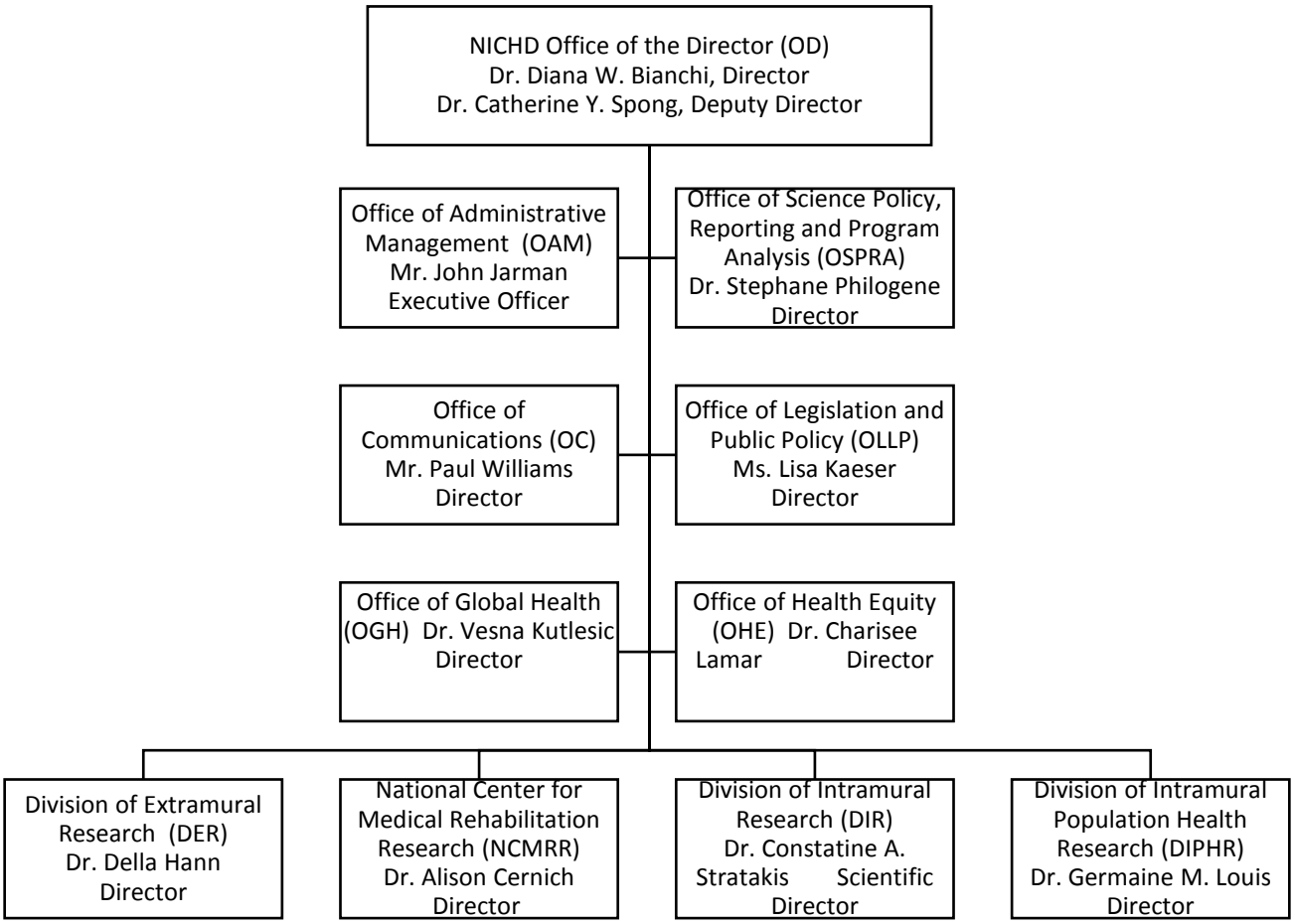
DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)

Eunice Kennedy Shriver
National Institute of Child Health and Human Development



NATIONAL INSTITUTES OF HEALTH

Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)

For carrying out section 301 and title IV of the PHS Act with respect to child health and human development, $1,032,029,000 .

NATIONAL INSTITUTES OF HEALTH
National Institute of Child Health and Human Development

Amounts Available for Obligation[1]

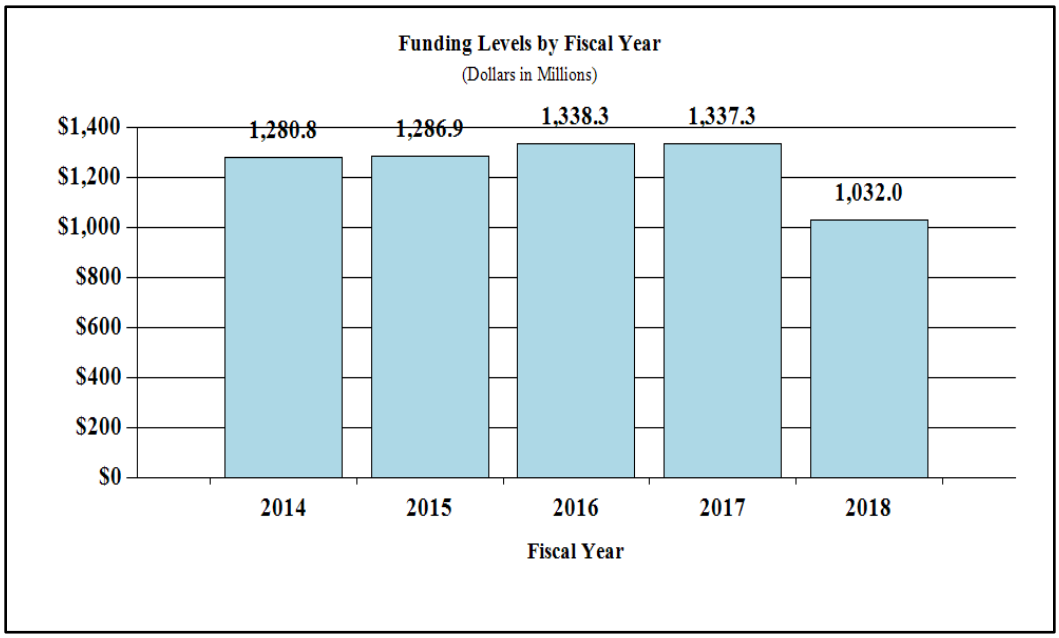
(Dollars in Thousands)

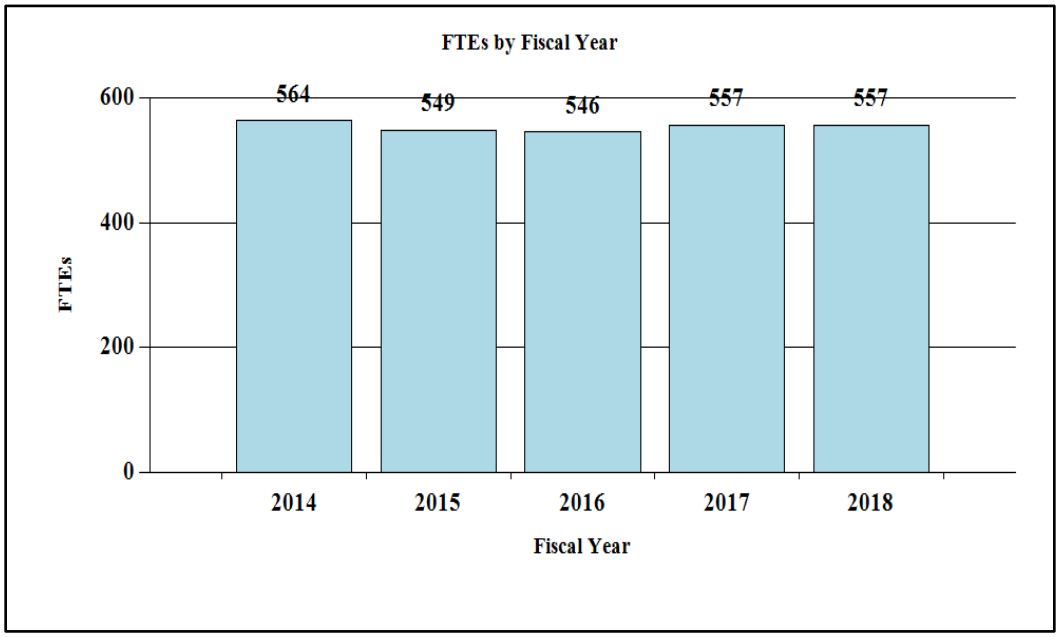
Source of Funding	FY 2016 Final	FY 2017 Annualized CR	FY 2018 President's Budget
Appropriation	$1,339,802	$1,339,802	$1,032,029
Mandatory Appropriation: (non-add)			
Type 1 Diabetes	*(0)*	*(0)*	*(0)*
Other Mandatory financing	*(0)*	*(0)*	*(0)*
Rescission	0	-2,547	0
Sequestration	0	0	0
Zika Intra-NIH Transfer	0	0	0
Subtotal, adjusted appropriation	$1,339,802	$1,337,255	$1,032,029
OAR HIV/AIDS Transfers	-1,454	0	0
Subtotal, adjusted budget authority	$1,338,348	$1,337,255	$1,032,029
Unobligated balance, start of year	0	0	0
Unobligated balance, end of year	0	0	0
Subtotal, adjusted budget authority	$1,338,348	$1,337,255	$1,032,029
Unobligated balance lapsing	-68	0	0
Total obligations	$1,338,280	$1,337,255	$1,032,029

[1] Excludes the following amounts for reimbursable activities carried out by this account:
FY 2016 - $30,236 FY 2017 - $31,000 FY 2018 - $25,000

Fiscal Year 2018 Budget Graphs

History of Budget Authority and FTEs:





NATIONAL INSTITUTES OF HEALTH
National Institute of Child Health and Human Development

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2017 Amount Authorized	FY 2017 Annualized CR	2018 Amount Authorized	FY 2018 President's Budget
Research and Investigation	Section 301	42§241	Indefinite	$1,337,255,000	Indefinite	$1,032,029,000
National Institute of Child Health and Human Development	Section 401(a)	42§281	Indefinite		Indefinite	
Total, Budget Authority				$1,337,255,000		$1,032,029,000

NATIONAL INSTITUTES OF HEALTH
National Institute of Child Health and Human Development

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
2008	$1,264,946,000	$1,273,863,000	$1,282,231,000	$1,254,708,000
Rescission				$22,309,000
Supplemental				$6,673,000
2009	$1,255,920,000	$1,299,059,000	$1,290,873,000	$1,294,894,000
Rescission				$0
2010	$1,313,674,000	$1,341,120,000	$1,316,822,000	$1,329,528,000
Rescission				$0
2011	$1,368,894,000		$1,366,750,000	$1,329,528,000
Rescission				$11,674,048
2012	$1,352,189,000	$1,352,189,000	$1,303,016,000	$1,323,900,000
Rescission				$2,502,171
2013	$1,320,600,000		$1,324,603,000	$1,321,397,829
Rescission				$2,642,796
Sequestration				($66,325,085)
2014	$1,339,360,000		$1,330,459,000	$1,282,595,000
Rescission				$0
2015	$1,283,487,000			$1,286,571,000
Rescission				$0
2016	$1,318,061,000	$1,305,586,000	$1,345,355,000	$1,339,802,000
Rescission				$0
2017[1]	$1,338,348,000	$1,373,408,000	$1,395,811,000	$1,339,802,000
Rescission				$2,547,000
2018	$1,032,029,000			

[1] Budget Estimate to Congress includes mandatory financing.

Justification of Budget Request

Eunice Kennedy Shriver National Institute of Child Health and Human Development

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

Budget Authority (BA):

	FY 2016 Actual	FY 2017 Annualized CR	FY 2018 Budget Request	FY 2018 + / - FY 2017
BA	$1,338,348,000	$1,337,255,000	$1,032,029,000	-$305,226,000
FTE	546	557	557	0

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

Director's Overview

The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) supports a broad research portfolio uniquely focused on human health and development, from before birth through adulthood. In scientific domains encompassing developmental biology, reproductive health, pediatrics, population sciences, and medical rehabilitation, NICHD supports research that helps us better understand how health and disease develop over time, to prevent, reduce, and treat illness and disability in current and future generations.

The lifelong process of human development is shaped by an array of complex physiological processes that interact with behavioral, social, and environmental factors. Fundamental scientific knowledge about how these processes work may not yield commercially-viable new treatments quickly – or at all. Yet fundamental research is the foundation of medical progress. Basic research helps identify crucial points in the disease process for treatment or prevention; reveals new compounds for testing as candidate therapies; pinpoints previously unsuspected risk factors for multiple conditions; and generates new approaches to prevention and cure.

NICHD's support for fundamental science emphasizes technologies and tools to understand both normal development and disease, as well as creating new ways to measure progress in improving health. NICHD actively promotes data sharing and supports publicly-available databases and biobanks to help ensure that relevant materials are available for translational research in maternal, pediatric, and reproductive health. NICHD's continuing efforts to understand the crucial role of the human placenta has already begun to provide an unprecedented wealth of information on how placental function affects maternal and fetal health. NICHD also continues to prioritize continuing investment in basic and translational research related to structural birth defects, which are a major cause of infant death in the United States.

Populations of primary interest to NICHD -- children, pregnant women, and persons with physical and intellectual disabilities – have too often and for too long been prescribed drugs, devices, and other treatments that were designed for and tested in groups from which they differ physiologically. Parents, pregnant women, individuals with disabilities, and their health care providers are often put in an extremely difficult position in which they have little or no information to assess whether the treatment is more dangerous than the disease. NICHD supports clinical research that specifically focuses on these populations, in the real-world settings where they receive treatment—including neonatal and pediatric intensive care units; fertility, rehabilitation, and HIV clinics; day care and schools; and physicians' offices. For example, the neonatal intensive care units across the United States that form NICHD's Neonatal Research Network are currently conducting clinical trials on potential treatments for neonatal sepsis, necrotizing enterocolitis, and anemia to help the smallest and most vulnerable infants. The Zika in Infants and Pregnancy (ZIP) study intends to enroll 10,000 pregnant women in areas where Zika virus is prevalent, including Puerto Rico, Brazil, and Colombia. Continuing this line of research will allow scientists to obtain data on the developmental effects of the virus on children, including understanding the relationship between timing of exposure and development of microcephaly. This will help clinicians, parents, and educators to better support children affected by prenatal exposure to Zika.

Fundamental biomedical and behavioral science is essential to prevention and health promotion. Recent scientific findings show that pregnancy is a "stress test" that indicates a higher risk for more serious problems as women age. For example, NICHD-supported research has shown that women with pregnancy complications such as preeclampsia and gestational diabetes have a higher risk of developing heart disease and type 2 diabetes later in life. NICHD research has also demonstrated that lifestyle factors such as nutrition and exercise can mitigate these risks.

Physical activity is a key component to maintaining physical health and decreasing secondary health conditions throughout life. However, individuals with disability experience a number of physical, social, and environmental barriers that make it more difficult for them to participate in physical activity. NICHD's National Center for Medical Rehabilitation Research (NCMRR) studies interventions that can promote, monitor, and sustain physical activity programs for people with disabilities in real-world settings (e.g., home, community, workplace, and school). This includes the use of engineering and social-science approaches to understand the effect of environmental factors, monitor individual participation, and promote overall health and independence.

NICHD continues to prioritize funding for new and early-stage investigators, to ensure that there is a pipeline of scientists and clinicians who are focused on the health problems of the communities NICHD serves, and to make certain that scientific progress continues to the next generation. Over the past two years NICHD has convened a Training Task Force that has examined outcomes for a variety of different training pathways. NICHD will use the evidence gathered from the Task Force's analysis to preferentially fund mechanisms that require individuals, rather than institutions, to apply for training opportunities.

The broad scientific opportunities at NICHD come with the recognition that thoughtful prioritization and careful stewardship are essential. NICHD has implemented data-driven

approaches to portfolio analysis, program evaluation, and performance assessment. This will help the Institute make strategic funding choices, focusing on areas that hold the most promise to improve the health of children, pregnant women, individuals with disabilities, families, and communities. Through a visioning process that has occurred over the past several years, NICHD has identified scientific research priorities that have been shared with the research community and the public. NICHD will use these priorities to identify key areas for continued support.

Overall Budget Policy: The FY 2018 President's Budget request is $1,032.029 million a decrease of $305.226 million compared with the FY 2017 Annualized CR level. These reductions are distributed across all programmatic areas and basic, epidemiology, or clinical research.

Program Descriptions and Accomplishments

Reproductive Health, Pregnancy, and Perinatology: The program in reproductive health, pregnancy, and perinatology supports basic, clinical, and translational research on a variety of topics, including gynecologic disorders, contraception, fertility and infertility, pregnancy, and newborn care.

NICHD manages a broad research portfolio to understand, treat, and prevent common, painful, costly reproductive health conditions, including uterine fibroids, vulvodynia, pelvic floor disorders, and endometriosis. For example, NICHD's Pelvic Floor Disorders Network currently is conducting several studies to compare surgical and non-surgical treatments for women with urinary incontinence. Recently, a group of NICHD-supported scientists analyzed the medical records of more than 190,000 women enrolled in one of the largest commercial health plans in the United States. They found that for women with uterine fibroids, cholesterol-lowering drugs known as statins reduced fibroid-related symptoms and surgeries. Program research on contraceptive development encompasses discovery of new pharmaceutical targets, contraceptive devices, and other methods to increase the range of safe, effective, and acceptable options for both women and men.

Research on infertility is a primary concern for the five percent of couples across the United States who have difficulty conceiving or carrying a child. NICHD's Reproductive Medicine Network is conducting studies to assess the benefits of lifestyle interventions in improving fertility. Epidemiological studies from the NICHD analyze the relationships between environmental exposures and fertility in both women and men. Recently, results from one of these studies provided additional evidence that adult exposure to air pollution increases the risk of infertility in women, and chronic exposure over time may worsen this risk. Other researchers studying infertility recently discovered, to their surprise, that only three genes are required for the development of healthy sperm in mice. Identifying the minimum genetic sequences needed for producing healthy sperm may be the first step in developing new approaches to male partner infertility, which accounts for 40% of all cases of infertility.

Pregnancy-related research spans preconception care, pregnancy, fetal growth, labor and delivery, and maternal and neonatal health. NICHD-supported researchers recently documented a troubling rise in maternal mortality. In the United States, deaths related to complications of pregnancy have been rising steadily, although such deaths have been falling in other developed

countries. Between 2000 and 2014, the estimated maternal mortality rate for 48 states and the District of Columbia increased by 26.6 percent, from 18.8 per 100,000 live births in 2000 to 23.8 per 100,000 live births in 2014.[1] This finding resulted from an analysis of vital statistics data, which researchers adjusted to account accurately for changes over time in state reporting of pregnancy-related deaths. Risks to maternal health include gestational diabetes, a type of diabetes that occurs during pregnancy; preeclampsia, a condition involving high blood pressure, liver and kidney damage during pregnancy; placental conditions, such as placenta previa, which occurs when the placenta blocks or partially blocks the opening of the uterus and interferes with normal delivery; substance use; and postpartum depression. NICHD-supported scientists are working to discover better ways to prevent and treat each of these conditions. For example, epidemiologists and biologists at NICHD are studying risk factors for gestational diabetes and its long-term consequences, while also taking advantage of metabolomics technology to investigate biochemical markers related to glucose intolerance in pregnancy. NICHD's ongoing Human Placenta Project, designed to provide information about placental health noninvasively and in real time, may yield new information to improve maternal health and pregnancy outcomes.

NICHD supports prevention research to help reduce rates of high-risk pregnancies and preterm birth, as well as the associated lifelong morbidities for mother and child. Preeclampsia, for example, not only leads to high blood pressure in pregnant women, but also is associated with long-term risk of heart disease in women and is a major cause of preterm birth. Because preeclampsia shares some characteristics with cardiovascular disease, researchers funded by NICHD conducted a trial of the cardiovascular drug Pravastatin to see if it could lower the risk for preeclampsia. Twenty pregnant women with a history of prior preeclampsia – and thus at high risk for recurrence – completed the trial, with ten taking the drug Pravastatin beginning with the second trimester (after completion of fetal organ formation) and ten taking a placebo. None of the women taking Pravastatin developed preeclampsia, while four in the placebo group did– about the same rate as is typical for women in the general population with a prior history of preeclampsia. No identifiable safety risks were associated with the drug. Researchers hope to continue this research to assess fully the safety and effectiveness of Pravastatin for preventing preeclampsia in high-risk pregnant women.

Infants born too small or too soon are particularly vulnerable to a range of infections and other conditions that can result in death or disability. Preterm infants are at particularly high risk for necrotizing enterocolitis (NEC), a potentially fatal inflammation of the intestines. NICHD's Neonatal Research Network is comparing the effectiveness of two different surgical procedures – laparotomy versus drainage – that are commonly used to treat NEC or isolated intestinal perforations in extremely low birth weight infants (< 1,000 g). Like many life-saving treatments delivered in the neonatal intensive care unit, these surgeries may have long-term effects. NICHD's research portfolio in preterm infants includes long-term studies that assess treatment effects and monitor children's progress as they grow. In a follow-up study of preschool children who were born preterm and treated early with medications to protect their developing brains, scientists found new evidence that the drugs had lasting positive effects on how the children functioned. In the original clinical trial, the newborns in the "treatment" group had been treated with drugs known as erythropoiesis-stimulating agents (ESAs), which stimulate production of

[1] MF MacDorman, E Declercq, H Cabral, and C Morton (2016). "Recent Increases in the U.S. Maternal Mortality Rate: Disentangling Trends from Measurement Issues", Obstetrics and Gynecology, 128, 1-10.

red blood cells. Preterm newborns in the trial's control group received placebo medication. Assessed at age two, three, and four, toddlers who were treated with ESAs had significantly better neurocognitive outcomes than did the placebo control group. A generation ago, many of these vulnerable infants would not have survived. Thanks to medical advances, many supported by NICHD studies, today these infants are surviving and thriving in far greater numbers.

Program Portrait: The Zika Generation
FY 2017 Level: $0.794 million
FY 2018 Level: $2.954 million
Change: +$2.16 million

When Zika virus infects adults, they typically experience mild symptoms or none at all, lasting for less than a week. However, after the 2015 outbreaks in South America, Zika virus infection was linked to microcephaly, a condition in which a newborn's brain is significantly smaller than normal and with abnormal, disorganized development. Zika infection also has been linked to fetal loss and miscarriage, stillbirth, and fetal eye and joint abnormalities. To date, no vaccine exists. In Brazil, increased numbers of Zika infections have correlated with a 35-fold increase in microcephaly cases, cited by The World Health Organization as a "public health emergency of international concern." Public health agencies across the world, including NICHD, are tracking the outbreaks in different regions, and are supporting research on Zika infection. Cases of Zika virus infection have been documented in travelers residing in most states in the US, with local outbreaks occurring in Texas and Florida.

NICHD is at the forefront of studying the Zika virus in pregnancy and identifying the best way to help the "Zika Generation," children born with conditions linked to Zika infection. Scientists from around the world joined NICHD and NIH partners at a meeting in 2016 on "Bridging Knowledge Gaps to Understand How Zika Virus (ZIKV) Exposure and Infection Affect Child Development." Already, researchers supported by NICHD and other NIH ICs have made progress in understanding how Zika affects development. Researchers using a mouse model have discovered that Zika virus infects and crosses the placentas, causing death or severe damage in fetal mice throughout development, as well as infertility in adult male mice. Models of Zika virus infection will enable rapid initial testing of experimental drugs to prevent birth defects. Research that explains the virus's impact, its range of complications, and its long-term outcomes will allow health care providers to advise people of reproductive age, including couples who are planning families, on how to promote healthy pregnancies.

NIH, along with researchers in Brazil, began The Zika in Infants and Pregnancy (ZIP) study. This multi-country study aims to enroll 10,000 pregnant women across Latin America and the Caribbean to examine the health risks of Zika virus on pregnant women and the developing fetus. The study will document rates of microcephaly and other complications among women who have had Zika compared to those who have not, as well as women who have shown symptoms of Zika infection and women who have been infected by Zika without experiencing symptoms. The study also will evaluate how the timing of Zika infection affects pregnancy outcomes, and what role environmental and other factors may play in the health of study participants and their newborns. Additional funds will support a follow-up study planned to monitor the progress of Zika-exposed children for several years, aimed at identifying and addressing their longer-term health needs.

Child Health: Child health research ranges from basic scientific investigations of biological processes that control healthy and atypical development to clinical studies in pediatric pharmacology, pediatric HIV and associated infections, nutrition science, pediatric endocrinology, pediatric trauma and critical illness, and other aspects of pediatric medicine. NICHD's strong fundamental science portfolio in developmental biology has paved the way for efforts to understand and ultimately prevent structural and functional birth defects, a leading cause of death and disabilities in children. Through intramural and extramural programs, NICHD supports collaborative teams of basic and clinical scientists studying the developmental biology, epidemiology, and genetics of structural birth defects. Scientists also are utilizing and

expanding the genomic sequencing data developed under the Common Fund's Gabriella Miller Kids First Pediatric Research Program, with one of its two focal areas on structural birth defects.

Because children differ physiologically from adults, medications developed and tested in adults often work differently in children. In some cases, children's bodies clear medications more quickly, which may mean that effective doses need to be higher or given more often than the doses suggested by adult health care guidelines. In other cases, a proportionally lower dose may be effective in children and reduce the potential for damaging side effects. Lacking specific information on the safety and effectiveness of drugs in children, yet needing to treat the child, physicians often prescribe medications "off label" – that is, they prescribe medications that have been approved and "labeled" for use in adults but not in children. NICHD is working to expand the limited existing scientific knowledge base on the safety, efficacy, and appropriate doses of pharmaceuticals for children. For example, NICHD has launched a study to assess the risks and benefits of two drugs (risperidone and aripiprazole), which are commonly used to treat schizophrenia and bipolar disorder in children and adolescents, but are not labeled for pediatric use. Recently, researchers tested the efficacy and safety of drugs used for gastric reflux in low birth weight infants. Histamine-2 receptor blockers (brand names include Zantac and Pepcid) have been shown to be safe and effective against gastric reflux in adults and older children. Because of concerns about the adverse effects of gastric reflux, which exposes the esophagus to stomach acids, the drugs also have been commonly used in very low birth weight infants, although the drugs' efficacy and safety have not been tested specifically in these most fragile babies. Many of these infants are susceptible to necrotizing enterocolitis, an infection-triggered intestinal inflammation, as well as sepsis, an overwhelming, systemic inflammatory reaction to infection. Both conditions are difficult to prevent or treat and can swiftly prove fatal. The research showed that use of the histamine-2 receptor blockers in very low birth weight infants was associated with a significantly increased risk of death, necrotizing enterocolitis, or sepsis. This finding supports efforts to minimize exposure to these drugs in low birth weight infants, thus improving their care.

Children and adolescents with HIV, or who were exposed to HIV in the womb, are surviving and living full lives in greater numbers than ever before. However, research supported by NICHD shows that both HIV and the drugs used to treat it can cause long-term health issues. For example, NICHD-supported scientists compared two antiretroviral drug regimens in South African children with HIV. They found that one of the drugs (efavirenz) was associated with less risk to bone formation than the other (ritonavir-boosted lopinavir or LPV/r). Adults with HIV are known to be at elevated risk of osteoporosis and bone fractures, apparently due to the effects of HIV, inflammatory proteins (cytokines), and antiretroviral therapy on bone cells and bone turnover. Any interference with bone formation in childhood and adolescence is of concern, because 85 to 90 percent of adult peak bone mass is achieved during this period, and shortfalls set the stage for osteoporosis and fractures in adulthood. The LPV/r regimen, recommended by the World Health Organization, is widely used for children with HIV. The results of this study suggest limiting LPV/r exposure in HIV positive children once viral suppression has been achieved, and using other medications to keep HIV in check.

For children affected by trauma or critical illness, evidence-based emergency and critical care can be lifesaving. NICHD's Collaborative Pediatric Critical Care Research Network

(CPCCRN), including seven pediatric intensive care units across the United States, aims to improve care for critically ill and injured children. For example, one of CPCCRN's current studies is assessing the drug Granulocyte Macrophage Colony Stimulating factor (GM-CSF) for use in severely injured children. Already FDA-approved for use in children with blood disorders, GM-CSF helps to improve immune function. Because injured children in the pediatric intensive care unit are especially vulnerable to infection, the researchers aim to establish the optimal dose of this medication that will help improve immune function for children with severe traumatic injury. Ultimately, scientists hope GM-CSF can reduce the risk of serious infection in these children. Another research team seeks to learn more about developing new approaches to lessen the effects of severe burns over a large proportion of a child's body. In addition to the initial skin damage, serious burns can have long-term effects of multi-organ dysfunction, degradation of muscle protein, insulin resistance (pre-diabetes), and increased risk for infection. The scientists found that even two years after a burn, mitochondrial (energy-producing structures within the muscle cells) function was altered, compared with healthy mitochondria. The researchers hope that understanding the role of mitochondrial alterations could help pave the way for interventions to address long-term effects of severe burns.

Program Portrait: Best Pharmaceuticals for Children Act

FY 2017 Level:	$7.0 million*
FY 2018 Level:	$5.6 million*
Change:	-$1.4 million

Many of the drugs that are safe and effective for adults have never been tested in children and, in fact, behave very differently in children. Simply adjusting drug doses to a child's weight or age is inadequate. In addition to being smaller, children's brains, bones, and metabolism differ from those of adults. To make sure that drugs used in children are safe and effective for children's specific needs, Congress passed the Best Pharmaceuticals for Children Act (BPCA). NIH established a trans-NIH effort, led by NICHD, to prioritize therapies in need of study, sponsor pediatric clinical trials that are declined by industry, and to submit data to the Food and Drug Administration (FDA) for pediatric labeling.

In prioritizing pediatric therapeutic needs, NICHD consults with colleagues from across the NIH, experts in pediatrics, and the FDA, to identify and test drugs used to treat children. Current drugs under study include furosemide (a diuretic) for preterm infants at risk of bronchopulmonary dysplasia, a severe lung condition; timodol (a beta-blocker) for treatment of benign tumors in children; and TMP/SMX (an antibiotic) for treatment of soft tissue infections. In addition, a new study was very recently launched to assess the use of risperidone and aripiprazole (two mental health drugs) in children.

Based on results from previous BPCA-supported research, pediatric labeling changes have been submitted or completed for antibiotics (ampicillin, piperacillin/tazobactam, and meropenem); lorazepam, an anti-epileptic drug; sodium nitroprusside, used to lower blood pressure; pralidoxime, a drug to treat poisoning by certain pesticides; and others. Several recent studies have provided key information required by the FDA to support future labeling changes. For example, a recent BPCA-supported study assessed the drug hydroxyurea, which had been approved by the FDA to treat adults with sickle cell anemia, but not children. Although the drug has not been approved for pediatric use, it is frequently prescribed "off-label" for children, especially older children, in capsule form. Researchers measured children's response to hydroxyurea in both capsule and liquid form. The scientists found that the liquid and capsule forms were equivalent, and that dosages based on a child's weight provided consistent and predictable drug exposure. The results of the study support approval of the drug in children, and will help to develop a liquid form for children who are unable to swallow a capsule.

**These figures reflect NICHD funds only and do not include additional funds for BPCA activities provided by other ICs. These funds would bring the total to $25 million in FY 2017 and $20 million in FY 2018.*

Intellectual and Developmental Disabilities: The program in intellectual and developmental disabilities (IDD) supports basic, translational, and clinical research and research training to advance knowledge of origins of common and rare disorders such as Down syndrome (DS), Fragile X syndrome, Rett syndrome, inborn errors of metabolism, and autism spectrum disorders (ASD). Evidence shows that early detection of conditions that impair a child's intellectual development, and beginning therapy as soon as possible may increase the likelihood of better outcomes. Accordingly, IDD research encompasses studies of newborn screening, as well as the earliest diagnosis, treatment, and management of IDDs and other conditions. The IDD program also supports research to understand the complex processes through which these disorders compromise cognitive, emotional, social, and physical development in infants and children and throughout the lifespan. In searching for the origins of ASD, for example, NICHD-supported researchers recently found that activation of maternal immune responses midway through a pregnancy may increase the risk of both ASD and intellectual disability (ID) in a child.

For years, many scientists believed that IDs were permanent and that it was not feasible to improve cognitive function. Recent animal research suggests otherwise, showing that it may be possible to develop medications to improve brain function and learning in people with some types of ID. With NICHD support, scientists are taking a critical step to develop ways to measure cognitive changes in people with ID over time. Using NIH-developed cognitive tests originally tested in the general population, researchers conducted a pilot study with people of varying ages with Fragile X syndrome, DS, autism, and other causes of ID. They discovered that the tests could be used to measure important functions like working memory, processing speed, and vocabulary in individuals with IDs, and to track these changes over time. With these tools, researchers will be better able to assess both clinical and behavioral interventions to improve or maintain cognitive function in individuals with IDs.

Another core component of the IDD program focuses on understanding, describing, and managing comorbid conditions in individuals with ID. For example, now that people with DS are living far longer than they were 50 years ago, it has become apparent that middle-aged adults with DS have a much higher risk than the general population of developing Alzheimer's disease. Both conditions are characterized by neurodegeneration, the breakdown of proteins and other structures of the brain. In a recent comparison of postmortem brain tissues from individuals with DS, DS and Alzheimer's, and those with healthy brains, researchers focused on a specific process (ubiquitinylation) in the protein breakdown. They found patterns in this process that varied in the atypical tissue by diagnosis and by age. The patterns suggested inefficiencies in the process that can result in a buildup of damaged proteins, which may contribute to Alzheimer's symptoms. Further study of the process could lead to insights on how to track or treat neurodegenerative disorders, which in turn may also have relevance for the general population of aging adults.

Research that can assist clinicians and others in helping families keep children with ID healthy and safe is an important area of IDD research. Results from a recent analysis of national emergency department data on pediatric injury-related visits found significantly higher rates of injuries in youth with ID, especially those with ASD. The investigators stressed the need for developing prevention and monitoring programs to keep youth with ASD or ID safe in their communities. Additionally, individuals with DS are known to experience sleep problems,

including obstructive sleep apnea and/or behavioral sleep problems, such as waking up for long periods at night and needing parental attention. Testing for sleep problems and follow-up treatment if needed is recommended for all young children with DS. However, NICHD-supported researchers analyzed electronic health records at a large specialized children's hospital, and found that fewer than half of young patients with DS had undergone the recommended diagnostic testing. These findings emphasize the importance of screening for sleep problems in children with DS, referring children with sleep problems to appropriate specialists, and educating families about the importance of diagnosing and treating any sleep problems.

Demography and Behavior: The program in demography and behavior supports research and research training in the characteristics and dynamics of populations and subpopulations, to increase understanding of the causes and consequences of population structure and change in such areas as fertility, family demography and functioning, urbanization, migration, and subsequent implications for behavioral and social influences on health. Researchers supported by this program analyze how demographic factors relate to health and health behavior. One team of researchers used data from a nationally representative survey of over 30,000 adolescents to assess prescription opioid misuse in adolescents aged 12-17 years. An estimated 6.8 percent of rural teens and 5.3 percent of teens in large urban areas reported misusing opioids in the previous year.[2] Rural adolescents perceived substance use to be less risky, and were more likely to smoke and engage in binge drinking but were less likely to use marijuana. Regardless of whether they lived in a rural or urban area, teens that misused opioids most commonly reported friends or family as the source of the drug. Rural teens were more likely than urban teens to report having received opioids from a physician or dealer. These results may help public health officials improve programs to decrease opioid misuse, particularly in rural areas.

The demography and behavior program encompasses research in a wide range of developmental science areas, from trajectories of typical cognitive, affective, and social development to studies of language, attention, reasoning, problem-solving and multiple mechanisms underlying typical learning and learning disabilities. The NICHD's Learning Disabilities Research Centers support research to identify genetic and neurobiological characteristics of children, adolescents, and adults with learning disabilities; develop and validate classification systems for learning disabilities; expand knowledge about ways to improve comprehension for individuals who struggle with reading; assess the impact of ADHD on reading; and investigate the relationship between executive function skills and learning. Complementing the Centers, the NICHD's Learning Disabilities Innovation Hubs focus on understudied research topics that address the causes, symptoms, and treatments of learning disabilities that impact reading, writing, and mathematics.

Recently, NICHD researchers showed that children who do not know how to read can still recognize that written words symbolize meanings differently than pictures do. This is an important developmental aspect in learning how to read; though this concept can appear fundamental to literate adults, it shows that children at a very early age already know more than previously thought. Researchers presented more than 100 preschool children (aged three- to

[2] SM Monnat and KK Rigg (2016). "Examining Rural/Urban Differences in Prescription Opioid Misuse Among US Adolescents", Journal of Rural Health, 2016, 32, 204-218.

five-years-old) with a drawing or a written word, said what the word or drawing portrayed, then had a puppet illustrate the same or a different word, and asked the children whether the puppet knew what the word or drawing was. For example, if the puppet indicated that the word "dog" was a "baby" or a "puppy," then many children said that the puppet was wrong. However, many children were more likely to accept synonyms for the pictures, showing that the written words had more specific meanings than pictures. By using a novel, straightforward task that did not require the children to write, the researchers demonstrated that children possess some of the most basic conceptual knowledge of the symbolic nature of printed words before they can actually read.

Finally, the research interests of the demography and behavior program also include studies that identify the relationships among behavior, prevention, and risks to health. For example, NICHD supported a study to obtain objective data on the frequency of risk factors in the infant night-time sleep environment associated with Sudden Infant Death Syndrome (SIDS) and sleep-related infant deaths, such as accidental suffocation, entrapment, and strangulation in bed. The researchers recruited healthy newborns and their parents, and then videotaped the infants sleeping in their homes for one night at one month, three months, and six months of age. The researchers analyzed the videos, finding that even when parents are aware they are being recorded, they often place their infants in unsafe sleep environments, including non-recommended sleep surfaces, placing infants on their sides or stomachs to sleep, or allowing loose items on the sleep surface such as bedding, bumper pads, pillows, and stuffed animals. The results indicate that still more parent education is needed, particularly regarding safe sleep environments.

Rehabilitation: Through the National Center for Medical Rehabilitation Research (NCMRR), NICHD fosters research and research training to enhance the health, productivity, independence, and quality of life of people with disabilities. With a dedicated budget, this program supports a broad range of research, including efforts to understand the underlying biology of injury and disability, and the body's mechanisms of recovery and adaptation.

Rehabilitation research investments are guided by the comprehensive five-year NIH Research Plan on Rehabilitation, developed in 2016. The plan[3] was developed under the leadership of NCMRR in collaboration with stakeholders across the NIH and other Federal agencies, as well as researchers and representatives of individuals with disabilities and practitioners. The plan identifies six priority areas and details research plans and opportunities in each of them:

- *Rehabilitation across the lifespan:* Models of rehabilitation may require different approaches or considerations at different stages in life. For example, play-based rehabilitation approaches can help young children build muscle strength and learn new skills, while adaptive physical exercise programs can assist seniors in maintaining their motor functions.
- *Family and community*: Recovery may start in a hospital, but outpatient services like speech or physical therapy and mental health services are key to successful daily and long-term functioning. Caregivers play an essential but understudied role in rehabilitation management and improving quality of life for people with disabilities.

[3] https://www.nichd.nih.gov/publications/pubs/Documents/NIH_ResearchPlan_Rehabilitation.pdf

- *Technology use and development*: Technology has played a significant role in research and clinical applications in rehabilitation science, including assistive technology, orthotics, prosthetics, and others. Computational science has also played a significant role, especially in providing advanced algorithms for device control and increased use of modeling and simulation. Interdisciplinary collaboration will continue to be essential to harnessing technology to improve rehabilitation services.
- *Research design and methodology*: Improved research approaches are needed to address challenges in rehabilitation research, such as generating consistent clinical data from individuals with a variety of underlying conditions.
- *Translational science*: Rehabilitation research is poised to capitalize on advances in fundamental science. Genomic and other cell-based, process-level contributors to plasticity and healing are now better understood, potentially allowing precision medicine approaches to be used in rehabilitation research.
- *Building research capacity and infrastructure*: To expand the potential of rehabilitation research, NIH will continue its support for training the next generation of rehabilitation scientists, and supporting interdisciplinary collaboration through courses, consultation, and collaboration.

NCMRR places a special emphasis on translational research to apply gains in fundamental science to creating real-world interventions that can help people with disabilities where they live and work. In particular, NCMRR-supported researchers study the body's self-repair mechanisms so they can understand and potentially harness those mechanisms. In a recent study, scientists found that people with cerebral palsy have muscle weakness that is not related to the oxygen-fueled processes within mitochondria, the specialized structures within cells that produce the energy that cells and tissues need to function. This may open other avenues to understanding potential causes and treatments for cerebral palsy.

The rehabilitation program's activities include a special emphasis on research related to rehabilitation for stroke, spinal cord injury, and traumatic brain injury (TBI), frequently in collaboration with other NIH ICs and outside organizations. The long-term effects of TBIs are not well understood, since most studies are limited to irregular observations of TBI patients during a short period of time. Researchers analyzed years of annual cognitive testing on over 7,000 participants in three longitudinal studies, with a subset consenting to autopsy. The scientists found that people who had experienced TBI with loss of consciousness had a higher risk for symptoms of Parkinson's disease and related conditions.

NCMRR takes a collaborative approach to rehabilitation science, working with other NIH institutes, federal agencies, the business community, advocates, and other stakeholders. In a project supported by NCMRR and NINDS, scientists tested a new imaging technique that may one day permit diagnosis of the progressive brain disorder known as chronic traumatic encephalopathy (CTE) while a patient is still alive. CTE is most commonly associated with repetitive blows to the head (concussions, TBI), such as those that occur in football, boxing, and hockey. Currently, the only way to diagnose CTE definitively is examination of postmortem brain tissue, for distinctive deposits of the tau protein and other abnormalities that characterize the neurodegeneration of CTE. The new technique uses a type of imaging known as positron emission tomography (PET) with a novel ligand a radioactive substance that localizes to the

proteins of interest, which enabled the PET scans to produce visual images of tau abnormalities in the brain. When the scientists tried the technique with a retired professional football player with early CTE symptoms and a history of 22 concussions, they found a ligand pattern that suggested extensive abnormal tau deposits. Though further development and testing of the technique is needed, it may one day inform decisions for patients still functioning at relatively high levels despite CTE symptoms about continuing or halting high risk activities. The technique could also help to evaluate therapies to interrupt CTE progression.

Program Portrait: Improving Quality of Life for People with Disabilities through Rehabilitation Research
FY 2017 Level: $69.6 million
FY 2018 Level: $52.6 million
Change: -$17.0 million

According to the CDC, about 53 million Americans have some type of disability. Over the past two decades, our understanding and diagnosis of disabilities has advanced tremendously, along with new technologies that have led to implants and devices that help alleviate many obstacles to daily living for people who need them the most. Two core goals for rehabilitation scientists are to improve pain management and to help restore motor function in people with disabilities.

Pain is a fact of life for many people with disabilities, but researchers are working to reduce it. For example, many amputees experience painful sensations that seem to come from the part of the limb that is no longer there. In one recent project, scientists demonstrated that two weeks of treatment with a device that delivers repetitive transcranial magnetic stimulation (rTMS) significantly reduced this "phantom limb pain" in amputees who had lost limbs to land mine explosions. This technology, which uses a magnet to stimulate certain areas of the brain, has been used for decades to treat depression. Although the reduction in phantom pain was not permanent, the study may be a first step towards a safe and effective treatment to reduce phantom limb pain in amputees. Another research team analyzed data from a randomized controlled trial of two different chronic pain self-management interventions, for individuals with spinal cord injury, amputation, and multiple sclerosis. The results indicated that factors in individuals' resilience and vulnerability contribute equally to their experience of physical pain, but resilience factors make a larger contribution than vulnerability to mental health outcomes. The researchers suggested that more attention to strengthening resilience could ultimately help individuals with chronic pain.

A wide range of very different conditions affect motor function – cerebral palsy, spinal cord injury, and multiple sclerosis, among others. Movement is vital to overall fitness, independent living skills, and being able to participate in community life. Working with other NIH ICs and other federal agencies, NCMRR has helped develop new mobility devices. For example, brain-computer interface systems allow the brain to directly coordinate prosthetic limbs. NIH also has developed software that turns brain signals into commands for useful devices, from computers to wheelchairs. A study of physical therapy strategies in children with motor difficulties on one side of the body, caused by unilateral spastic cerebral palsy, compared the therapeutic effects of two intensive play-based training programs. Both highly structured therapy and a less structured approach improved movements in the affected hand and children's speed with use of both hands. Children with the structured training also had increases in the size and strength of the brain region controlling the affected hand, and more improvement toward completing functional tasks. The decrease in FY 2018 funding for this progam will bring commitments in line with available resources.

Intramural Research: NICHD's Division of Intramural Research (DIR) conducts interdisciplinary research to answer basic biomedical research questions and to solve difficult clinical problems in human health and development, placing special emphasis on translational research. DIR also focuses on innovative diagnostics for endocrine, metabolic, and reproductive diseases; behavioral research; and the impact of pediatric cancer on child development. DIR research includes investigations in genetics, genomics, and epigenetics, and how these factors and processes influence typical and atypical development and disease and healing processes.

Recently, intramural scientists, using 3D imaging of cellular processes, found that so-called "ghost fibers" of skeletal muscle fibers, which remain after injury-induced degeneration of muscle tissue, play a critical role in post-injury muscle regeneration. The technology enabled the scientists to visualize these processes in a mouse model, focusing on stem cells as well as "progenitor cells," which were farther along the pathway of differentiating into muscle cells. They found that stem cells were, in effect, not involved in the regenerative process but that progenitor cells migrated and divided after the injury. An unexpected discovery was that progenitor cell divisions and migrations were aligned in such a way that the progenitors spread throughout the ghost fibers, ultimately causing disorganization of regenerated muscle fibers. The scientists concluded that the ghost fibers are necessary for proportional regeneration after tissue injury, and that fabrication of bioengineered matrices that mimic living tissue matrices is needed for use in tissue regeneration therapies.

The intramural program emphasizes the importance of fundamental investigations into the physics, chemistry, and biology of cells, their component parts, and the processes that govern and regulate their function as the foundation of disease and health. Scientists in the NICHD intramural program also study the basic biophysical mechanisms that underlie cell biology and tissue function and how these factors influence development, specifically targeting the nervous, endocrine, and reproductive systems. DIR scientists recently investigated a specific physiological process that appears to lead to Smith-Lemli-Opitz syndrome (SLOS), a rare genetic disorder that disrupts the nervous system and causes a spectrum of physical and neurological symptoms, often similar to autism. The scientists discovered that the buildup of a compound, 7-dehydrocholesterol (7DHC), is an important step in how the body produces cholesterol, an essential molecule involved in several biological functions, including neurological development and function. They created a new model of SLOS by inducing stem cells from the skin of patients with the disease to form cells resembling neurons, and then tested how 7DHC interacts with cell signaling processes. They found that 7DHC caused the loss of a key signaling protein (β-catenin), which normally regulates how neurons develop. They were subsequently able to stabilize the protein, using a drug may be a potential treatment for SLOS. Detecting a specific process that results in a symptom allows researchers to identify potential new treatment targets.

Research Management and Support (RMS): RMS activities include administrative and technical functions that support and enhance the effectiveness of the Institute's research investments. Included among these functions are public communications; budget, contracts, and grants management; peer review; reporting; program evaluation; public policy; and information technology. The RMS budget also supports NICHD's health-related outreach activities. For example, the NICHD-led Safe to Sleep® campaign, formerly the Back to Sleep® campaign, provides information to educate parents and caregivers about a safe sleep environment, including the importance of placing healthy babies on their backs to sleep, for naps and at night to reduce the risk of SIDS. The NICHD's National Child and Maternal Health Education Program (NCMHEP) involves a coalition of the nation's most prominent health care provider associations, federal agencies, nonprofit maternal and child health organizations, and other partners to help translate and disseminate research findings in maternal and child health. NCMHEP's "Mom's Mental Health Matters" initiative, launched in early 2016, enables women to recognize warning signs of depression and anxiety during or after pregnancy, and encourages

them to get help. The “Mom’s Mental Health Matters” initiative includes information for fathers and partners, providers, family and friends as well as mothers.

As part of NICHD’s communications strategy, to better provide information to families, investigators and journalists on mobile platforms, a website redesign was initiated in 2016.

To support responsible stewardship of valuable resources, NICHD will continue to support systematic evaluations of NICHD’s administrative and scientific programs, helping to identify ways to ensure program effectiveness. NICHD continues to track the results of changes made related to recent reviews of NICHD’s training and career development programs and Office of Health Equity, among others.

NATIONAL INSTITUTES OF HEALTH
National Institute of Child Health and Human Development

Detail of Full-Time Equivalent Employment (FTE)

OFFICE/DIVISION	FY 2016 Final			FY 2017 Annualized CR			FY 2018 President's Budget		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
DIPHR									
Total:	28		28	28		28	28		28
Division of Extramural Research									
Total:	131	-	131	134	1	135	134	1	135
Division of Intramural Programs									
Total:	271	10	281	278	8	286	278	8	286
National Center for Medical Rehabilitation Research									
Total:	9	-	9	8	-	8	8	-	8
Office of the Director									
Total:	95	2	97	99	1	100	99	1	100
DIPHR									
Reimbursable:	-	-	-	-	-	-	-	-	-
Office of the Director									
Direct:	80	2	82	83	1	84	83	1	84
Division of Extramural Research									
Direct:	131	-	131	134	1	135	134	1	135
Reimbursable:	-	-	-	-	-	-	-	-	-
National Center for Medical Rehabilitation Research									
Direct:	9	-	9	8	-	8	8	-	8
Reimbursable:	-	-	-	-	-	-	-	-	-
Division of Intramural Programs									
Direct:	271	10	281	278	8	286	278	8	286
Reimbursable:	-	-	-	-	-	-	-	-	-
DIPHR									
Direct:	28		28	28		28	28		28
Office of the Director									
Reimbursable:	15	-	15	16	-	16	16	-	16
Total	534	12	546	547	10	557	547	10	557
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
2014	12.0
2015	12.2
2016	12.2
2017	12.2
2018	12.2

NATIONAL INSTITUTES OF HEALTH
National Institute of Child Health and Human Development

Detail of Positions[1]

GRADE	FY 2016 Final	FY 2017 Annualized CR	FY 2018 President's Budget
Total, ES Positions	1	1	1
Total, ES Salary	185,100	185,100	185,100
GM/GS-15	57	57	57
GM/GS-14	78	79	79
GM/GS-13	75	77	77
GS-12	58	65	65
GS-11	25	25	25
GS-10	2	2	2
GS-9	17	17	17
GS-8	17	17	17
GS-7	22	22	22
GS-6	2	2	2
GS-5	5	5	5
GS-4	2	2	2
GS-3	1	1	1
GS-2	0	0	0
GS-1	0	0	0
Subtotal	361	371	371
Grades established by Act of July 1, 1944 (42 U.S.C. 207)	0	0	0
Assistant Surgeon General	0	0	0
Director Grade	9	9	9
Senior Grade	1	1	1
Full Grade	0	0	0
Senior Assistant Grade	0	0	0
Assistant Grade	0	0	0
Subtotal	10	10	10
Ungraded	191	191	191
Total permanent positions	372	372	372
Total positions, end of year	562	572	572
Total full-time equivalent (FTE) employment, end of year	546	557	557
Average ES salary	185,100	185,100	185,100
Average GM/GS grade	12.2	12.2	12.2
Average GM/GS salary	106,476	108,712	110,778

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