DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute on Alcohol Abuse and Alcoholism

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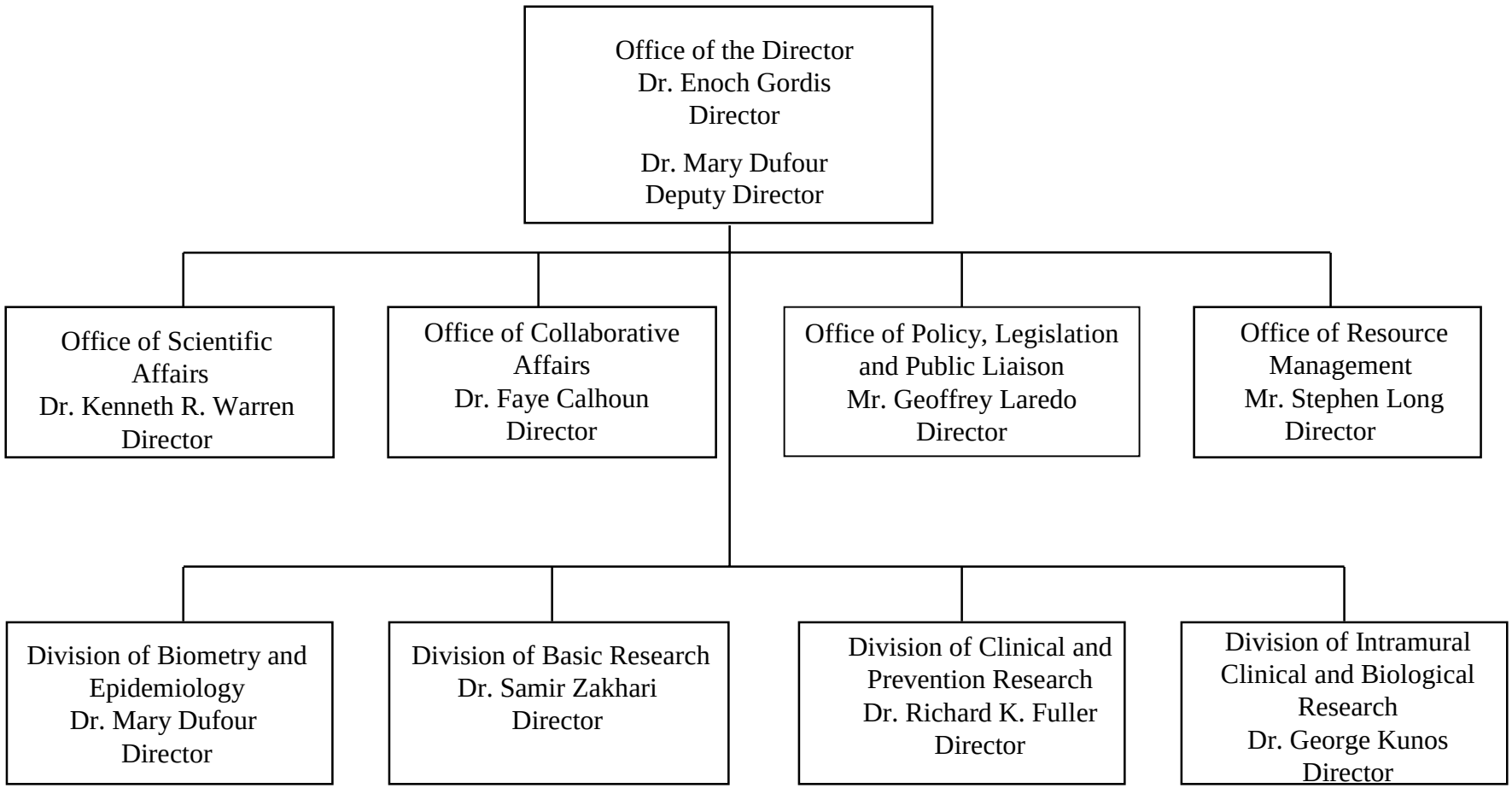
Organization Structure



NATIONAL INSTITUTES OF HEALTH

National Institute on Alcohol Abuse and Alcoholism

For carrying out section 301 and title IV of the Public Health Service Act with respect to alcohol abuse and alcoholism, [$340,678,000] *$381,966,000*.

[Departments of Labor, Health and Human Services, Education, and Related Agencies Appropriations Act, 2001 (P.L. 106-554)]

National Institutes of Health

National Institute on Alcohol Abuse and Alcoholism

Amounts Available for Obligation 1/

Source of Funding	FY 2000 Actual	FY 2001 Estimate	FY 2002 Estimate
Appropriation	$293,935,000	$340,678,000	$381,966,000
Enacted Rescission	(1,566,000)	(154,000)	---
Subtotal, Adjusted Appropriation	292,369,000	340,524,000	381,966,000
Real transfer to:			
Other NIH Institutes through the NIH Director's one-percent transfer authority	(245,000)	---	---
Other HHS Agencies through Secretary's one-percent transfer authority	(61,000)	---	---
Real transfer to HHS for the Office of Human Research Protection	(0)	(71,000)	---
Comparative transfer from:			
Office of the Director for the Academic Research Enhancement Award program	143,000	149,000	
Comparative transfer to:			
Other NIH Institutes as a result of a change in assessment formula for Central Services funding	865,000		
Subtotal, adjusted budget authority	293,071,000	340,602,000	381,966,000
Unobligated balance lapsing	(135,000)	---	---
Total obligations	292,936,000	340,602,000	381,966,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: FY 2000 - $4,123,000
FY 2001 - $ 4,300,000 FY 2002 - $4,511,000
Excludes $ in FY 2000 and $ in FY 2001 for royalties.

Justification

National Institute on Alcohol Abuse and Alcoholism

Authorizing Legislation: Section 301 and Title IV, Sections 464H and 487d of the Public Health Service Act, as amended. Reauthorizing legislation will follow.

FY 2000 Actual		FY 2001 Estimate		FY 2002 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
217	$293,071,000	237	$340,602,000	264	$381,966,000	27	$41,364,000

Budget Authority:
This document provides justification for the Fiscal Year 2002 activities of the National Institute on Alcohol Abuse and Alcoholism (NIAAA), including HIV/AIDS activities. A more detailed description of NIH-wide Fiscal Year 2002 HIV/AIDS activities can be found in the NIH section entitled AOffice of AIDS Research (OAR).@

Introduction

Second only to tobacco, alcohol is among the most abused substances in the United States. Alcohol abuse and alcohol dependence cost U.S. society an estimated $185 billion annually, according to the 1998 update of *The Economic Costs of Alcohol and Drug Abuse in the United States, 1992* (a publication of the Department of Health and Human Services, National Institutes of Health). Unlike other drugs of abuse, alcohol can damage any tissue in the body, with major consequences. It not only injures the brain, resulting in the behavioral and cognitive deficits that tend to be the most visible problems associated with alcohol misuse, but also damages other organs and systems. For example, alcohol damages the liver and alters functions of the immune and endocrine systems, with far-reaching effects.

Our mission is to develop optimal prevention and treatment strategies for alcohol-use disorders and the medical consequences of alcohol misuse. As part of this mission, we include the dissemination of our findings to clinicians and the public, to ensure that these findings reach people who suffer from alcohol-use disorders or are at risk of developing them.

Among substances of abuse, alcohol is unique in the pervasiveness of its effects on all of the body=s tissues. In the nervous system, alcohol can trigger Ahardwiring@ changes that lead to physical dependence. We are making significant advances in understanding what the molecular and genetic mechanisms that underlie these changes are; the series of cellular biochemical reactions, all of them directly or indirectly related to each other, that are involved in alcohol=s

actions. Within these cascades lie points of opportunity; for example, proteins that we can pharmaceutically block so that alcohol no longer binds with them, thus interfering with biochemical pathways that lead to alcohol-related behaviors.

The complexity of alcohol=s actions in the body calls for research in an array of disciplines, including molecular biology, genetics, neuroscience, endocrinology, and immunology, to name a few. Compounding this complexity is the fact that environmental factors also influence whether or not people develop alcohol-use disorders, and in this area, too, we conduct and support research. If we can prevent at-risk people from drinking through behavioral interventions, we can prevent the biologic changes in the brain that promote alcohol dependence. This is particularly important for young people, since those who begin drinking earlier rather than later in life stand a dramatically higher chance of becoming alcoholic.

On a broader scale, our prevention research includes social and policy issues. For example, drinking among college students is a complex problem entrenched in campuses and communities. Minority groups provide another example. Certain minority groups appear to respond differently to alcohol, physically and behaviorally, than does the general population. Our epidemiology research identifies these kinds of public-health issues, and these findings lead to basic and behavioral research that investigates root causes and potential interventions.

We bring our research findings to the public in a variety of ways. Our Research to Practice Initiative is an excellent example. In collaboration with the Substance Abuse and Mental Health Services Administration=s Center for Substance Abuse Treatment, we arrange with States to meet with treatment providers and administrators. After exchanging information about our current research findings and the practitioners= obstacles to providing treatment, we place experts in temporary residencies in treatment programs that have identified specific areas of need.

We bring our findings to the public via Alcohol Screening Day, a nationwide event that enables people to receive free screening for alcohol problems and, if needed, referrals. Last year, almost 1,500 sites across the country participated, more than 370 of them college campuses. We also are dealing with the difficult issue of college drinking through our Advisory Council=s Subcommittee on College Drinking. The Subcommittee, a unique collaboration between researchers and college presidents, has been meeting since 1998 and has commissioned 23 papers and developed two panel reports to determine how to prevent drinking by students.

Drinking by youth is not limited to college students, and we are reaching children and adolescents through our Governors= Spouses Initiative. Spouses of governors in 28 states have joined this project to reduce drinking by young people; a crucial effort, given our research findings that early initiation of drinking portends dramatically higher risk of alcoholism later in life. We also are preparing to release public service announcements on underage drinking. This report presents highlights of some of our accomplishments of the past year and describes how we can build on previous findings to advance further toward effective prevention and treatment.

Story of Discovery: Looking in Cells for the Sources of Alcoholism

Alcohol researchers are finding that at least part of the source of alcoholism can be found in certain cellular activities. Cells produce substances the body needs to function, and hundreds of synchronized biochemical reactions -- Apathways@ -- take place in them. Ultimately, these pathways influence people=s physical appearances and behaviors, including, scientists believe, drinking behaviors. Identifying pathways involved in drinking behaviors will help researchers design medications that biologically interrupt them.

None of these cellular activities happen in a vacuum. Constantly bombarding cells are molecular stimuli that tell cells what=s needed in the rest of the body. For example, some stimuli trigger conditions for nerve cells to carry electrical impulses to one another; others act as chemical messengers and receivers between nerve cells, activating pathways in them. Among these pathways is one, the cyclic AMP or AcAMP@ signaling system, that occurs inside cells and is crucial in signaling initiation of yet more cellular activities.

Alcohol researchers have built on a body of work on cAMP, conducted by investigators from a variety of fields, that began in the 1950s. Early on, investigators identified much of how the cAMP signaling system normally works. They found that the cAMP pathway acts on protein kinase A (PKA), a protein that alters the functions of other proteins by adding a phosphate molecule to them, with important results. Proteins are the chief regulators of cellular activities, and many become active only on addition of this phosphate molecule. The result is that cells can control the timing and placement of proteins= activities with the necessary precision. These activities are possible because cAMP causes the subunits that comprise PKA to split, activating one of them, the catalytic subunit. On activation, this subunit goes throughout the cell=s interior (cytoplasm), adding phosphate molecules to proteins at the right time and place.

Equally important is the catalytic subunit=s subsequent migration into the nucleus of the cell. This is where genes, the DNA blueprints that tell cells what kinds of proteins to make, reside. Here, the subunit adds phosphate to a molecule that turns on a wide variety of genes, which then Adirect@ the cells to produce specific kinds of proteins. The catalytic subunit leaves the nucleus and returns to the cytoplasm, where it re-attaches to the other subunit (PKA-R) from which cAMP had separated it earlier, making it inactive again. When the cell receives the right external signal, cAMP causes the PKA subunits to split up again, and the cycle repeats.

For the most part, external signals tell cells what they need to do by temporarily binding onto docking sites made of protein molecules that are on, or embedded in, the protective membranes that surround cells. This binding activates a cell-membrane protein that makes cAMP.

To alcohol researchers, nowhere are these activities more important than in the nervous system -- the brain -- because this is where alcohol exerts its effects on behavior. In the 1970s, alcohol researchers found that rodents= brain tissue and cultured nerve cells increased in cAMP levels when they were exposed to alcohol. The implications were significant. cAMP performs crucial functions not only in

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Story of Discovery, cont=d.

the cytoplasm of the cell, but also in its nucleus, where genes reside. These early researchers found that *acute* alcohol exposure (a bout of heavy drinking, for example) raised cAMP levels by affecting the activity of the cell-membrane protein that makes cAMP. Subsequent studies revealed that cells adapted to *chronic* alcohol exposure by reducing cAMP levels, resulting in a decrease in events farther along in its biochemical pathway. Chronic alcohol exposure reduced the amount or activity of the cell-membrane proteins that produce cAMP.

Within the past 5 years, researchers have demonstrated that alcohol promotes the rapid migration of PKA=s catalytic subunit -- the one involved in turning genes on, thereby activating protein production by cells -- to the nucleus of the cell. Normally, the catalytic subunit leaves the nucleus quickly when its function there is done, but researchers found that it stayed in the nucleus as long as alcohol was present. Thus engaged, the catalytic subunit is unavailable to return to the cell=s cytoplasm, to add phosphates to other proteins; these proteins are deprived of the normal alterations that make them work properly. The catalytic subunit=s prolonged presence in the nucleus also results in an excess of its normal activity there; that is, to add phosphate to a substance that turns on genes. Scientists are not sure of the results of this excessive turning on of genes, but they believe it may be responsible for neurophysiologic changes that lead to alcohol dependence. Research continues in this area.

At the same time scientists were exploring the involvement of cAMP signaling in *chronic* alcohol exposure, others were exploring the role of this system in alcohol=s *acute* intoxicating effects. They took a different tack. Epidemiology studies had revealed that half of the risk for alcoholism is genetic. Fruit flies are valuable research tools, because their genetic makeup is similar to that of humans, and genetic findings in one species provide clues about where to look in the other. These scientists knew that the fruit fly=s cAMP signaling system also is similar to humans=. They demonstrated that mutations in several genes involved in the cAMP system increased fruit flies= sensitivity to alcohol. Proper functioning of the cAMP signaling system, they thus demonstrated, is required for control of sensitivity to alcohol in the fly. The significance of this is that previous studies had revealed that a person=s baseline sensitivity to alcohol is directly related to his or her risk for alcoholism.

In the most recent study of the cAMP pathway=s role in alcohol dependence, scientists genetically altered mice so that the gene that encodes the PKA-R subunit B the one whose normal function is to temporarily disable the catalytic subunit B was itself inactivated. Among the potential implications were that the catalytic subunit then would go unchecked, now that PKA-R was unavailable to disable it, and would over-engage in its normal activities: adding phosphate to other proteins, including those that turn on certain genes. The result of this experiment was that the PKA-R-deficient mice were resistant to alcohol=s effects and drank more of it than did normal mice, both of which appear to portend greater risk of alcohol addiction. Thus, cAMP signaling is involved in control of alcohol sensitivity in both mice and flies, an indication that it is likely to play the same role in humans.

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Story of Discovery, cont=d.

Among drugs of abuse, alcohol is unique in the pervasiveness and complexity of its actions in the nervous system, and other pathways are likely to emerge in the search for the origins of drinking behaviors. Taken alone, none of the these studies is the last word in what causes people to become alcoholic. Taken together, however, they lend considerable weight to the assertion that the cAMP pathway is a front-runner in the search for mechanisms -- and ways to therapeutically alter them -- that lead to alcoholism.

This is how stories of discovery grow in scientific research: in steps that build on steps that came before. Ultimately, they provide scientists with the information they need to design interventions for diseases like alcoholism, an illness that destroys minds, bodies, and families.

Science Advances

Molecule Shape Determines If Alcohol Disrupts Process Crucial to Fetal Brain Development

For the brains of fetuses to develop normally, nerve cells must attach to each other via Acell-adhesion@ proteins on the cells= surfaces. Ethanol, the kind of alcohol contained in beverages, interferes with this crucial process. Different kinds of alcohols have differently shaped molecules, and researchers now have evidence that these shapes determine if an alcohol interferes with cell adhesion. The deciding factor appears to be whether or not the molecules= shapes can fit into binding sites in the cell-adhesion proteins. Presumably, if an alcohol=s molecules can fit into the binding sites, they usurp the sites= normal cell-adhesion function.

This new finding has significant implications for fetal alcohol syndrome (FAS) and fetal alcohol effects (FAE), which are caused by drinking during pregnancy and can result in lifetime neurologic deficits. FAS is the leading cause of preventable birth defects in the United States. The research described here is an important step in identifying the mechanisms involved in alcohol-related fetal damage and potential targets at which to direct pharmaceutical design.

A key task for scientists is to identify the structures of the protein binding sites and to design pharmaceuticals that will block ethanol=s deleterious interactions with them, without interfering with their normal cell-adhesion function. This would provide clinicians with a valuable tool for preventing the harmful effects of maternal drinking on the fetus.

Vitamin E Prevents Alcohol=s Damage to the Developing Mammal Brain, A Leading Cause of Mental Retardation in the U.S.

For the first time, researchers have shown that a common antioxidant B vitamin E B can prevent alcohol-induced damage in the developing brains of mammals. Researchers based their work on previous evidence that alcohol not only induces free radicals in nerve cells, but also inhibits the cells= own production of protective antioxidants. (Free radicals are damaging molecules, and

antioxidants neutralize them.) *In vitro* studies also had shown that vitamin E prevented damage to isolated nerve cells grown in culture dishes. Fetal damage resulting from maternal drinking manifests as the debilitating fetal alcohol syndrome (FAS) or as fetal alcohol effects (FAE), a cluster of more subtle cognitive and behavioral defects that often go undiagnosed but, as in FAS, may result in life-time deficits.

Scientists know that more than one biologic mechanism contributes to the development of FAS and FAE, free radicals and antioxidant inhibition being prominent among them. The finding described here is an important step in a progressive body of work aimed at identifying and therapeutically altering the neuropathology of these conditions.

Absence of Mother Biologically Linked to Stress Hormone, Alcohol Problems

For the first time, researchers have established a direct link between overproduction of a specific stress hormone by infants separated from their mothers and heavy alcohol use by the infants when they become adults. The research, conducted in primates genetically and behaviorally close to humans, suggests that stress-induced, high levels of the hormone cortisol are a powerful predictor of alcohol problems in adulthood. This, in turn, suggests new avenues for prevention and treatment of alcoholism in people at risk of these kinds of early-life, stress-related conditions.

While it might seem intuitive that anxious or stressed individuals would drink more, the question researchers are asking is Awhy?@ What are the molecular events that occur in the brain in response to stress and promote drinking behaviors? What accounts for the persistence of these molecular events that lead to heavy drinking many years after an early-life stressor, such as maternal separation, has occurred? Can we do anything to therapeutically alter the body=s stress response in these individuals, at the biologic level, to alter the stimulus to drink?

Cortisol appears to be a major player in this scenario, and researchers continue to study the molecular biology of stress hormones and alcohol. For example, alcohol investigators recently showed that pharmacologically blocking the molecules that bind to, and activate, corticotrophin-releasing hormone, a stimulator of cortisol, reduced stress responses in monkeys.

The Adolescent Brain Is Vulnerable to Alcohol-Induced Damage

Adults who go through repeated bouts of heavy alcohol use and withdrawal run the risk of changes in brain functions like memory and learning, studies show. Now, researchers have shown that children who follow the same drinking pattern also risk brain damage.

Among a group of 15- to 16-year-old alcohol-dependent children who also used but were not dependent on other substances, scientists found deficits in memory and the ability to comprehend and conceptualize pictures and other visual cues (visuospatial cognitive function). Adolescents with a history of long-time, heavy drinking had more difficulty remembering and recalling verbal and nonverbal information. Children who reported recent alcohol withdrawal symptoms were

more likely to have poorer visuospatial function. Compared to others, children reporting several withdrawals had more difficulty retrieving verbal and nonverbal information.
Adolescent brains are still developing physically. How the biologic changes that take place during this time influence alcohol=s effects on the brain remains unknown. Repeated heavy alcohol use and withdrawal could interfere with developmental changes and lead to unique kinds of brain damage. On the other hand, developmental changes could protect the brain from the damage that alcohol would cause in an adult.

The results of this study suggest that a pattern of heavy drinking and withdrawal puts adolescents at risk for brain damage. Researchers also must ask whether the neuropsychologic deficits seen in these adolescents were present before they began drinking, perhaps predisposing them to, and compounding, their problems with alcohol. These kinds of studies can lead to methods of identifying teens at risk and optimal points for intervention.

Alcohol or Mental Illness: What Does the Damage?

Among alcoholics with schizophrenia, even comparatively small amounts of drinking over the life-span result in brain damage previously thought to be associated with schizophrenia itself, new research reveals. The alcohol-induced injury occurs in the cerebellum, a part of the brain that governs motor coordination and the ability to pay attention and execute complex tasks essential for routine activities and job success. The new findings suggest that, for reasons that remain to be clarified, the cerebellum is supersensitive to alcohol in people with schizophrenia. Whether this supersensitivity is the result of biologic brain abnormalities that pre-exist schizophrenia is, as yet, unknown.

These results have diagnostic and treatment implications for the thousands of Americans who abuse alcohol and whose brains simultaneously are compromised by other illnesses associated with brain injury. Examples include people with attention deficit hyperactivity disorder, post-traumatic stress disorder, and neurologic deficits that occur in some people whose mothers drank during pregnancy. As in people with schizophrenia, these individuals= alcohol misuse places them at greater risk of brain damage, compared to people without these pre-existing conditions. Among people with schizophrenia, 24 percent are alcoholic and an additional 10 percent abuse alcohol (binge-drink, for example). Because clinicians sometimes do not consider the issue of alcohol use among their schizophrenic patients, the percentages might be higher.

Comorbidity, the appearance of alcoholism with one or more other illnesses, is a major issue in alcohol and mental-health research. Understanding the effects these conditions have on each other will have a major impact on how health-care providers design prevention programs and diagnose and treat people with both mental illness and alcohol misuse. This study underscores the importance of alcohol-abuse treatment and rehabilitation for people whose potential for independent function and contributions to society already are limited by mental illness.

New Activities

College Drinking Requires Joint Effort by Researchers, Colleges, and Communities

Media reports of alcohol-related deaths of college students are just one manifestation of a complex problem deeply entrenched in the college culture and in the communities surrounding colleges. The NIAAA has devoted considerable effort to identifying factors involved in college drinking and to designing interventions to prevent it. We plan to add research initiatives that will further our understanding and result in better-informed intervention design.

We have reviewed existing research on the contexts in which college drinking occurs and its consequences, and on prevention and treatment, and have identified gaps in the research. For example, studies have shown that partnerships between community organizations reduce drinking in the general population, but we need to evaluate whether partnerships between community organizations and colleges can reduce drinking among students. We also need to evaluate the effects of specific campus alcohol policies. In addition, investigators would benefit from capturing data on the effects of alcohol-related policy changes that occur outside their purview, such as those imposed independently by lawmakers in the community or by campus administrators. The lack of longitudinal studies that track alcohol-related behaviors from high school through young adulthood also presents a gap in the data. A NIAAA-supported data and surveillance system will facilitate research in all of these areas.

As part of our new college drinking research initiatives, we also plan to disseminate our findings. For example, we will sponsor regional and national workshops for college presidents and administrators and will distribute educational material developed for specific groups, such as students and administrators.

Medications for Alcoholism: New Advances Create New Opportunities

Advances in knowledge of how alcohol acts on the brain and other organs are providing an unprecedented opportunity to develop new medications for the treatment of alcoholism and alcohol-related organ injury. New medications introduced by NIAAA investigators in the past few years are important advances, but they represent only the beginning of the search for pharmaceuticals that are highly effective in treating alcoholism across a wide population.

In the past, we had not yet elucidated many of the biologic mechanisms in the brain that interact to cause alcohol addiction. Without this understanding, we cannot pinpoint the molecular sites responsible for alcohol addiction; thus, we cannot design medications to target these sites. The same is true of sites in the liver that are affected by alcohol. We can now apply new advances in our understanding of these mechanisms to the development of medications that will be effective in a much broader range of people with alcoholism.

We already are pursuing a number of leads in medication development. We are, for example, supporting studies of new kinds of medications B Aantisense@ drugs B that interfere with genes involved in alcohol-induced liver injury, and are evaluating other promising gene-therapy approaches for alcoholic liver disease. We also are exploring promising medications that

interact with receptors in various biochemical cell-signaling systems and with key sites in the series of reactions they trigger in brain cells, to prevent or reduce the desire to drink

However, additional potential compounds for treating alcohol disorders can come from a number of sources and should be explored, given our better understanding of alcohol=s actions. For example, some of the compounds we use in experiments to study the molecular actions of alcohol could themselves be promising medications, with more development. We can identify prototype medications from existing compounds or create new ones.

To proceed to clinical trials, compounds identified through any of these sources must undergo extensive safety and efficacy studies. The extent of the problem B14 million Americans who abuse or are dependent on alcohol and 2 million who have alcoholic liver disease B and the lack of highly effective medications to treat these diseases call for increased scientific inquiry.

Health Disparities: Research Collaboration on Toxic Effects of Alcohol

The NIAAA has a strong tradition of establishing partnerships with minority organizations, clinicians, and alcohol and other researchers. These activities lay the groundwork for addressing further a pressing issue in alcohol research: health disparities in the toxic effects of alcohol, particularly organ damage and pregnancy outcomes.

Data suggest that deaths associated with alcohol abuse are higher for African Americans, even though a higher percentage abstain from alcohol, compared to Whites. The death rate from alcohol-related cirrhosis is almost 74 percent higher in African-American males than in White males. Among White Hispanic males, the alcohol-related mortality rate is double that of their non-Hispanic counterparts. The incidence of fetal alcohol syndrome is several times higher in African Americans and some American Indian communities than in the general population. Clinical observations suggest a higher incidence of alcoholic cardiomyopathy and pancreatitis among African Americans, compared to the general population. Discussions with the National Institute of Child Health and Human Development suggest a link between alcohol consumption and sudden infant death syndrome in American Indians and Alaska Natives.

Data also suggest that ethnic groups show genetic diversity in their sensitivity to alcohol, which may result from genetic differences in metabolic factors and nervous-system reactivity.

Our collaborative research initiative will integrate the work of several disciplines and institutions. In addition to continued efforts to enable alcohol research by minority investigators and institutions, the initiative will include disparity-related studies of:

$ variations in alcohol-metabolizing genes;
$ behavioral, neuroendocrine, and electrophysiologic risk factors for organ damage;
$ below-average survival rates of cardiomyopathy patients;
$ physiologic, genetic, and environmental factors as potential causes of adverse pregnancy outcomes and increased infant morbidity and mortality; and
$ cultural and environmental issues and alcohol consumption patterns (for example, factors that

contribute to preference for specific types of beverages, such as wine, beer, or malt liquor) in specific groups, results of which will contribute to the design of physiologic studies.

Biosensor Creates New Possibilities for Tracking Alcohol Levels

Researchers and clinicians lack accurate methods of continuously measuring long-term drinking in humans. Technological advances now have made possible the development of a tamper-proof biosensor that continuously measures alcohol levels. Currently, long-term alcohol use is measured through personal interviews or questionnaires, and these self-reports are subject to memory and the desire to give socially acceptable answers.

By measuring how much and when people drink as a matter of course, in daily life, the proposed biosensor could provide accurate assessments of whether clinical interventions are effective in preventing drinking. The biosensor also could contribute to our understanding of changes that take place in the brain as it adapts to chronic alcohol use. Continuous measurements of alcohol levels in various organs could contribute to our understanding of how the body disposes of alcohol.

Other kinds of biosensors, such as those used for monitoring glucose or blood pressure, could benefit from the technology developed by this research.

The Next Step in Research on Adolescent Alcohol Use: Nonhuman Primates

Alcohol is the drug most commonly abused by adolescents and may result in unique damage to the still-developing brains of people in this age group. However, most of the neurobiologic and behavioral research on alcohol use by adolescents has been on rodents. The NIAAA is planning the preferable approach of studying mechanisms and consequences of alcohol use in adolescent primates. While research on rodents has contributed essential information, research in nonhuman primates will yield data that studies of rodents cannot. Rodents undergo only 2 to 4 weeks of adolescence, but nonhuman primates experience a 2- to 4-year adolescence and have complex social systems. The longer primate adolescence will enable us to observe relatively long-term effects of adolescent alcohol use on brain structures and functions and behaviors.

Understanding the changes that alcohol imposes on the developing adolescent brain could, for example, eventually explain why 40 percent of people who begin drinking before age 13 will become alcoholic, compared to only 10 percent of those who begin drinking as adults. Animal studies show that adolescents develop more acute tolerance to the adverse effects of alcohol than do adults. Tolerance to alcohol manifests as the need for larger doses to achieve the same effects, raising the risk of alcohol addiction. Biologic changes that occur in the brains of adolescents who develop tolerance, and how these changes, along with environmental influences, translate into behavior are examples of the kinds of issues this research initiative will address.

This research initiative will rely heavily on positron emission tomography and single-photon emission computed tomography neuroimaging, with concurrent measures of behavior, to achieve its goals.

Integrating Alcohol-Research Disciplines Captures Potential for New Neuroscience and Treatment Advances

Recent advances in various disciplines B neuroscience, behavior, and molecular genetics B can contribute valuable information to the search for new strategies to treat alcoholism. However, such strategies require an approach that integrates these advances and the disparate research of their disciplines. The depth of analysis required for this kind of integrative approach is beyond the scope of any single investigator or research group.

To capture this potential, the NIAAA last year received partial support for the Integrative Neuroscience Initiative on Alcoholism (INIA). This program fosters collaboration among research teams from various laboratories, each focusing on an issue highly specific to its own discipline and highly applicable to the problem of alcoholism. Our goal is to integrate this work, to enable us to identify mechanisms that underlie the brain=s response to alcohol. This year, NIAAA plans to increase INIA support to include three crucial areas of investigation:

Improvements in genetic engineering: Newly developed methods enable researchers to disrupt a gene=s function at specific stages of the animal=s development and in specific tissues, rather than in the whole animal and in all stages of its development. These newer technologies will enable us to determine the time, brain region, and cell type in which the protein that a gene produces normally mediates alcohol=s effects on behavior.

High-Throughput Gene Expression Assays: Research on alcoholism-related gene expression would benefit from simultaneous monitoring of changes in expression of tens of thousands of genes. Technology to conduct this kind of research is now available. Information about gene expression can help us identify brain proteins that can be therapeutically blocked from the effects of alcohol, to prevent or treat alcoholism.

Computational Neuroscience Research: INIA researchers will develop computer simulations of how alcohol affects brain functions. These simulations can generate data unobtainable through current methods.

Other Areas of Interest

Alcohol Injures All Organs -- What Are the Mechanisms of Damage Common to All Cell Types?

Alcohol=s damage is not limited to the brain and to behavior; unlike other drugs of abuse, it can damage any organ system in the body, and it frequently does so. For example, alcohol is responsible for a significant proportion of death and disability associated with the liver and heart; it alters the immune and endocrine systems; and it contributes to cancer risk. Recent techniques have enabled us to establish that a core group of interrelated biochemical processes shared by all cells of the body are particularly prone to disruption by alcohol. Integrating research on biologic mechanisms, common to a variety of cell types, that underlie alcohol-induced organ damage would contribute to design of improved treatment and prevention strategies for alcoholism.

The processes in question are involved in biologic activities crucial to survival; for example, cells produce antioxidants to protect themselves from damage that their own metabolism creates, and alcohol disrupts this balance. Alcohol disrupts normal cellular activities that lead genes to produce proteins, with ominous implications, given the multitude of cell functions that proteins regulate. Alcohol=s disruption of these and other processes result in a host of medical conditions.

Imaging Studies Can Link Brain Chemistry and Behavior in Animal Models

Noninvasive functional imaging technologies enable us to observe activities that occur in specific structures of the living brain and how changes in those structures change their functions, in real time. We have used these technologies to link alcohol-induced changes in brain structure (for example, tissue damage) to changes in function in specific parts of the brain. An unexploited potential of imaging technology is the contribution it could make to determining how chemical activities in the brain are linked to specific behaviors.

Imaging studies of animals could (1) explore how the brain adapts to chronic alcohol use and the effects of discontinuing alcohol on recovery of metabolic function in the brain, (2) define networks of nerve cells associated with craving of alcohol or cognitive deficits, and (3) assess whether the alcohol-induced damage that occurs in specific structures of the brain result in reversible or irreversible changes in cognitive function. The NIAAA has an interest in developing the animal models, techniques, and materials necessary for these kinds of studies, in concert with development and dissemination of informatics tools that would facilitate sharing of data across laboratories.

Genetically Engineered Rodents: A Valuable Tool for Alcohol Research

More than a year ago, we joined other NIH Institutes in providing funding for establishment of mouse mutagenesis centers. In this approach, scientists create random, single-gene mutations in many mice. By screening them, scientists from different fields can select mice whose mutations have resulted in traits of interest, for use in studies. We are now prepared to screen these mice to identify those whose mutations cause altered responses to alcohol. Next, we will pinpoint the locations of the altered genes, which will provide us with information for finding those genes in humans. We then can test whether the human genes play a role in heavy drinking among people.

Of particular interest is identification of genes, in rats and mice, that underlie biological mechanisms that permit an animal to drink alcohol to such excess that it is physically unable to drink any more. In the case of this trait--the ability to drink to that point--we suspect that genetic variations in the physiologic feedback loop that normally would signal animals to stop drinking play a role.

New ASNP@ Techniques Increase Precision of Search for Alcoholism Genes

Because the risk of developing alcoholism is about 50 percent genetic, the search for genes that may contribute to this disease is essential. We have successfully identified some chromosomal regions likely to contain genes that influence alcoholism. However, at this point, the methods necessarily used for this type of preliminary work limit our ability to pinpoint the genes themselves. Now, we are proceeding to the next step: application of newly developed methods that will greatly increase our ability to find the exact locations of genes that may contribute to alcoholism.

Like previous methods, the newer approaches depend on markers, variations in chromosomal DNA whose locations are known on the map that visually lays out all the genes contained in humans (that is, the genome). These markers act as points of reference when researchers try to find out where other genes that govern specific physical or behavioral traits are located on the map. Geneticists now have identified markers that are distributed at much more frequent intervals in the genome, making possible more precise gene localization. Using these newer markers, Asingle nucleotide polymorphisms@ (SNPs), scientists now can scan the entire genome for genes likely to play a role in alcoholism.

Several circumstances contribute to the timeliness of this opportunity. Previous studies conducted or supported by the NIAAA have generated several large groups of subjects ideal for this kind of genetic analysis. These groups have been thoroughly evaluated for alcohol dependence and related behavioral and physiologic traits, and samples of their DNA are readily available. Joint public and private efforts have identified a sufficient number of SNPs to cover the whole genome at the density required for scanning it. Some of the new technologies required for this work are orders of magnitude faster and less expensive than are older methods.

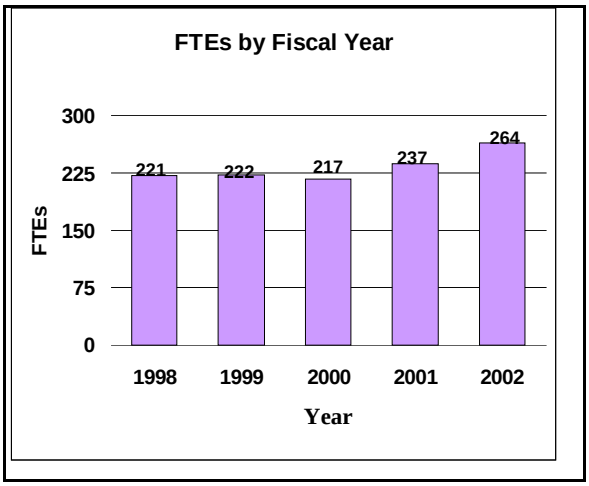
The search for genes involved in alcoholism is difficult; multiple genes interact with each other and with environmental factors to influence vulnerability to the disease. However, identification of these genes will have great potential for developing medications that target the biologic products of gene activity that promote alcoholism.

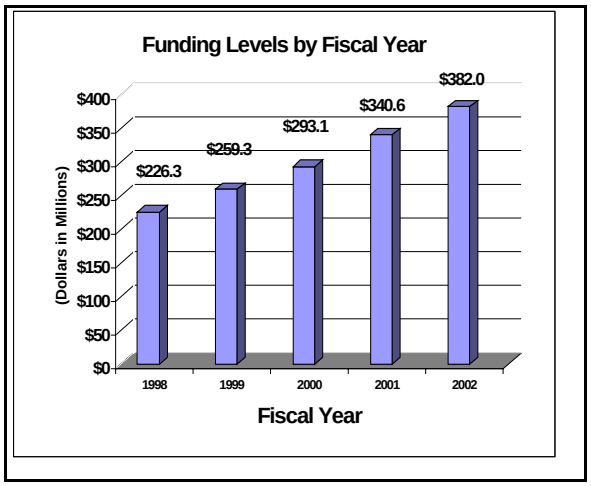
HIV and Alcohol

Alcohol is both a behavioral and biologic variable in the AIDS epidemic. People who use alcohol heavily have significantly higher rates of HIV infection and are significantly less likely to comply with AIDS medication regimens, compared to the general population. Although these findings might seem intuitive at the behavioral level, they belie the complexity of the relationship between alcohol and AIDS. For example, the changes that alcohol use induces in organ systems may influence HIV pathogenesis. We also have found that, among gay men who are infected with HIV, those who drink heavily seroconvert more quickly than do those who do not drink heavily. Increasing evidence suggests that heavy alcohol use and HIV interact to cause deficits in brain function and cognitive processes. Our goal is to develop and test improved interventions that prevent HIV infection related to alcohol use.

Budget Policy

The Fiscal Year 2002 budget request for the NIAAA is $381,966,000, including AIDS, an increase of $41,364,000 and 12.1 percent over the FY 2001 level, and $88,895,000 and 30.3 percent over FY 2000.





A five year history of FTEs and Funding Levels for NIAAA are shown in the graphs below :

One of NIH=s highest priorities is the funding of medical research through research project grants (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while providing new research opportunities. The Fiscal Year 2002 request provides average cost increases for competing RPGs equal to the Biomedical Research and Development Price Index (BRDPI), estimated at 4.3 percent. Noncompeting RPGs will receive increases of 3 percent on average for recurring costs. In FY 2002, total RPGs funded will be 730 awards, an increase of 47 awards over the FY 2001 estimate, the highest annual total ever awarded.

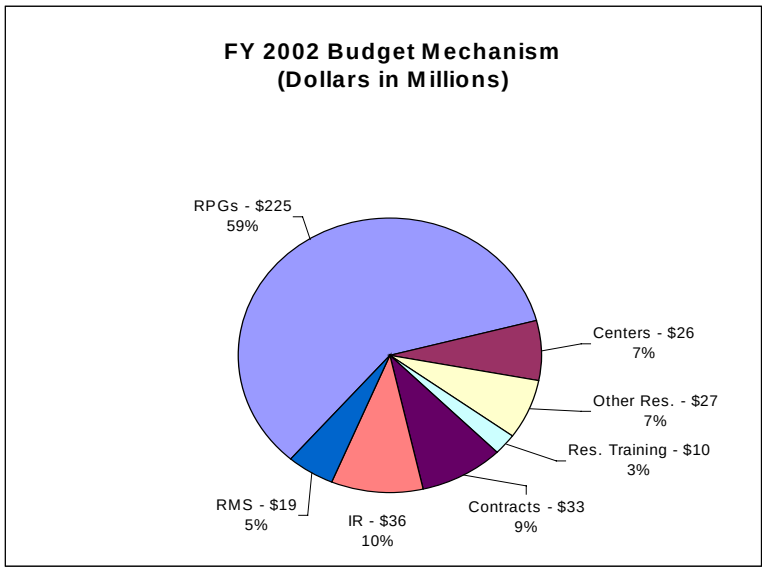
Promises for advancement in medical research are dependent on a continuing supply of new investigators with new ideas. In the Fiscal Year 2002 request, NIAAA will support 265 pre- and postdoctoral trainees in full-time training positions. An increase of 10 percent over Fiscal Year 2001 levels is provided for stipends and other training-related expenses (e.g., health insurance, research supplies and equipment, and travel to scientific meetings.

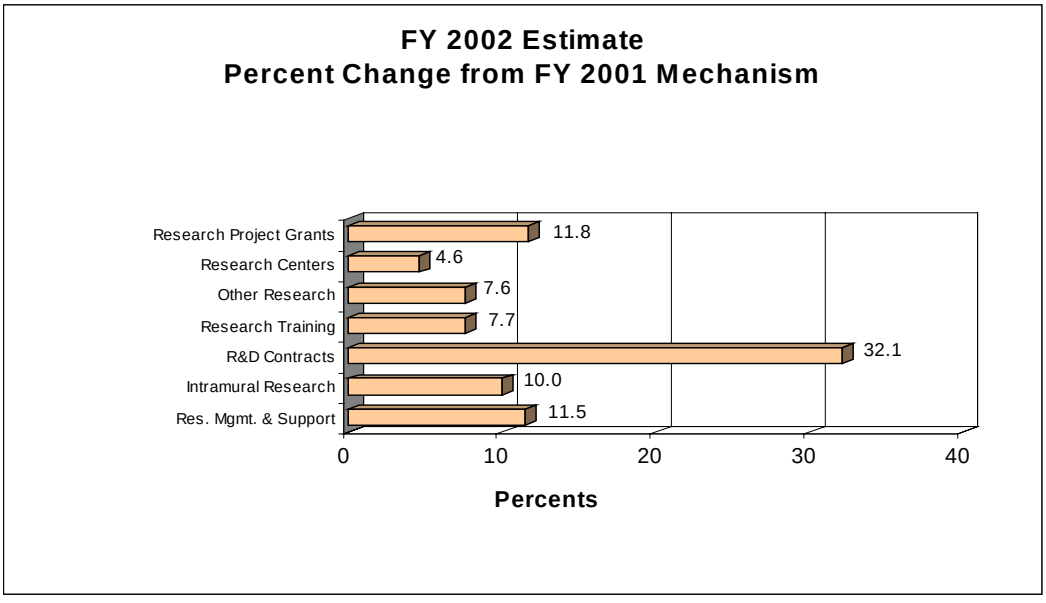
The Fiscal Year 2002 request includes funding for 15 research centers, 103 other research grants, including 6 new clinical career awards, and 40 R&D contracts. The R&D contracts mechanism also includes support for 8 contracts for the Extramural Clinical and Pediatric Loan Repayment Programs.

The FY 2002 NIAAA Research Management and Support budget request of $19,291,000, an increase of 11.5% or $1,990,000 will support the administrative costs of providing responsible

stewardship for the rapidly expanding extramural science portfolio and infrastructure costs. This level also provides support to better address the dimensions of Health Disparities and respond to the information dissemination requests of our multi-lingual constituents.

The mechanism distribution by dollars and percent change are displayed below:





NATIONAL INSTITUTES OF HEALTH

National Institute on Alcohol Abuse and Alcoholism

Budget Mechanism

MECHANISM	FY 2000 Actual		FY 2001 Estimate		FY 2002 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount
Research Projects:						
Noncompeting	441	124278000	469	146807000	503	164564000
Administrative supplements	39	1836000	27	1360000	27	1500000
Competing:						
Renewal	46	16102000	48	17563000	54	19578000
New	137	32737000	141	35707000	148	39804000
Supplements	0	0	0	0	0	0
Subtotal, competing	183	48839000	189	53270000	202	59382000
Subtotal, RPGs	624	174953000	658	201437000	705	225446000
SBIR/STTR	22	5426000	25	5170000	25	5450000
Subtotal, RPGs	646	180379000	683	206607000	730	230896000
Research Centers:						
Specialized/comprehensive	15	24157000	15	25000000	15	26150000
Clinical research	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0
Comparative medicine	0	0	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0
Subtotal, Centers	15	24157000	15	25000000	15	26150000
Other Research:						
Research careers	74	8330000	80	9717000	80	10104000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	13	11748000	13	12000000	13	12000000
Biomedical research support	0	0	0	0	0	0
Minority biomedical research support	0	0	0	0	0	0
Other	11	2338000	10	3000000	10	4500000
Subtotal, Other Research	98	22416000	103	24717000	103	26604000
Total Research Grants	759	226952000	801	256324000	848	283650000
Training:	FTTPs		FTTPs		FTTPs	
Individual awards	47	1294000	65	1873000	65	2028000
Institutional awards	188	6479000	200	6995000	200	7519000
Total, Training	235	7773000	265	8868000	265	9547000
Research & development contracts	39	17319000	36	25109000	40	33178000
(SBIR/STTR)	5	1146000	7	2489000	7	2350000
	FTEs		FTEs		FTEs	
Intramural research	92	26083000	103	33000000	115	36300000
Research management and support	125	14944000	134	17301000	149	19291000
Cancer prevention & control	0	0	0	0	0	0
Construction		0		0		0
Total, IC	217	293071000	237	340602000	264	381966000
(Clinical Trials)		-35457000		-38300000		-40600000

NATIONAL INSTITUTES OF HEALTH

National Institute on Alcohol Abuse and Alcoholism

Budget Authority by Activity
(dollars in thousands)

ACTIVITY	FY 2000 Actual FTEs	Amount	FY 2001 Estimate FTEs	Amount	FY 2002 Estimate FTEs	Amount	Change FTEs	Amount
Extramural Research:								
Alcohol Biomedical and Behavioral Research		252044		290301		326375		36074
Subtotal, Extramural research		252044		290301		326375		36074
Intramural research	92	26083	103	33000	115	36300	12	3300
Research management and support	125	14944	134	17301	149	19291	15	1990
Total	217	293071	237	340602	264	381966	27	41364

NATIONAL INSTITUTES OF HEALTH

National Institute on Alcohol Abuse and Alcoholism

Summary of Changes

2001 Estimated budget authority	340602000
2002 Estimated budget authority	381966000
Net change	41364000

CHANGES	2001 Current Estimate Base FTEs	2001 Current Estimate Base Budget Authority	Change from Base FTEs	Change from Base Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase		10008000		123000
b. Annualization of January 2001 pay increase		10008000		93000
c. January 2002 pay increase		10008000		270000
d. One extra day of pay		10008000		40000
e. Payment for centrally furnished services		5953000		595000
f. Increased cost of laboratory supplies, materials, and other expenses		17039000		577000
Subtotal				1698000
2. Research Management and Support:				
a. Within grade increase		12907000		230000
b. Annualization of January 2001 pay increase		12907000		119000
c. January 2002 pay increase		12907000		348000
d. One extra day of pay		12907000		51000
e. Payment for centrally furnished services		1595000		160000
f. Increased cost of laboratory supplies, materials, and other expenses		2799000		140000
Subtotal				1048000
Subtotal, Built-in				2746000

NATIONAL INSTITUTES OF HEALTH

National Institute on Alcohol Abuse and Alcoholism

Summary of Changes--continued

CHANGES	2001 Current Estimate Base		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	469	148,167,000	34	17,897,000
b. Competing	189	53,270,000	13	6,112,000
c. SBIR/STTR	25	5,170,000	0	280,000
Total	683	206,607,000	47	24,289,000
2. Centers	15	25,000,000	0	1,150,000
3. Other research	103	24,717,000	0	1,887,000
4. Research training	265	8,868,000	0	679,000
5. Research and development contracts	36	25,109,000	4	8,069,000
Subtotal, extramural				36,074,000
	FTEs		FTEs	
6. Intramural research	103	33,000,000	12	1,602,000
7. Research management and support	134	17,301,000	15	942,000
Subtotal, program		340,602,000		38,618,000
Total changes	237		27	41,364,000

NATIONAL INSTITUTES OF HEALTH

National Institute on Alcohol Abuse and Alcoholism
Budget Authority by Object

	FY 2001 Estimate	FY 2002 Estimate	Increase or Decrease
Total compensable workyears:			
Full-time employment	237	264	0
Full-time equivalent of overtime and holiday hours	1	1	0
Average ES salary	128488	130800	2312
Average GM/GS grade	11.5	11.6	0.1
Average GM/GS salary	65109	66281	1172
Average salary, grades established by act of July 1, 1944 (42 U.S.C. 207)	66232	68682	2450
Average salary of ungraded positions	94320	97809	3489

OBJECT CLASSES		FY 2001 Estimate	FY 2002 Estimate	Increase or Decrease
	Personnel Compensation:			
11.1	Full-Time Permanent	13735000	15495000	1760000
11.3	Other than Full-Time Permanent	2365000	2782000	417000
11.5	Other Personnel Compensation	380000	400000	20000
11.8	Special Personnel Services Payments	2243000	2725000	482000
11.9	Total Personnel Compensation	18723000	21402000	2679000
12.0	Personnel Benefits	4189000	4954000	765000
13.0	Benefits for Former Personnel	2000	2000	0
	Subtotal, Pay Costs	22914000	26358000	3444000
21.0	Travel & Transportation of Persons	422000	460000	38000
22.0	Transportation of Things	108000	222000	114000
23.1	Rental Payments to GSA	2018000	2083000	65000
23.2	Rental Payments to Others	181000	182000	1000
23.3	Communications, Utilities & Miscellaneous Charges	691000	710000	19000
24.0	Printing & Reproduction	371000	406000	35000
25.1	Consulting Services	740000	869000	129000
25.2	Other Services	1683000	1727000	44000
25.3	Purchase of Goods & Services from Government Accounts	28221000	33015000	4794000
25.4	Operation & Maintenance of Facilities	44000	68000	24000
25.5	Research & Development Contracts	10914000	16547000	5633000
25.6	Medical Care	363000	363000	0
25.7	Operation & Maintenance of Equipment	290000	377000	87000
25.8	Subsistence & Support of Persons	0	0	0
25.0	Subtotal, Other Contractual Services	42255000	52966000	10711000
26.0	Supplies & Materials	2958000	3181000	223000
31.0	Equipment	3492000	2201000	-1291000

32.0	Land and Structures	0	0	0
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	265192000	293197000	28005000
42.0	Insurance Claims & Indemnities	0	0	0
43.0	Interest & Dividends	0	0	0
44.0	Refunds	0	0	0
	Subtotal, Non-Pay Costs	317688000	355608000	37920000
	Total Budget Authority by Object	340602000	381966000	41364000

NATIONAL INSTITUTES OF HEALTH

National Institute on Alcohol Abuse and Alcoholism

Salaries and Expenses

OBJECT CLASSES	FY 2001 Estimate	FY 2002 Estimate	Increase or Decrease
Personnel Compensation:			
Full-Time Permanent (11.1)	13735000	15495000	1760000
Other Than Full-Time Permanent (11.3)	2365000	2782000	417000
Other Personnel Compensation (11.5)	380000	400000	20000
Special Personnel Services Payments (11.8)	2243000	2725000	482000
Total Personnel Compensation (11.9)	18723000	21402000	2679000
Civilian Personnel Benefits (12.0)	4189000	4954000	765000
Benefits to Former Personnel (13.0)	2000	2000	0
Subtotal, Pay Costs	22914000	26358000	3444000
Travel (21.0)	422000	460000	38000
Transportation of Things (22.0)	108000	222000	114000
Rental Payments to Others (23.2)	181000	182000	1000
Communications, Utilities and Miscellaneous Charges (23.3)	691000	710000	19000
Printing and Reproduction (24.0)	371000	406000	35000
Other Contractual Services:			
Advisory and Assistance Services (25.1)	740000	869000	129000
Other Services (25.2)	1683000	1727000	44000
Purchases from Govt. Accounts (25.3)	14769000	17172000	2403000
Operation & Maintenance of Facilities (25.4)	44000	68000	24000
Operation & Maintenance of Equipment (25.7)	290000	377000	87000
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	17526000	20213000	2687000
Supplies and Materials (26.0)	2956000	3179000	223000
Subtotal, Non-Pay Costs	22255000	25372000	3117000
Total, Administrative Costs	45169000	51730000	6561000

NATIONAL INSTITUTES OF HEALTH

National Institute on Alcohol Abuse and Alcoholism (NIAAA)

SIGNIFICANT ITEMS IN HOUSE AND SENATE
APPROPRIATIONS COMMITTEE REPORT

FY 2001 House Appropriations Committee Report Language (H.R. Report 106-645)

Item

Alcohol-Induced Liver Disease - The committee encourages NIAAA to continue its work on the role of tumor necrosis factor-alpha (TNF-alpha) and with gene knockouts, which holds promise for development of interventions to mitigate or disrupt the liver-damaging effects of TNF-alpha. (p. 87)

Action taken or to be taken

We are funding a project, in response to a request for applications (RFA), in which the gene that encodes the receptor for TNF-α has been knocked out in an animal model. Investigators will determine if this will prevent liver scarring, part of the pathogenesis of alcoholic liver disease (ALD), in mice exposed to alcohol.

The NIAAA also issued an RFA, in FY 2000, called *Microarray-Based Research on Alcohol=s Effects on Behavior, Nervous System Functions, and Organ Pathophysiology*. This research will inform investigators= efforts to design a gene therapy that blocks the action of TNF-α, for treatment of ALD.

The NIAAA is planning a symposium on the roles of various leukocytes, blood cells with immune functions, in the pathogenesis of ALD. Among the topics of discussion will be the role of TNF-α in the increased transcription of genes that encode substances involved in the migration of leukocytes to the liver.

We also have found a link between TNF-α and the greater susceptibility of women to ALD. In animals given alcohol, females produced TNF-α at levels three times greater than those of males and developed more liver injury more rapidly than did males. We will pursue this disparity further.

Item

Biological Basis of Recovery B Alcohol researchers have the initial data to begin to explore the biology of why some patients are able to recover from alcoholism, while others fail. The

Committee encourages NIAAA to enhance research in this area and to apply its findings to developing interventions that promote recovery through all available mechanisms, as appropriate, including clinical trials. (p. 87)

Action taken or to be taken

The NIAAA is developing an initiative to identify the biologic mechanisms that underlie both success and failure to recover from alcoholism. Four promising areas of research will be part of this initiative: genotyping/gene expression, neuroimaging, cognitive function, and hormonal and other changes that occur during sleep. During FY 2001, NIAAA will sponsor a workshop to develop the initiative. Based on the results of the workshop, we will issue an RFA, and we will make awards before the end of the fiscal year. We plan to fund approximately three to five grants in the first year of the initiative=s operation. Data from the initiative will aid in developing interventions that target specific biologic mechanisms that impede recovery. Promising findings will proceed to clinical trial, pending results of animal and safety studies.

Item

Minority and Ethnic Groups - The Committee encourages the Institute to continue research on the prevention and treatment of alcohol-use disorders among minority groups and, particularly, to continue research on the genetic differences in alcohol dependence among ethnic groups. (p. 87)

Action taken or to be taken

The NIAAA has developed a major plan for research on alcohol-related health disparities. This plan will be available and will be posted on the worldwide web by the time of the 2001 appropriations hearings.

In October 2000, the Institute convened a working group that reviewed methodologies for studying ethnic minorities. Among other topics, the working group discussed use of genetics as a variable in prevention studies and establishment of links between environmental factors (for example, preference for types of alcohol beverage, including malt liquor) and physical and behavioral characteristics influenced by genes. Based on the findings of the working group, the NIAAA is planning a Request for Applications.

In FY 1999, Howard University, a minority-serving institution, became one of eight NIAAA-supported sites defining genetic mechanisms and clarifying heritable phenotypes that contribute to susceptibility to alcoholism and severity of it. The University is studying African-American families with members who are alcoholic. Meanwhile, NIAAA intramural scientists are using genetic linkage analysis to look for correlations between alcoholism and certain psychiatric disorders in several Native American tribes.

FY 2001 Senate Appropriations Committee Report Language (Senate Report 106-293)

Item

Alaska native substance abuse - The Committee urges NIAAA to sponsor a Research to Practice Forum with the Substance Abuse and Mental Health Services Administration and the State of Alaska, to focus on bridging the gap between researchers and practitioners and translating scientific research into clinical applications, and encourages NIAAA to support the implementation of any recommendations developed at the forum. (p. 159)

Action taken or to be taken

NIAAA intends to establish its Research to Practice Initiative in all of the States, in partnership with SAMHSA=s Center for Substance Abuse Treatment (CSAT). We have conducted the initiative in New York and North Carolina, and NIAAA and CSAT have held preliminary discussions regarding the expansion of the program into Alaska. The first phase of the program, the Research to Practice Forum, would be designed specifically to enable clinical supervisors and directors in Alaska to incorporate current research findings into their programs. At the same time, the clinical supervisors and directors would inform researchers about obstacles to practice in the clinical setting.

In the next phase, the Researcher in Residence program, participating sites across the State would implement recommendations from the Forum. They would identify areas of need for clinical improvement, and NIAAA staff would recruit researchers with expertise in those areas. These experts would serve residencies at the requesting sites. Based on our success in moving from Phase I to Phase II in New York and North Carolina, we expect to implement the same strategy in Alaska, with attention to cultural and environmental differences.

Item

Alcohol consumption and hepatitis C B It is well established that alcohol consumption in patients with hepatitis C increases the damage caused by the disease. Less well known is the mechanism by which this happens, as well as why alcohol inhibits the success of standard treatments for the disease. Both of these areas are important for dealing with this disease, and the Committee strongly encourages the Institute to pursue them both individually and collectively with other interested Institutes. (p. 159)

Action taken or to be taken

We devoted $3.1 million to the study of alcohol consumption and the hepatitis C virus (HCV) in FY 2000. Six grant applications submitted in response to a recent RFA, *Hepatitis C Infection and Alcoholic Liver Disease*, have been funded by the NIAAA and other Institutes.

We expanded our research on alcohol and HCV in FY 2000. For example, we co-sponsored an alcohol/HCV RFA, *Hepatitis C Cooperative Research Centers,* with the National Institute of Allergy and Infectious Diseases (NIAID), the National Institute on Diabetes, Digestive and Kidney Diseases (NIDDK), and the National Institute on Drug Abuse (NIDA). This RFA facilitates collaborative research on HCV pathogenesis and recovery and explores therapeutic strategies.

A second RFA, co-sponsored by the NIAAA, NIAID, the National Cancer Institute, and the National Center for Research Resources, solicited small business applications to develop inexpensive models for HCV research, which has been hampered by a lack of appropriate animal models and *in vitro* culture systems.

The NIAAA has joined with other Institutes in co-sponsoring multi-faceted initiatives on HCV and other infections, such as HIV. In partnership with NIDA, the NIAAA issued a RFA, *Viral Hepatitis and HIV in Drug and Alcohol Users.* NIAAA, NIAID, NIDA, NIDDK, and the National Institute of Mental Health co-sponsored a research initiative, *Collaborations for Advanced Strategies in Complications of HIV Infection,* which seeks to integrate clinical and basic studies from diverse disciplines and foster collaborations for sharing of resources and expertise.

Item

Alcohol treatment services - Given the rapid growth of managed behavioral health care, the Committee is concerned that more needs to be known about how alcohol treatment services are delivered under managed care arrangements and the specific characteristics of behavioral health components of health insurance plans and managed care organizations. The Committee is supportive of the NIAAA Advisory Council's comprehensive plan for health services, particularly its recommendation to prioritize research to understand the effects of managed care on the access, utilization, quality, costs, and outcomes of alcohol treatment services. The Committee acknowledges NIAAA's progress in implementing this recommendation and encourages NIAAA to consider supporting additional research in this area. (p. 159/160)

Action taken or to be taken

We have expanded our research on how managed care affects alcohol treatment services, as our Advisory Council recommended in its report, *Improving the Delivery of Alcohol Treatment and Prevention Services: A Plan for Alcohol Health Research*. Since the Council issued its report in 1997, we have significantly increased our existing support of research in this area, supporting 20 grants and three contracts, totaling $11.8 million. During FY 2000 alone, we funded 16 grants and one contract, totaling more than $3.8 million. With this investment, the NIAAA has nearly doubled the funding that focuses explicitly on alcohol treatment under managed care systems, compared to the amount spent in FY 1996. Our overall spending on health services research rose 32 percent during that same period.

We plan to continue this expansion. In May 2000, we reissued a Program Announcement that solicited research on the impact of managed care on alcohol treatment and prevention services, among other topics. Later in FY 2001, we will reissue our general Program Announcement for health services research. This announcement, too, will emphasize the study of alcohol treatment under managed care and will encourage qualified investigators to apply for grants.

Item

Binge drinking - Alcohol abuse, particularly binge drinking and drinking with the intent to get drunk, continues to pose significant problems for college communities. The Committee strongly supports the efforts of NIAAA=s Advisory Council Subcommittee on College Drinking and encourages the Subcommittee to identify the context and consequences of college drinking and provide recommendations on the prevention and treatment of the problem.

College drinking - The Committee continues its strong support of the NIAAA Advisory Council's Subcommittee on College Drinking and its efforts to create a dialogue among college presidents, administrators, and alcohol researchers. The Committee understands that the full report will be submitted to the National Advisory Council for approval next February. This report will be organized around recommendations from the research community and college presidents. The Committee requests that the Director of NIAAA be prepared to communicate these recommendations at upcoming congressional hearings. (p. 160)

Action taken or to be taken

Members of the NIAAA Subcommittee on College Drinking have been meeting regularly, since late 1998, to address the complex problem of alcohol abuse among college students. This collaboration between college presidents and alcohol researchers is analyzing the current state of research on college drinking, various approaches to the problem, and strategies to improve communication between school administrators and the research community. The goals of the Subcommittee are to (1) advise NIAAA and policy makers as to what gaps in knowledge about college drinking need to be addressed and (2) inform college presidents and policy makers about the effectiveness of current interventions and encourage these authorities to adopt research-based solutions.

The Subcommittee commissioned 23 papers and developed two panel reports. In addition, the Subcommittee received input from students, community organizations, industry representatives, foundations, and other Federal agencies in preparing its report. The final Subcommittee report is under review by college and university presidents and researchers. When the project is complete, NIAAA and Subcommittee staff will present a summary and recommendations to college and university presidents across the country, through a series of regional workshops. The Subcommittee also is developing plans for reaching other audiences; for example, students and parents.

The NIAAA Director is prepared to discuss the Subcommittee=s recommendations at the Congressional hearings.

Item

Fetal alcohol syndrome - The Committee commends NIAAA for its sponsorship of fetal alcohol syndrome (FAS) research and prevention activities. The Committee recognizes that collaborations between many agencies and organizations are needed to address the multiple issues central to FAS. The Committee is pleased with membership of the collaborative Interagency Coordinating Committee on Fetal Alcohol Syndrome (ICCFAS) and with the progress of the ICCFAS. The Committee requests that the NIAAA, because of its leadership role in the ICCFAS, be prepared to present an update on the progress of the ICCFAS at next year=s hearings. (p. 160)

Action taken or to be taken

We devoted an estimated $21.2 million to basic-science and prevention research on fetal alcohol syndrome (FAS) in FY 2000 and will increase that amount to 23.1 million in FY 2001. In addition to our research on FAS, we continue our leadership of the Interagency Coordinating Committee on Fetal Alcohol Syndrome (ICCFAS), which is developing a 5-year strategic plan for FAS research. The plan reflects the input of the ICCFAS= membership, which includes seven organizations of the Department of Health and Human Services, the U.S. Department of Education=s Office of Special Education, and the U.S. Department of Justice=s Office of Juvenile Justice and Delinquency Prevention.

The Institute has distributed the ICCFAS Working Group report, *Prevention of Risk Drinking in Pregnancy*, for use in training clinicians and health educators. In March 2000, the ICCFAS convened a workshop to review neurobehavioral assessment techniques for early detection of developmental deficits. Experts in teratology discussed how to distinguish the neurobehavioral deficits of prenatal alcohol exposure from those of other substances or disorders. The workshop will contribute to development of a screening technique that can differentiate alcohol-related neurobehavioral deficits from others, so that health-care providers can initiate earlier and more appropriate interventions.

Item

National advertising campaign **-** The Committee encourages the National Institute on Alcohol Abuse and Alcoholism to partner with the appropriate Federal agencies on a national advertising campaign against underage drinking. (p. 160)

Action taken or to be taken

The NIAAA, in partnership with SAMHSA, is developing two television and two radio advertisements designed to address underage drinking. They are scheduled for airing in the coming months.

Item

National Alcohol Research Centers - The Committee recognizes the significant contributions these centers have made to the understanding of alcohol abuse and alcoholism and encourages the NIAAA to continue supporting these centers. (p. 160)

Action taken or to be taken

We recently issued an RFA to ensure continuation of the present number of Centers. Seven of the currently active 15 Centers are required to submit applications for renewal in 2003. The RFA also provides opportunity for new applicants to seek support through this program. At the same time, we are exploring the feasibility of raising the funding cap for the Centers program. The intent is to expand community outreach and education activities relevant to the Centers= research by providing up to $100,000 per Center.

In 2001, we will conduct a major evaluation of the program, to determine how we can strengthen it even further. Among the issues we will be reviewing are the kinds of research best suited for the Centers approach and recruitment of new and established investigators, including minority researchers, to the alcohol field, as well as retention of investigators.

Item

Alcoholic liver disease - The committee recognizes that alcoholic liver disease (ALD) is a major cause of morbidity and mortality in the United States today. Developing effective interventions for this disease is of paramount importance. The Committee is pleased that the Institute has begun to focus greater attention on this problem and encourages NIAAA to sponsor additional research on treatment. The Committee encourages NIAAA to continue its work on the role of tumor necrosis factor-alpha (TNF-alpha) and with gene knockouts, which holds promise for development of interventions to mitigate or disrupt the liver-damaging effects of TNF-alpha.
(p. 160)

Action taken or to be taken

NIAAA-supported scientists recently developed a successful *in vivo* delivery, in liver cells of rats, of a substance that blocks the mRNA involved in making the TNF-α protein. (mRNA provides cells with a copy of the genetic code for a specific protein, and the cell produces that protein.) Following two daily injections of the substance, TNF-α antisense phosphorothioate oligodeoxynucleotide liposome, TNF-α levels were reduced by 55 percent in rat livers. We plan to test the safety of this substance in rats. Results of these tests will be included in an FDA Investigational New Drug application for initiation of human studies.

Item

Prevention and treatment of violence associated with alcohol abuse - The Committee is supportive of NIAAA=s efforts to understand the relationships between alcohol use and violence. The committee encourages NIAAA to consider supporting more research in this area, particularly to understand individual characteristics and environmental conditions, situations, and circumstances under which alcohol use and violent behavior are connected. The Committee also encourages NIAAA to consider supporting additional research on the prevention and treatment of violence by persons with alcohol problems. (p. 160/161)

Action taken or to be taken

In FY 2000, the NIAAA devoted an estimated $11.3 million to the study of alcohol-related violence. During this time, we participated in a NIH-wide initiative on reducing violence among youth. We also co-funded a large grant, with the Office of Behavioral and Social Science Research, that includes the study of alcohol-related violent and criminal offenses throughout the life-span.

We are developing an intervention to prevent rape and other violent abuse in adolescent dating, in part by reducing alcohol use. Also underway is a study examining alcohol=s role in rape and other sexual assault, to provide data for design of preventive interventions. A supplement to this study assesses the problem among ethnically diverse populations. We also are studying alcohol=s impact on decision-making during marital situations that involve provocation, threat, and high levels of anger.

Another study is developing and testing a training program that will help bar managers, waiters, and waitresses reduce alcohol-related aggression in drinking environments.

New fellowships and mentored-scientist studies are developing interventions to reduce alcohol-related violence among high-school students and are examining genetic contributions to the risk of so-called Aantisocial alcoholism,@ the comorbid occurrence of alcohol abuse and antisocial behavior or antisocial personality disorders, which have been associated with violent and aggressive behavior.

In 2001, the NIAAA and the National Institute of Justice will collaborate in publishing a special issue of the NIAAA=s journal, *Alcohol Research and Health*, that focuses on alcohol and violence.

NATIONAL INSTITUTES OF HEALTH

National Institute on Alcohol Abuse and Alcoholism

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2000 Amount Authorized	2001 Estimate	2002 Amount Authorized	2002 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite	$331,734,000	Indefinite	$372,419,000
National Institute on Alcohol Abuse and Alcoholism	Section 464H(d)	42§285	Indefinite		Indefinite	
	Section	42§241				
National Research Service Awards	Section 487(d)	42§288	a/	8,868,000	b/	9,547,000
Total, Budget Authority				340,602,000		381,966,000

a/ Funding provided under the Departments of Labor, Health and Human Services, Education, and Related Agencies Appropriations Act, 2001 (P.L. 106-554).

b/ Reauthorizing legislation will be submitted.

NATIONAL INSTITUTES OF HEALTH

National Institute on Alcohol Abuse and Alcoholism

Appropriation History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1993	N/A	N/A	$180,169,000	$176,619,000 2/
Rescission				(0)
1994	173,615,000	184,700,000	184,700,000	185,617,000
Supplemental				
1995 3/	182,498,000	181,328,000	181,328,000	181,256,000 4/
Rescission				(106,000)
1996	185,712,000 3/	198,607,000	183,733,000 3/	198,607,000
Rescission				(195,000)
1997	192,280,000 3/	212,079,000	195,891,000 3/	211,870,000 5/
1998	208,112,000 3/	226,205,000	228,585,000	227,175,000
1999	229,551,000 3/6	248,778,000	259,747,000	259,747,000
Rescission				(172,000)
2000	248,916,000 3/	265,497,000	265,497,000	293,935,000
Rescission				(1,566,000)
2001	308,661,000 3/	349,216,000	336,848,000	340,678,000
Rescission				(154,000)
2002	381,966,000			

1/ Reflects enacted supplementals, recissions, and reappropriations. Prior to the FY 1999 Senate Allowance, NIAAA was a component of the ADAMHA apapropriation.

2/ Excludes enacted administrative reductions of $1,430,000, $61,000 and $601,000.

3/ Excludes funds for HIV/AIDS Research Activities consolidated in the NIH Office of Aids Research.

4/ Excludes enacted administrative reductions of $117,000, $4,000 and $68,000.

5/ Excludes enacted administrative reductions of $134,000.

6/ Reflects a decrease of $692,000 for the budget amendment for bioterrorism.

NATIONAL INSTITUTES OF HEALTH

National Institute on Alcohol Abuse and Alcoholism

Detail of Full-Time Equivalent Employment (FTEs)

OFFICE/DIVISION	FY 2000 Actual	FY 2001 Estimate	FY 2002 Estimate
Division of Intramural Clinical and Biological Research	92	103	115
Office of the Director	9	9	9
Office of Resource Management	38	38	38
Office of Scientific Affairs	21	23	27
Office of Policy, Legislation and Public Liaison	6	6	7
Office of Collaborative Research	6	10	12
Division of Clinical and Prevention Research	19	17	17
Division of Basic Research	14	17	24
Division of Biometry and Epidemiology	12	14	15
Total, NIAAA	217	237	264
FTEs supported by funds from Cooperative Research and Development Agreements	(0)	(0)	(1)

FISCAL YEAR	Average GM/GS Grade
1998	11.1
1999	11.2
2000	11.5
2001	11.5
2002	11.6

NATIONAL INSTITUTES OF HEALTH
National Institute on Alcohol Abuse and Alcoholism
Program Administration

Detail of Positions

GRADE	FY 2000 Actual	FY 2001 Estimate	FY 2002 Estimate
ES-6	0	0	0
ES-5	0	0	0
ES-4	1	1	1
ES-3	1	0	0
ES-2	1	2	2
ES-1	0	0	0
Subtotal	3	3	3
Total - ES Salary	$378,289	$385,466	$399,728
GM/GS-15	26	23	23
GM/GS-14	36	36	52
GM/GS-13	28	34	34
GS-12	24	29	29
GS-11	19	17	17
GS-10	1	1	1
GS-9	22	24	24
GS-8	7	8	8
GS-7	13	13	13
GS-6	4	3	3
GS-5	1	4	4
GS-4	3	6	6
GS-3	3	6	6
GS-2	0	0	0
GS-1	1	0	0
Subtotal	188	204	220
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	1	1	1
Director Grade	2	0	0
Senior Grade	4	4	4
Full Grade	2	2	2
Senior Assistant Grade	0	0	0

Assistant Grade	0	0	0
Co-Step	0	0	0
Subtotal	9	7	7
Ungraded	27	38	45
Total permanent positions	188	193	213
Total positions, end of year	229	252	275
Total full-time equivalent (FTE) employment,end of year	217	237	264
Average ES level	ES-3	ES-3	ES-3
Average ES salary	$126,096	$128,488	$130,800
Average GM/GS grade	11.5	11.5	11.6
Average GM/GS salary	$63,958	$65,109	$66,281

NATIONAL INSTITUTES OF HEALTH

National Institute on Alcohol Abuse and Alcoholism

New Positions Requested

	Grade	FY 2002 Number	Annual Salary
Section Chief, Intramural	AD	3	110000
Tenure Track, Intramural	AD	1	75000
Research Fellow, Intramural	AD	3	50000
Secretary, Intramural	GS-11	2	50000
Subtotal, Intramural		9	
Health Science Administrator	AD	1	110000
Health Science Administrator	GS-14	13	85000
Health Science Administrator	GS-13	1	72000
Deputy Branch Chief, OSA	GS-14	1	85000
Program Evaluation Officer	GS-14	1	85000
Internet Web Manager	GS-13	1	72000
Program Analyst	GS-9	1	42000
Grants Assistant	GS-5	1	27000
Office Automation Clerk	GS-4	1	25000
Subtotal, RMS		21	
Total Requested		30	