DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute on Alcohol Abuse and Alcoholism

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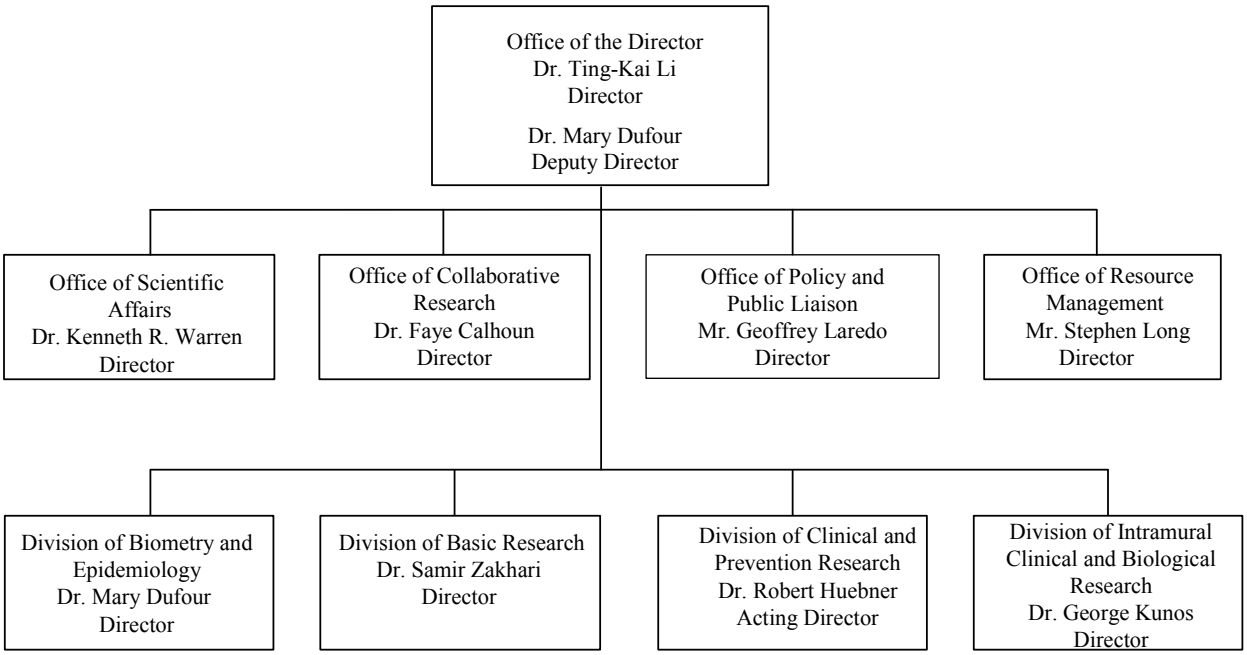
Organization Structure



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, $430,121,000.

National Institutes of Health
National Institute on Alcohol Abuse and Alcoholism

Amounts Available for Obligation 1/

Source of Funding	FY 2002 Actual	FY 2003 Amended President's Budget	FY 2004 Estimate
Appropriation	$384,238,000	$415,310,000	$430,121,000
Enacted Rescissions	(623,000)	(0)	---
Subtotal, Adjusted Appropriation	383,615,000	415,310,000	430,121,000
Real transfer to:			
Other HHS Agencies through Secretary's one-percent transfer authority	(415,000)	(0)	(0)
Comparative transfer from:			
Fogarty International Center for International Services Branch	16,000	16,000	0
Comparative transfer to:			
Office of the Director for program changes	(377,000)	(407,000)	(0)
Subtotal, adjusted budget authority	382,839,000	414,919,000	430,121,000
Unobligated Balance, start of year	0	0	0
Unobligated Balance, end of year	0	0	0
Subtotal, adjusted budget authority	382,839,000	414,919,000	430,121,000
Unobligated balance lapsing	(26,000)	---	---
Total obligations	382,813,000	414,919,000	430,121,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2002 - $6,129,000; FY 2003 - $6,245,000; FY 2004 - $6,370,000
Excludes $5,652 in FY 2002 and $4,000 in FY 2003 for royalties.

Justification

National Institute on Alcohol Abuse and Alcoholism

Authorizing Legislation: Section 301 of the Public Health Service Act, as amended. Reauthorizing legislation will be submitted.

Budget Authority:

FY 2002 Actual		FY 2003 Amended President's Budget		FY 2004 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
244	$382,839,000	245	$414,919,000	241	$430,121,000	(4)	$15,202,000

This document provides justification for the Fiscal Year 2004 activities of the National Institute on Alcohol Abuse and Alcoholism (NIAAA), including HIV/AIDS activities. A more detailed description of NIH-wide Fiscal Year 2004 HIV/AIDS activities can be found in the NIH section entitled "Office of AIDS Research (OAR)."

Introduction

In October, the World Health Organization issued *The World Health Report 2002: Reducing Risks, Promoting Healthy Life*. The report reveals that in developed countries, such as the United States, alcohol is exceeded only by tobacco and hypertension as a preventable risk factor for premature death. Alcohol is listed as a greater risk factor than are cholesterol, obesity, low fruit and vegetable intake, lack of exercise, illicit drugs, and unsafe sex, in that order.

In the WHO report's list of the 10 highest-ranking preventable risk factors for premature death globally, alcohol and tobacco are the only substances of abuse included. The report reveals that 40 percent of deaths world-wide are attributable to these 10 risk factors, with the 10 next-highest factors contributing only 10 percent of the risk.

Part of alcohol's power as a risk factor is that it not only leads to addiction and behavioral consequences that result in morbidity and mortality, as do some illicit drugs, but also may act as a toxic agent in almost any organ of the body. A portion of alcohol's disability and death rate thus is attributable to physical illness, sometimes protracted, that results from alcohol's actions on tissues and organs, at the cellular level. For example, alcohol damages the liver and alters

functions of the immune and endocrine systems, and disrupts development of fetuses, with far-reaching effects.

The mission of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) is to generate new knowledge about the causes of alcohol-use disorders and their medical consequences, and to use this knowledge to develop optimal prevention and treatment strategies. As part of this mission, we disseminate our findings to clinicians and the public, sometimes partnering with them and with Federal and State agencies, to ensure that our results reach people who suffer from alcohol-use disorders or are at risk of developing them.

Who Is Vulnerable?

Alcoholism is caused by a variety of factors, both biological and environmental. We now know that about half of the risk of alcoholism can be attributed to multiple genes. These genes produce key substances, such as proteins, in pathways of biochemical reactions that determine brain functions and thus influence behavioral responses to alcohol. Similar pathways determine physiological responses to alcohol, which may include organ damage and fetal injury. Unlike other substances of abuse, alcohol can have toxic effects in almost any tissue or organ.

In the nervous system, alcohol can trigger "hardwiring" changes – neuroadaptation – in these pathways; changes that lead to physical dependence. They involve nerve-cell responses at the genetic, molecular, and cellular levels. Meanwhile, environmental factors can moderate or exacerbate the biological influences that either predispose people to alcohol-use disorders or protect them from it.

A key question in our research is "Who among us is vulnerable to the harmful effects of alcohol?" The key to the answer lies in understanding variability; identifying the variations among us in our genes, which produce variations in our proteins – which in turn cause variations in the biochemical pathways that influence our brain functions, and thus behaviors, and our tissues' and organs' susceptibility to alcohol-induced damage. Some variations predispose the people who have them to alcoholism and organ damage, while others protect the people who have them.

Variations in our genes, and thus proteins (and thus biochemical pathways), also influence how we respond to medications for alcoholism; why the same medication results in sustained recovery for one person, but not for another. This fact has powerful implications for our medication-development research, and underscores the importance of understanding the biological underpinnings of alcohol-use disorders and alcohol-induced organ damage.

Our research is designed to help us understand not only the impact of variability in genes and proteins, but also the impact of environmental variations – such as family, peers, and socioeconomic status – on development of alcohol-use disorders. Neither type of factor, biological nor environmental, acts in a vacuum; they interact with each other to influence how a given individual, or given populations, such as different ethnic groups, responds to alcohol. Part of our research is aimed at understanding the interactions of these factors.

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Within the pathways of biological events that influence our response to alcohol or treatments for alcohol problems are points of opportunity; for example, we could pharmaceutically alter proteins so that alcohol no longer affected them, thus blocking harmful behaviors or tissue damage. Environmental factors that contribute to development of alcohol-use disorders also provide points of opportunity. Part of our research focuses on preventive interventions, at the individual, family, community, college, and policy levels, that are intended to reduce alcohol misuse and its consequences.

Outreach

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. We also are addressing the difficult issue of college drinking through our Advisory Council's Task Force on College Drinking. The Task Force, a collaboration between researchers and college presidents, recently released a major report that provides recommendations for preventing the consequences of abusive drinking by students (http://www.collegedrinkingprevention.gov/Reports/#task).

Drinking by youth is not limited to college students, and we are reaching children and adolescents through another project, the Leadership to Keep Children Alcohol-Free. Thirty-three State governors' spouses have joined this effort to reduce drinking by young people. We also have released television and radio public service announcements aimed at preventing underage drinking.

Story of Discovery: Brief Interventions for Risky Drinking

Most people would agree that preventing alcohol dependence and alcohol-induced organ damage is preferable to treating it. Preventing risky drinking prevents the biological machinery that leads to alcohol dependence and organ damage from going into motion. This story of discovery describes the development of an intervention that is reducing risky drinking.

Almost two-thirds of Americans drink beer, wine, or liquor. Most of them aren't alcoholics. However, more than 70 percent of drinkers age 21 or older exceed Department of Health and Human Services (DHHS) and Department of Agriculture (DOA) guidelines for low-risk drinking: up to two drinks per day for men and one drink per day for women and older people.

While the people who comprise the 70 percent of drinkers who exceed DHHS and DOA guidelines might not be alcohol-dependent, they are high-risk drinkers. So are people who drink heavily periodically. For example, a drink a day adds up to 14 drinks over two weeks – moderate drinking -- but anyone who has 14 drinks *in a row* once every two weeks is at high risk. Excessive alcohol use is a significant cause of car crashes, injuries, illnesses, and other consequences. Most people who exceed the daily guidelines don't seek help from alcohol-treatment professionals, so their excessive drinking, and the consequences that result, go unchecked. Many, however, are likely to have regular contact with a doctor or other healthcare provider, and therein lies an opportunity.

A strategy called "brief intervention" has emerged as a promising way to address risky drinking by nonalcoholics. It's a short therapy delivered by a healthcare provider. The intervention typically consists of four or fewer sessions lasting from a few minutes to an hour, and focuses on changing behaviors. The basic elements of a brief intervention include an assessment of how much and *how often* a patient drinks and of any alcohol-related problems the patient has experienced. If the patient's responses show high-risk alcohol use, the healthcare provider advises the patient to quit drinking or establishes a goal for reducing the patient's drinking, and suggests specific ways to help the patient attain that goal. The healthcare provider monitors the patient's progress through follow-up office visits and supportive telephone calls.

Researchers in the United Kingdom first demonstrated the effectiveness of brief intervention in primary-care settings in the late 1980s and early 1990s. One study, for example, found that after a year, alcohol consumption had declined among high-risk drinkers who received two brief interventions, followed by two supportive phone calls, from their doctors. The patients also had lower blood pressure and healthier liver-enzyme levels.

In 1997, NIAAA-supported scientists reported the results of Project TrEAT (Trial for Early Alcohol Treatment), the first large-scale U.S. study on the effectiveness of brief intervention. The study found that two 10- to 15-minute counseling visits, by physicians, followed by two 5-minute follow-up phone calls led to significant reductions in drinking by high-risk drinkers. Follow-up studies four years after Project TrEAT interventions, published in 2002, revealed that the beneficial effects were sustained. Even 5- to 10-minute interventions are effective, an NIAAA study (Project Health, published in 1999) showed.

NIAAA-supported researchers recently have extended the brief intervention concept to the emergency room. In a 1999 study, patients admitted to a trauma center for alcohol-related injuries took part in a single "motivational interview" with a psychologist. One year later, the patients' alcohol use had decreased significantly, particularly among those who initially had mild-to-moderate drinking problems. Another 1999 study evaluated the use of a 30-minute motivational interview, in the ER, for adolescents who had been involved in alcohol-related incidents. Six months later, the adolescents who had received the motivational interview had lower rates of drinking and driving and fewer traffic violations and alcohol-related injuries, compared with patients who received standard care.

Within the past 5 years, NIAAA-supported scientists have shown that brief interventions reduce problem drinking in other groups. Alcohol-related health problems are common among elderly persons. An estimated 15 percent of men and 12 percent of women over age 60 regularly drink in excess of the recommended limits. In the NIAAA-supported Project GOAL (Guiding Older Adult Lifestyles), two brief counseling sessions from their doctors significantly reduced drinking by older problem drinkers.

Researchers also have found that heavy-drinking college students who received a one-hour counseling session and a discussion of drinking risks and norms decreased their alcohol use and binge drinking over two years. Individual "motivational interviews" with high-risk first-year college students also reduced their alcohol use and alcohol-related problems.

Cost-benefit analyses offer evidence that brief interventions for problem drinkers can generate positive net benefits for patients, the health-care system, and society. A 2000 NIAAA-supported study of the economic benefits of brief intervention in primary-care settings estimated a benefit-to-cost ratio of more than 5 to 1. In other words, $10,000 invested in brief intervention yields more than $56,000 in benefits from reduced hospitalizations and emergency room use, fewer car crashes, and other cost savings (http://www.rwjf.org/reports/grr/027204s.htm). Taken together, these findings are telling us that brief interventions can reduce alcohol use and related problems by various subpopulations of nonalcoholic, high-risk drinkers in different settings.

Science Advances

Alcohol Researchers Discover First Genetic Link to Brain Waves

For the first time, researchers have linked a cluster of genes to a brainwave detected by electroencephalogram (EEG). EEG readings are reflections of electrical signals that pass from nerve cell to nerve cell in the brain. Networks of these nerve cells work in concert to enable us to process information, ultimately influencing how we behave. Variations in the EEG frequencies these electrical impulses produce correlate with certain pathological behaviors. People at risk of alcoholism, for example, tend to have different beta frequencies than do other people.

Gaba-aminobutyric acid type A ($GABA_A$), which is produced by a cluster of genes on chromosome 4, is one of the molecular receptor systems on nerve cells that govern the brain's flow of electrical traffic, thereby preventing chaos. Alcohol interferes with the speed and synchronization of the traffic flow, and alcohol is known to interfere with the $GABA_A$-receptor regulatory system.

In this new finding, scientists have linked the cluster of genes on chromosome 4 that produce $GABA_A$ receptors to the beta brain wave. Scientists from the Collaborative Study on the Genetics of Alcoholism used two types of statistical analyses, linkage and linkage disequilibrium, to come to their conclusions.

These kinds of findings will help scientists identify genes that produce the neural machinery for information processing, biomarkers for diseases like alcoholism, and points for therapeutic intervention in molecular pathways.

One Brief Counseling Session Reduces Drinking by College Students for Four Years

A single, brief counseling session appears to have long-term effects in reducing heavy drinking by college students. As a group, college students have a high rate of heavy drinking, which often results in violence, date rape, accidents, and other serious consequences, including death.

Among the few interventions that have been documented to reduce drinking in this population are brief, nonconfrontational counseling sessions. Previous studies showed that a single session greatly reduced alcohol-related problems for two years among students at high risk.

In this study, researchers examined whether the benefits of this single intervention persisted even after four years. They found that high-risk students who had received the brief counseling session continued to drink less alcohol and to experience far fewer alcohol-related problems than did high-risk students who had not received the intervention. The intervention's most significant effect was to reduce the consequences of drinking, consistent with the overall goal of harm reduction.

Alcohol consumption also declined in the control group, suggesting that much of the heavy drinking done by college students is transitory. The finding described here suggests that brief interventions can hasten this naturally occurring decline in consumption. Subsequent studies will identify the critical content and delivery components of the brief intervention.

Scientists Discover a Mechanism of Alcohol-Induced Liver Damage

For the first time, scientists have pinpointed one way that alcohol alters part of the genetic production process for tumor necrosis factor (TNF), an inflammatory protein of the immune system, to result in liver damage. Inflammation is a protective response; for example, it helps destroy some bacteria and viruses. But in excess, inflammation can do damage.

Alcoholic liver disease is an example. It progresses when alcohol enables toxins from the intestine (lipopolysaccharides, or "LPS") to leak into the blood and travel to the liver. There, the LPS toxin stimulates macrophages – cells that destroy toxins and other invaders -- to produce TNF. In small amounts, TNF helps regenerate damaged liver tissue. On exposure to alcohol, however, macrophage cells produce TNF in excess, resulting in damage.

Production of TNF starts with a gene, in the nucleus of a macrophage cell, which holds the blueprint (genetic code) that "tells" the cell how to make TNF. The gene makes a copy of this code and sends it outside the nucleus, via a molecule called mRNA, into the "production area" of the cell. In the production area, the cell translates the copy of the code and makes TNF.

Other molecules activate and synchronize the various stages of this production process. An enzyme called MAP kinase is one example. MAP kinase regulates the stage in which mRNA carries a copy of the code for TNF into the production area of inflammatory cells. LPS, the bowel toxin that increases TNF production in liver macrophage cells, activates MAP kinase.

How much TNF is produced depends on the synchronization of these stages. Alcohol results in an overproduction of TNF, and in this study, scientists asked where in the production process the problem is. They tested macrophage cells from rats fed alcohol, and mouse macrophages exposed to alcohol in culture dishes, and compared them with cells not exposed to alcohol.

Macrophage cells exposed to alcohol produced more LPS-induced TNF. The stage in which mRNA carries a copy of the code for TNF from the nucleus of the cell into its "production area" lasted longer in cells exposed to alcohol. Usually, mRNA degrades after a specific amount of time, putting an end to this stage of the production process. In alcohol-exposed macrophages, this degradation didn't take place as quickly as usual, allowing mRNA more time to "tell" the cells to make TNF.

Alcohol also potentiated the activity of LPS-stimulated MAP kinase in the cells. When investigators treated the cells with a compound that blocks the actions of one particular kind of MAP kinase ("p38"), the LPS-induced prolongation of the mRNA stage also was blocked. In other words, without activation of p38 MAP kinase, this problem doesn't occur.

Environmental Factors Are a Major Contributor to Early Alcohol Use

People who start using alcohol at young ages, in the childhood or early teen years, have a dramatically higher risk of becoming alcoholic at some point in life. This finding has raised a number of questions. Does early initiation of drinking *lead to* alcoholism? Or do certain characteristics predispose some people to engage in problem behaviors like early alcohol use *and* alcoholism, in addition to others? In either case, does the correlation between early alcohol use and alcoholism have a biological basis or an environmental basis, or both?

This study compared twin siblings and found, through genetic and statistical analyses, that environmental factors played a major role in determining whether or not the children began using alcohol by age 14. Factors associated with early alcohol use included reduced parental monitoring, less supportive home atmosphere, behavior problems in school, being female, having a twin of the opposite sex, and early puberty.

The question of whether or not there is a cause-and-effect relationship between early drinking and subsequent alcoholism remains unanswered. Another study suggests that a common vulnerability underlies not only early alcohol use, but also a number of other behavioral and psychological problems that precede early drinking. That study suggests that the common vulnerability is, at least in part, biologically based.

Whether or not early drinking leads to alcoholism, and regardless of why children begin to drink, alcohol use by children and teens is associated with immediate harm, such as injury. Preventive interventions are essential. If further research indicates that early alcohol use does, in fact, lead to alcoholism later in life -- an unknown, at this point, -- such preventive efforts will have even more far-reaching benefits.

Moderate Alcohol Use Reduces Heart-Disease Risk in Men with Adult-Onset Diabetes

A new study has found that moderate drinking is associated with lower risk of coronary heart disease (CHD) in men with Type 2 diabetes, regardless of the kind of alcoholic beverage they consume. The finding held true when other health and lifestyle factors were eliminated as potential contributors to this effect. Type 2 diabetics are an especially high-risk group for CHD.

The potential health and lifestyle confounders that researchers ruled out included body mass, smoking, family history of heart attack, high blood pressure, high cholesterol, duration of diabetes, physical activity, vitamin E supplements, and dietary intake of fats, fiber, and folate (part of the B-vitamin complex).

If scientists can discover the biological mechanisms that underlie alcohol's apparent protective effect against CHD, they can attempt to develop medications that mimic or enhance these mechanisms. Type 2 diabetics who must avoid alcohol for any one of a number of important reasons could then reap alcohol's apparent benefits without its risks.

At this time, however, clinicians can't make blanket recommendations about alcohol use for diabetic patients. Examples of reasons that diabetics and others might be prohibited from even light alcohol use are psychiatric problems, a history of drinking problems (or family history of drinking problems, which might indicate a genetic predisposition to alcoholism or high environmental risk), or potential for medication interactions with alcohol. Heavy drinking has serious health consequences and shouldn't be advised for anyone. In Type 2 diabetes, it increases risk of nerve and retinal damage, among other serious or fatal problems.

A Type of Alcohol Blocks Mechanisms that Contribute to Fetal Alcohol Syndrome

Although exposure to ethanol (the kind of alcohol in beverages) in the womb is the leading nongenetic cause of mental retardation, clinicians have no treatments to prevent its damaging effects. In a new study, octanol, another member of the alcohol family, showed a striking ability to block two specific mechanisms of ethanol-induced fetal damage in cultured mouse embryos.

One of the ways that ethanol damages the fetus is by preventing cell adhesion, the stage of development when specialized cells stick to each other to form the various tissues of the body. During this and other stages, temporary cells die at specific, synchronized times, to make way for mature cells -- the normal process of apoptosis. Besides disrupting cell adhesion, ethanol also increases apoptosis inappropriately, which can have devastating consequences.

Researchers found that octanol appears to block ethanol's disruption of specific cell-adhesion molecules called "L-1" and inappropriate induction of apoptosis. Octanol dramatically reduced ethanol-induced growth stunting and apoptosis in mouse embryo cultures at a stage of development known to be vulnerable to damage.

Treating ethanol-exposed fetuses with octanol to prevent birth defects isn't an option, since octanol itself can be toxic. However, isolating the mechanism through which octanol exerts its apparently beneficial effects holds promise for design of compounds that can safely block ethanol's damage.

New Initiatives in Alcohol Research

Basic Research on Medications Development for Alcohol-Use Disorders

Basic-research findings are the fuel that feeds development of better medications to treat alcoholism and alcohol-related problems. The goal of this initiative is to develop a basic-research program that will facilitate discovery of new compounds to treat alcohol-use disorders and their medical consequences.

Behavioral therapies currently are the most widely used treatments and are effective for some people. We have the potential to greatly expand treatment success, in a substantially larger portion of the population, with medications designed to target the biological mechanisms that underlie alcohol-use disorders and organ damage. Ultimately, effective treatment for some patients might include new medications combined with behavioral therapies. At this juncture, however, developing medications based on an understanding of the biological underpinnings of alcohol-use disorders is a top priority.

Our research will include studies of genetic factors that influence whether or not a given medication will be effective from individual to individual. Pharmacogenetic research, which elucidates genetically controlled variations in absorption, distribution, and metabolism of medications, and variations in individuals' responses to them, is especially promising.

Another component of the initiative will identify neurobiological pathways of recovery, using neurocognitive imaging methods in humans and animal models. Behavioral, structural, molecular, and physiological studies in animal models also will provide valuable information.

In designing new compounds for alcohol dependence, we will use advances in our understanding of how nerve cells' molecular gateways (receptors and ion channels) contribute to alcohol's actions in the brain. New compounds for alcohol-induced tissue damage will be based on our understanding of how alcohol affects cell communication and the functions that depend on it.

The new laboratory models we develop will help us accurately predict clinical problems that may occur in humans as a result of alcohol abuse. We will establish research partnerships to test medications in laboratory models, then confirm results in targeted populations, using more clinically relevant measures.

In addition to designing new compounds, we will expand research to identify mechanisms of action of existing drugs that appear to be effective in treating aspects of alcohol-use disorders.

Genetic Studies of Vulnerability to Alcohol

Numerous steps in the intricate biochemical and molecular processes in the brain that contribute to development of alcoholism have not yet been identified. Our goal is to identify the genes that carry blueprints for proteins, and the proteins themselves, that participate in these steps. An NIAAA initiative supports several complementary approaches to identifying genes and proteins that influence vulnerability to alcohol-related problems. These proteins are potential targets for

prevention and treatment strategies for alcoholism and alcohol-induced organ damage. Key approaches to this research include the following.

- Determining whether alcoholics have different forms of specific genes than do nonalcoholics is one method of identifying the genes that influence vulnerability to alcoholism. Linkage-disequilibrium scanning, a gene-mapping method, locates chromosomal regions that are likely to contain genes that contribute to alcoholism. New resources under development make large-scale genetic analyses possible and include a genome-wide map of 3 million gene variants (single nucleotide polymorphisms, or "SNPs"). New methods of gene-typing are orders of magnitude faster and cheaper than older methods.

  By using SNPs and other genomic and proteomic approaches (which allow scientists to study the functions and interactions of genes and proteins, respectively), NIAAA expects to identify which genes and proteins are implicated in alcohol-related diseases. The proteins involved will become potential targets for pharmacotherapeutic agents.

- Another method is to alter genes in laboratory animals, either by targeting specific genes ("knockouts") or by a more random, large-scale application of gene-mutating chemicals. In either case, scientists observe the animals' responses to alcohol, with the ultimate goal of linking specific genes to alcohol-related behaviors and their biological underpinnings. The NIAAA will support both types of approaches in seeking the genes involved in alcohol-related behavioral, neuroanatomical, neurochemical, and neurophysiological traits.

  In anticipation of complete sequencing of both the mouse and rat genomes in the near future, NIAAA also will support comparative rodent and human genetic studies. The combination of these kinds of studies and information from rodent models will help us understand mechanisms that underlie human alcoholism.

Mechanisms and Markers of Alcohol-Induced Organ Damage and Organ Protection

Heavy alcohol use has toxic effects on tissues and organs, with potentially serious or fatal sequelae, while moderate use appears to protect against cardiovascular disease and, perhaps, dementia. This initiative will integrate research on a core group of biochemical processes, common to all cells of the body, that are particularly prone to disruption by alcohol. Understanding the mechanisms that underlie these shared processes will contribute to development of (1) genetic and molecular biomarkers of susceptibility and of cellular changes that initiate tissue injury, which can be used in prevention strategies, and (2) pharmacogenomic treatment strategies.

Of particular interest is the role of this core group of mechanisms in susceptibility to:

- fetal damage induced by maternal drinking, which often results in life-long defects;

- alcohol-related tumor formation, in general and in specific cancers (breast, hepatocellular, esophageal, mouth, pharynx, larynx);
- liver damage, especially the acceleration of hepatitis C in patients who use alcohol;
- alcohol-induced pancreatitis, which comprises 70 percent of all cases;
- cardiomyopathy, hypertension, and stroke associated with heavy alcohol use; and
- cardioprotection and dementia protection associated with light or moderate alcohol use.

Research will be based on processes implicated in medical conditions arising from alcohol-induced cellular dysfunction, including alterations in gene, protein, and enzyme activity; protein production; free-radical production; lipoproteins (fat and protein compounds that perform vital cellular functions); metabolites (products of metabolism); hormones; and immune-system components; and changes in DNA associated with alcohol-related depletion of S-adenosyl-methionine (a building block of proteins that serves the important cellular function of changing compounds into other compounds, including the neurotransmitters through which brain cells communicate).

Behavioral and Genetic Risk Factors for Alcoholism

We need to know what factors put people at risk of developing alcoholism, or protect people from it, in order to develop effective prevention strategies. About half of the risk appears to be genetic; the other half stems from environmental factors. These factors are numerous, change throughout the lifespan, and occur in multiple combinations. This initiative will identify these risk factors and determine how they interact with each other to result in alcohol-use disorders.

Large, longitudinal, multidisciplinary studies of the same individuals throughout life will provide the necessary data for analysis. In addition to on-going twin and family genetic studies (such as NIAAA's Collaborative Studies on the Genetics of Alcoholism) and population-wide epidemiology studies (such as NIAAA's National Epidemiologic Survey on Alcohol and Related Conditions), we will conduct natural experiments that measure and differentiate environmental and genetic risks. Cultural and ethnic minorities offer particular advantages for detecting genetic and environmental factors, and will be included in this initiative.

We are seeking collaborations with agencies and Institutes whose missions would be advanced by this kind of research.

Long-Term, Community-Based Prevention of Alcohol Problems at Different Life Stages

Each stage of life is characterized by unique environmental and developmental factors that influence vulnerability to alcohol-use disorders. This initiative will determine if community-based approaches successful in preventing alcohol-use disorders in the short-term can result in long-term prevention at different life stages.

> College Students are at exceptionally high risk of developing alcohol-related problems. Recent estimates suggest that, each year, 1,400 of the 500,000 college students who sustain alcohol-related injuries die from them, and 600,000 students are involved in alcohol-related assaults. In 1998, the NIAAA Task Force on College Drinking joined

researchers and college administrators together, to begin a major effort to address this problem. In 2002, after four years of research on the issue, the Task Force published a report, which includes recommendations. Among them are that college drinking be approached not only from the individual and campus perspective, but also from the community perspective.

High school students also have a high rate of episodic, heavy drinking, which predicts post-high school drinking patterns. Previous research suggests that reducing alcohol availability in the community is a key prevention strategy for this age group. In addition to school and community strategies, we will evaluate one-on-one sessions and the role of parental alcoholism.

Young children can be identified as being at high risk long before they begin drinking, based on family history; behaviors, such as conduct disorder; and beliefs about alcohol. We will focus on family training, including the effects of parental alcoholism, and the impact of community factors, such as teacher and health-professional involvement. Other NIH Institutes will be invited to participate in these studies.

The elderly are at risk of isolation and depression, and of onset of alcohol problems at lower drinking quantities than those of younger adults. Chronic diseases are common among the elderly, who are vulnerable to adverse interactions between medications and alcohol. They may suffer more severe sequelae from alcohol misuse than do other groups. Strategies effective in younger populations will be adapted for this age group, and tested.

Identifying the Neuroscientific Basis of Alcohol-Related Behaviors

We are preparing to undertake the final expansion of an initiative that is enabling us to link underlying neuroadaptive mechanisms, including those associated with stress, with the behaviors of alcoholism. The goal of the Integrative Neuroscience Initiative on Alcoholism (INIA), a collaborative effort, is to provide data for rational development of improved treatments for this disease.

The body's response to stress, a major contributor to drinking and inability to sustain recovery from alcoholism, is complex. Stress activates some of the same brain systems as does alcohol, suggesting that it contributes to molecular changes – "neuroadaptation" – that underlie the craving and compulsive drinking that are hallmarks of alcoholism. The final expansion of INIA addresses these and other molecular changes, and will introduce the following elements:

Proteomics Approach to Protein Modifications and Interactions: Alcohol-induced disruptions of protein-protein interactions that perturb brain-cell activity and cell-to-cell communication are understudied in alcohol research. The timing and amount of production of these proteins, and changes in their composition after they've been produced, are essential to this research, given the importance of proteins as regulators of biological and behavioral activities disrupted by alcohol.

Structural Plasticity: Nervous-system connections restructure during neuronal processing of functions like learning and memory. We expect that this structural plasticity also occurs during neuroadaptation to alcohol. Current studies of neural pathways and networks in neuroadaptive behavior formation will be expanded to include "synaptic connections," junctions where chemical messages transmit from nerve cell to nerve cell.

Translational Research: We will establish whether neurobiological changes observed in our animal models of alcohol-related behavior also occur in humans. Proposed methods include (1) electrophysiologic recording of neuronal activity in brain regions and neural circuits, networks of nerve cells that act in concert, (2) noninvasive brain-imaging techniques, to define neural networks that respond to acute alcohol exposure and to monitor progression of network involvement during development of neuroadaptive behaviors, and (3) measures of how the neuroendocrine system, which is very active in stress scenarios, changes with behavioral responses to alcohol.

INIA's collaborative approach is essential, because disparate models and methods from diverse fields, from behavior to molecular biology and genetics, were clouding the relevance of one set of results to another. The two consortia that comprise INIA removed bottlenecks in the research by developing new, standardized animal models and introducing technology and tools that enable integration of results. One consortium is characterizing alcohol-induced alterations in neuronal responses to stress and anxiety; the other is identifying neuronal responses to alcohol in the amygdala (putative locus of the brain's reward circuitry).

Other Areas of Interest in Alcohol Research

FAS: A Multi-site, Collaborative Initiative on Fetal Alcohol Syndrome

Children with fetal alcohol syndrome and alcohol-related neurodevelopmental disorders have serious neurobehavioral deficits and other physical problems that impair daily function and often persist throughout life. In the U.S., these conditions disproportionately affect American Indians, Native Alaskans, and African Americans. The NIAAA Collaborative Initiative on Fetal Alcohol Spectrum Disorders will support a consortium of individual investigators, multi-site collaborations, and collaborations between basic-science investigators and clinical scientists. This initiative will ensure that laboratory findings reach the clinical research setting and that they reach the populations most affected.

To develop preventive therapies and treatments, researchers must identify how alcohol damages the fetal nervous system at the molecular and cellular levels, and correlate these damaged areas with behavior problems. Recent technologies make this goal attainable. Emerging biomedical technologies, including noninvasive imaging, and newly developed neurobehavioral assessment techniques will accelerate research aimed at (1) preventing alcohol's damage to the fetal nervous system; (2) treating or reversing alcohol-induced damage once it has occurred (3) improving our understanding of specific neurobehavioral problems in children affected by prenatal alcohol exposure, so that we may develop early-education interventions.

Women, HIV/AIDS, and Alcohol

Alcohol consumption appears to play a role in the sexual transmission and progression of HIV/AIDS, rates of which have risen among women in recent decades. Collaborative NIAAA studies will examine the epidemiology, natural history, pathogenesis, prevention, treatment, and control of HIV/AIDS in this population. Our goals are to:

- understand the role of alcohol in HIV transmission and disease progression in women;
- develop and test interventions that (1) reduce risk of alcohol-related events of HIV transmission in women, including mother-to-child transmission, and (2) treat HIV-positive women who abuse alcohol or are dependent on it.
- disseminate research findings, including data, strategies, and models for prevention; and
- engage community-based networks in developing culturally-appropriate interventions.

The *UNAIDS Report on the Global HIV/AIDS Epidemic, 2002*, states that 18.5 million women are living with HIV/AIDS worldwide. In the United States, African-American and Hispanic women are affected disproportionately. To achieve our research goals for this population, we must understand (1) alcohol's impact on the immune system's susceptibility to HIV and opportunistic infections and (2) the liver's ability to metabolize anti-HIV medication, and other ways in which alcohol might contribute to accelerating the course of HIV infection in women.

Disparities in Adverse Effects of Alcohol

Gender and ethnic differences appear to play a role in the etiology and effects of alcoholism. Understanding these differences is a prerequisite for developing effective treatments for alcoholism and its sequelae in women and ethnic minorities. Among the issues that NIAAA will explore are risk factors that place women and some minority groups at higher risk of specific kinds of pathology, such as liver or heart disease, with alcohol use.

The Institute also will study genetic risk factors and will determine how sociocultural factors interact with genetic variations (in expression of alcohol-metabolizing enzymes, for example) to produce ethnic or gender differences in vulnerability to alcoholism and organ damage. Other studies will assess behavioral, neuroendocrine, and electrophysiological risk factors for alcoholism as a function of gender and ethnic background. Patterns of drinking and diet will be among the behavioral factors assessed.

Our efforts to increase alcohol research capacity at institutions in minority communities is expected to improve research in these areas. By increasing collaboration between research institutions and institutions that serve minority populations, the NIAAA intends to increase the number and quality of alcohol-related studies of minority communities.

Advancing Behavioral Therapies for Alcoholism

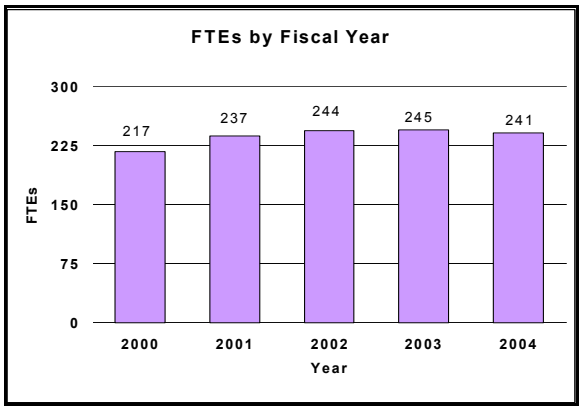
Behavioral, nonpharmacological therapies currently are the most widely used method of treating alcohol dependence and alcohol abuse. To advance the effectiveness of behavioral therapies, we are examining approaches to improving clinicians' abilities to engage and retain adults and adolescents in treatment. We intend to expand research on (1) the mechanisms of action of successful behavioral therapies, (2) behavioral therapies for alcohol-abusing patients who have

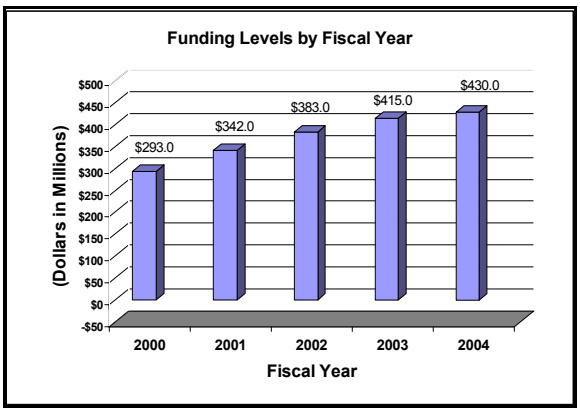
psychiatric disorders, which significantly complicates therapeutic interventions, and (3) combinations of new medications with behavioral therapies to sustain recovery.

In FY 2004, NIAAA will expand its collaboration with the Substance Abuse and Mental Health Services Administration in developing its health services research portfolio to enable a more rapid translation of research findings into the delivery of substance abuse treatment and prevention services.

Budget Policy

The Fiscal Year 2004 budget request for the NIAAA is $430,121,000, including AIDS, an increase of $15,202,000 and 3.7 percent over the FY 2003 amended President's Budget Request. A five year history of FTEs and Funding Levels for NIAAA are shown in the graphs below. Note that Fiscal Years 2001 and 2000 FTE's are not comparable for the NIH Human Resources functional consolidation.





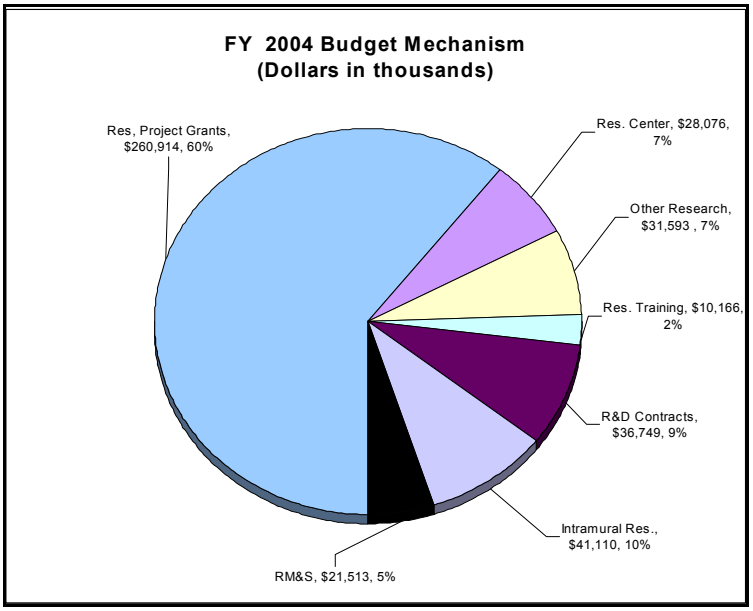
NIH's highest priority is the funding of medical research through research project grants (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while providing new research opportunities. NIAAA will provide an aggregate average cost increase of 2.6 percent for Research Project Grants (RPGs).

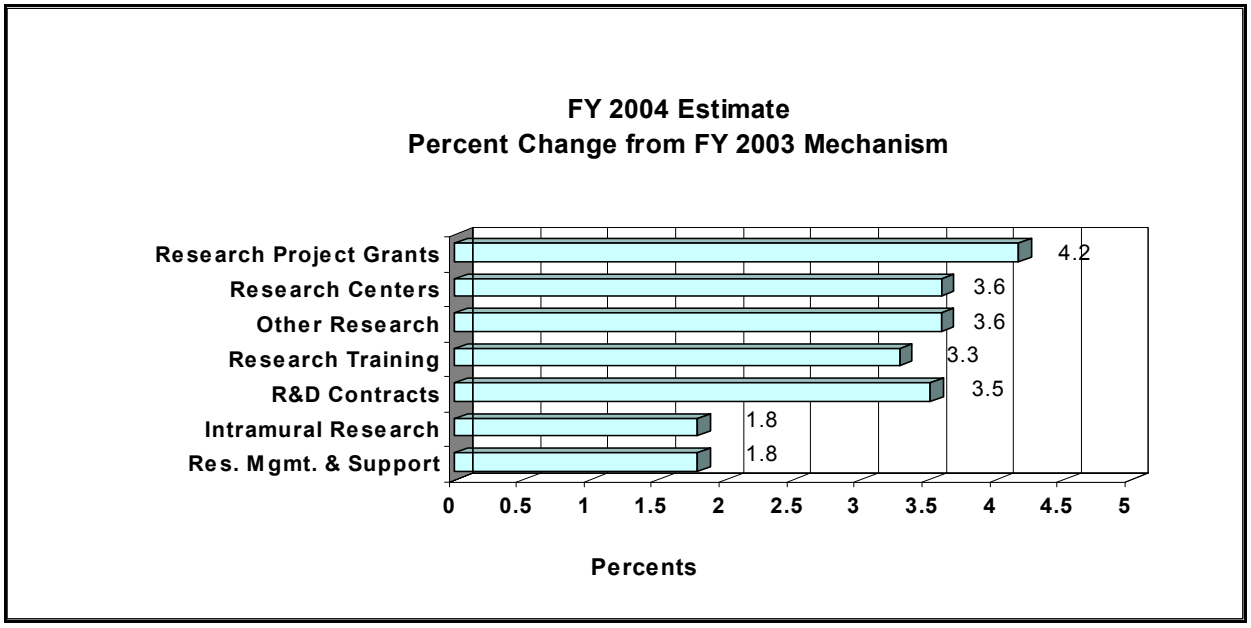
Also in FY 2004, NIAAA will fully fund 3 grants under the R15 mechanism. This mechanism is for Academic Research Enhancement Awards (AREA).

Promises for advancement in medical research are dependent on maintaining the supply of new investigators with new ideas. In the Fiscal Year 2004 request, NIAAA will support 247 pre- and postdoctoral trainees in full-time training positions, the same number as in FY 2003. Stipend levels for NRSA trainees will increase by 4 percent for predoctoral fellows, and from 4-1 percent, based on years of experience, for postdoctoral fellows.

The Fiscal Year 2004 request includes funding for 15 research centers, 112 other research grants, including 85 clinical career awards, and 49 R&D contracts. Intramural Research and Research Management and Support receive increases of 1.8 percent over FY 2003.

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


FY 2004 Budget Mechanism
(Dollars in thousands)
Res, Project Grants, $260,914, 60%
Res. Center, $28,076, 7%
Other Research, $31,593 , 7%
Res. Training, $10,166, 2%
R&D Contracts, $36,749, 9%
Intramural Res., $41,110, 10%
RM&S, $21,513, 5%


FY 2004 Estimate
Percent Change from FY 2003 Mechanism
Research Project Grants
Research Centers
Other Research
Research Training
R&D Contracts
Intramural Research
Res. Mgmt. & Support
4.2
3.6
3.6
3.3
3.5
1.8
1.8
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
Percents

NATIONAL INSTITUTES OF HEALTH

National Institute on Alcohol Abuse and Alcoholism

Budget Mechanism - Total

MECHANISM	FY 2002 Actual		FY 2003 Amended President's Budget		FY 2004 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount
Research Projects:						
Noncompeting	513	$170,266,000	526	$184,727,000	539	$191,589,000
Administrative supplements	(43)	3,308,000	(35)	2,715,000	(35)	2,786,000
Full funded	0	0	0	0	3	450,000
Single year	192	53,393,000	192	55,529,000	189	58,294,000
Renewal	26	11,894,000	38	11,106,000	38	11,659,000
New	166	41,499,000	154	44,423,000	151	46,635,000
Supplements	0	0	0	0	0	0
Subtotal, competing	192	53,393,000	192	55,529,000	192	58,744,000
Subtotal, RPGs	705	226,967,000	718	242,971,000	731	253,119,000
SBIR/STTR	20	8,207,000	35	7,495,000	35	7,795,000
Subtotal, RPGs	725	235,174,000	753	250,466,000	766	260,914,000
Research Centers:						
Specialized/comprehensive	15	25,750,000	15	27,100,000	15	28,076,000
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	141,000	0	0	0	0
Subtotal, Centers	15	25,891,000	15	27,100,000	15	28,076,000
Other Research:						
Research careers	80	9,429,000	85	10,910,000	85	11,303,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	13	11,665,000	15	12,900,000	15	13,364,000
Biomedical research support	0	0	0	0	0	0
Minority biomedical research support	0	0	0	0	0	0
Other	6	4,472,000	12	6,685,000	12	6,926,000
Subtotal, Other Research	99	25,566,000	112	30,495,000	112	31,593,000
Total Research Grants	839	286,631,000	880	308,061,000	893	320,583,000
Research Training:	FTTPs		FTTPs		FTTPs	
Individual awards	49	1,482,000	53	1,637,000	53	1,690,000
Institutional awards	188	8,000,000	194	8,205,000	194	8,476,000
Total, Training	237	9,482,000	247	9,842,000	247	10,166,000
Research & development contracts	31	30,291,000	49	35,500,000	49	36,749,000
(SBIR/STTR)	(3)	(300,000)	(8)	(1,900,000)	(9)	(2,200,000)
	FTEs		FTEs		FTEs	
Intramural research	106	37,049,000	106	40,383,000	104	41,110,000
Research management and support	138	19,386,000	139	21,133,000	137	21,513,000
Cancer prevention & control	0	0	0	0	0	0
Construction		0		0		0
Total, NIAAA	244	382,839,000	245	414,919,000	241	430,121,000
(Clinical Trials)		(38,553,000)		(41,597,000)		(43,138,000)

NATIONAL INSTITUTES OF HEALTH
National Institute on Alcohol Abuse and Alcoholism

Budget Authority by Activity
(dollars in thousands)

ACTIVITY	FY 2002 Actual FTEs	FY 2002 Actual Amount	FY 2003 Amended President's Budget FTEs	FY 2003 Amended President's Budget Amount	FY 2004 Estimate FTEs	FY 2004 Estimate Amount	Change FTEs	Change Amount
Extramural Research:								
Alcohol Biomedical and Behavioral Research		$326,404		$353,403		$367,498		$14,095
Subtotal, Extramural research		326,404		353,403		367,498		14,095
Intramural research	106	37,049	106	40,383	104	41,110	(2)	727
Res. management & support	138	19,386	139	21,133	137	21,513	(2)	380
Cancer Control & Prevention	0	0	0	0	0	0	0	0
Total	244	382,839	245	414,919	241	430,121	(4)	15,202

NATIONAL INSTITUTES OF HEALTH
National Institute on Alcohol Abuse and Alcoholism

Summary of Changes

2003 Amended President's Budget				$414,919,000
2004 Estimated Budget Authority				430,121,000
Net change				15,202,000
	2003 Amended President's Budget Base		Change from Base	
CHANGES	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase		$12,265,000		$152,000
b. Annualization of January 2003 pay increase		12,265,000		95,000
c. January 2004 pay increase		12,265,000		184,000
d. One extra day of pay		12,265,000		47,000
e. Payment for centrally furnished services		6,726,000		135,000
f. Increased cost of laboratory supplies, materials, and other expenses		21,392,000		333,000
Subtotal				946,000
2. Research Management and Support:				
a. Within grade increase		14,425,000		241,000
b. Annualization of January 2003 pay increase		14,425,000		112,000
c. January 2004 pay increase		14,425,000		216,000
d. One extra day of pay		14,425,000		55,000
e. Payment for centrally furnished services		2,485,000		50,000
f. Increased cost of laboratory supplies, materials, and other expenses		4,223,000		68,000
Subtotal				742,000
Subtotal, Built-in				1,688,000

NATIONAL INSTITUTES OF HEALTH
National Institute on Alcohol Abuse and Alcoholism

Summary of Changes--continued

CHANGES	2003 Amended President's Budget Base		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	526	$187,442,000	13	$6,933,000
b. Competing	192	55,529,000	0	3,215,000
c. SBIR/STTR	35	7,495,000	0	300,000
Total	753	250,466,000	13	10,448,000
2. Research centers	15	27,100,000	0	976,000
3. Other research	112	30,495,000	0	1,098,000
4. Research training	247	9,842,000	0	324,000
5. Research and development contracts	49	35,500,000	49	1,249,000
Subtotal, extramural				14,095,000
	FTEs		FTEs	
6. Intramural research	106	40,383,000	(2)	(219,000)
7. Research management and support	139	21,133,000	(2)	(362,000)
8. Cancer control and prevention	0	0	0	0
9. Construction		0		0
Subtotal, program		393,786,000		13,514,000
Total changes	245		(4)	15,202,000

NATIONAL INSTITUTES OF HEALTH
National Institute on Alcohol Abuse and Alcoholism

Budget Authority by Object

	FY 2003 Amended Pres. Budget	FY 2004 Estimate	Increase or Decrease
Total compensable workyears:			
Full-time employment	245	241	(4)
Full-time equivalent of overtime & holiday hours	1	1	0
Average ES salary	$142,278	$145,124	$2,846
Average GM/GS grade	11.5	11.5	0
Average GM/GS salary	$71,237	$72,662	$1,425
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$85,163	$86,866	$1,703
Average salary of ungraded positions	$140,257	$143,062	$2,805

OBJECT CLASSES		FY 2003 Amended Pres. Budget	FY 2004 Estimate	Increase or Decrease
	Personnel Compensation:			
11.1	Full-Time Permanent	$14,583,000	$15,000,000	$417,000
11.3	Other than Full-Time Permanent	3,607,000	3,703,000	96,000
11.5	Other Personnel Compensation	541,000	556,000	15,000
11.7	Military Personnel	506,000	519,000	13,000
11.8	Special Personnel Services Payments	2,411,000	2,481,000	70,000
	Total, Personnel Compensation	21,648,000	22,259,000	611,000
12.0	Personnel Benefits	4,612,000	4,741,000	129,000
12.1	Military Personnel Benefits	428,000	439,000	11,000
13.0	Benefits for Former Personnel	2,000	2,000	0
	Subtotal, Pay Costs	**26,690,000**	**27,441,000**	**751,000**
21.0	Travel & Transportation of Persons	666,000	681,000	15,000
22.0	Transportation of Things	156,000	159,000	3,000
23.1	Rental Payments to GSA	2,320,000	2,400,000	80,000
23.2	Rental Payments to Others	176,000	179,000	3,000
23.3	Communications, Utilities & Miscellaneous Charges	803,000	817,000	14,000
24.0	Printing & Reproduction	504,000	513,000	9,000
25.1	Consulting Services	1,843,000	1,856,000	13,000
25.2	Other Services	1,381,000	1,406,000	25,000
25.3	Purchase of Goods & Services from Government Accounts	32,090,000	33,131,000	1,041,000
25.4	Operation & Maintenance of Facilities	4,776,000	4,821,000	45,000
25.5	Research & Development Contracts	17,471,000	18,049,000	578,000
25.6	Medical Care	543,000	553,000	10,000
25.7	Operation & Maintenance of Equipment	693,000	705,000	12,000
25.8	Subsistence & Support of Persons	0	0	0
25.0	**Subtotal, Other Contractual Services**	**58,797,000**	**60,521,000**	**1,724,000**
26.0	Supplies & Materials	3,129,000	3,185,000	56,000
31.0	Equipment	3,775,000	3,476,000	(299,000)
32.0	Land and Structures	0	0	0
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	317,903,000	330,749,000	12,846,000
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	**388,229,000**	**402,680,000**	**14,451,000**
	Total Budget Authority by Object	**414,919,000**	**430,121,000**	**15,202,000**

National Institute on Alcohol Abuse and Alcoholism

Salaries and Expenses

OBJECT CLASSES	FY 2003 Amended Pres. Budget	FY 2004 Estimate	Increase or Decrease
Personnel Compensation:			
Full-Time Permanent (11.1)	$14,583,000	$15,000,000	$417,000
Other Than Full-Time Permanent (11.3)	3,607,000	3,703,000	96,000
Other Personnel Compensation (11.5)	541,000	556,000	15,000
Military Personnel (11.7)	506,000	519,000	13,000
Special Personnel Services Payments (11.8)	2,411,000	2,481,000	70,000
Total Personnel Compensation (11.9)	**21,648,000**	**22,259,000**	**611,000**
Civilian Personnel Benefits (12.1)	4,612,000	4,741,000	129,000
Military Personnel Benefits (12.2)	428,000	439,000	11,000
Benefits to Former Personnel (13.0)	2,000	2,000	0
Subtotal, Pay Costs	**26,690,000**	**27,441,000**	**751,000**
Travel (21.0)	666,000	681,000	15,000
Transportation of Things (22.0)	156,000	159,000	3,000
Rental Payments to Others (23.2)	176,000	179,000	3,000
Communications, Utilities and Miscellaneous Charges (23.3)	803,000	817,000	14,000
Printing and Reproduction (24.0)	504,000	513,000	9,000
Other Contractual Services:			
Advisory and Assistance Services (25.1)	748,000	761,000	13,000
Other Services (25.2)	1,381,000	1,406,000	25,000
Purchases from Govt. Accounts (25.3)	15,343,000	16,049,000	706,000
Operation & Maintenance of Facilities (25.4)	4,776,000	4,821,000	45,000
Operation & Maintenance of Equipment (25.7)	693,000	705,000	12,000
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**22,941,000**	**23,742,000**	**801,000**
Supplies and Materials (26.0)	3,123,000	3,179,000	56,000
Subtotal, Non-Pay Costs	28,369,000	29,270,000	901,000
Total, Administrative Costs	**55,059,000**	**56,711,000**	**1,652,000**

NATIONAL INSTITUTES OF HEALTH

National Institute on Alcohol Abuse and Alcoholism

SIGNIFICANT ITEMS IN SENATE
APPROPRIATIONS COMMITTEE REPORT

The following section represents FY 2003 Congressional requirements for reports and significant items derived from Senate Report 107-216. These actions discussed below are contingent on inclusion of similar language and funding in the final FY 2003 appropriation and related reports. Additional items may be transmitted at a later date as a result of the final Conference report.

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 continues its support 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 treatment services. The Committee acknowledges the NIAAA's progress in implementing this recommendation, and it encourages the Institute to consider supporting additional research in this area. (p. 38)

Action taken or to be taken

The Institute has devoted almost $22.5 million to research on improving delivery of alcohol treatment and prevention services since the NIAAA Advisory Council issued its recommendation. We currently fund 13 active grants in this area, and funding increased almost $0.5 million between FY 2001 to FY 2002. Awards for two additional grants in FY 2003 are pending.

We will hold a Spring 2003 conference, at which national-level experts will (1) assess existing research on alcohol treatment in managed-care settings and (2) recommend strategies to strengthen ongoing and future research in this area.

Item

Alcoholic liver disease – Alcoholic liver disease remains a major cause of morbidity and mortality in the United States. The Committee notes that recent research suggests that free radicals are a principal vehicle through which alcohol damages the liver, and that antioxidants look increasingly promising as a potential treatment. The Committee encourages the Institute to expand its research on alcoholic liver disease, particularly regarding the interaction between hepatitis C and alcohol in liver disease. (p. 38)

Action taken or to be taken

Last year, we reported that NIAAA's intramural program established a Section on Liver Biology. Investigators from this laboratory are collaborating with NIDDK researchers to study (1) the synergistic effect of alcohol and hepatitis C viral proteins on inflammatory and death-signaling pathways in the liver, and (2) the antioxidant potential of an immune-system protein, the cytokine interleukin-6, as protection against alcoholic liver disease (ALD).

NIAAA's extramural program also expanded its ALD research in 2002. The program will fund at least one ALD grant resulting from two Requests for Applications (RFAs) on new approaches to medication development and clinical evaluation of already-approved medications. To encourage research on early stages of ALD, we also issued Program Announcements on (1) cellular and molecular mechanisms that lead to alcoholic hepatitis and (2) mechanisms of alcohol-induced tissue injury.

NIAAA and the NIH Office of Dietary Supplements (ODS) cosponsored a symposium on the potential of a dietary supplement, S-adenosyl-L-methionine, as an ALD treatment. The symposium led to an RFA, co-funded by NIAAA, ODS, and NCCAM, which resulted in funding of eight grants. The NIAAA and ODS also co-sponsored a symposium on the role of dietary iron as a potential co-factor in alcohol-induced liver injury.

Following an NIAAA-sponsored workshop on potential use of stem cells for treatment of alcohol-related conditions, we issued an RFA to encourage research in this area. Several grant applications addressed ALD, and one of them is likely to be funded.

Like ALD, the harmful synergy resulting from hepatitis C infection and alcohol abuse is an ongoing research topic at NIAAA, and we also expanded in this area. We co-sponsored the NIH Consensus Development Conference on Management of Hepatitis C. Among the recommendations from the Conference is that patients with hepatitis C infection who abuse alcohol should not automatically be excluded from new or expensive treatments; they should be evaluated on a case-by-case basis. NIAAA joined NIDDK, NCI, NIAID, and NIDA in sponsoring a 2002 RFA on hepatitis C.

The Institute also sponsored a workshop on the direction that alcohol-specific research on hepatitis C should take to lead to advances in prevention and treatment. Recommendations from the workshop will be published in a scientific journal.

Item

Brain mapping and organ imaging in alcoholism **–** The Committee notes the rapid progress made through advanced imaging technology in mapping the brain pathways that are involved in

alcohol addiction and alcohol-related brain damage. The Committee urges the Institute to expand research on brain mapping in alcoholics. Where possible, the Institute should collaborate with the NIBIB and other NIH Institutes and agencies on the development of advanced instrumentation to further the understanding of alcohol dependence and alcohol-related medical disorders. (p. 38)

Action taken or to be taken

We know that heavy alcohol use can cause profound changes in the brain that ultimately may damage it. Our research links these changes to the neural circuitry of specific brain regions and resultant changes in brain functions -- neuroadaptation -- that promote alcoholism and inhibit recovery from it. Our goal is to discover which of these functions can be recovered and how to sustain their recovery. This last point is crucial, since we have found that some of the brain regions that alcohol damages regulate ability to learn the coping skills needed to sustain recovery.

We are necessarily approaching this "brain mapping" from several angles, from behavioral, cellular, and molecular-genetic studies of small-animal models to noninvasive, human functional-imaging studies of children, adolescents, and adults. Integrated data from these studies are revealing patterns of how alcohol-induced brain changes, and the molecular/genetic factors that underlie them, affect function, and how these disturbances impede sustainable recovery. Inherent in these kinds of discoveries are identification of markers of risk and of potential for recovery, and of mechanisms that are targets for therapeutic intervention.

Last year, we added two expansions to our ongoing research. In one expansion, we joined six other NIH Institutes in an initiative that will result in improved radiotracer techniques for imaging molecular events in preclinical and clinical studies. These techniques are essential for understanding the biological basis of normal brain function and the pathophysiology of brain disorders, including alcoholism. The scientific community currently has few versatile radiotracers for molecular targets implicated in alcoholism, which has impeded progress in our research.

The other expansion added anatomical-mapping and theoretical (computer) modeling components to NIAAA's Integrative Neuroscience Initiative on Alcoholism (INIA). This year, we are adding another INIA expansion: development of small-animal imaging techniques that will enable us to track alcohol-induced neuroadaptive changes in the same animal over time. Integrating these techniques with studies of how chronic alcohol use changes gene activity -- because genes produce proteins that act as intermediaries of alcohol's actions in the brain -- will provide important information on the pharmacology of alcohol and on resultant behavioral processes.

With the National Institute of Biomedical Imaging and Bioengineering having recently joined the Human Brain Project (in which six Institutes, including NIAAA, participate), more opportunities will arise for collaborations to develop instruments that will advance this research.

Item

Health disparities – Evidence suggests that alcohol affects genders and subpopulations differently, and that some groups suffer more adverse effects than others. The Committee encourages the Institute to work collaboratively with the NCMHD to study the role of gender, ethnicity, socioeconomic status, and other variables in determining the effects of alcohol use and abuse. (p. 39)

Action taken or to be taken

In FY 2002, NIAAA and NCMHD co-funded 11 projects, with two major goals in mind. One goal is to develop alcohol-research capacity at minority-serving institutions, through collaborations between students, faculty, and clinicians and established alcohol investigators. We are taking this approach because minority-serving institutions tend to have the cultural sensitivity and perspectives needed for alcohol research in the populations they serve. The grants we fund in this area are intended to develop sustained programs in alcohol research, increase the number of minority scientists who will successfully pursue biomedical and behavioral alcohol research careers, and emphasize research on alcohol problems in minority populations and communities. Collaborative projects involve American Indian, Native Hawaiian, and African- American institutions and communities.

Another goal is to support studies on specific risk and protective factors for alcohol-related problems according to gender, ethnicity, socioeconomic status, and other variables. Projects funded last year investigated fetal alcohol syndrome, risk factors for alcoholism, and prevention and treatment of alcoholism in American Indian or Alaska Native communities. Collaborative projects also included research on the genetics of alcoholism and treatment approaches for African-Americans.

Item

Longitudinal studies – The Committee encourages the Institute to undertake longitudinal studies that recruit subjects in early adolescence to examine gene-environment interactions impacting alcohol abuse and alcoholism during the course of an individual's life. The Institute is encouraged to partner with other institutes, agencies and organizations deemed appropriate, including the NICHD and SAMHSA. (p. 39)

Action taken or to be taken

About half of the risk of alcoholism is genetic; the other half stems from environmental factors. Since gene expression and environmental influences change throughout the lifespan, longitudinal

studies of gene/environment interactions are essential for identifying scenarios that predispose people to alcoholism.

We currently fund six longitudinal studies on the impact of gene/environment interactions, beginning in adolescence and throughout life, one of which is a component of our Collaborative Studies on the Genetics of Alcoholism. Our current studies examine such topics as markers; biological risk factors in relatives of alcoholics; and cognitive, personality, and social factors. They include genetic epidemiology studies of twins. Eight other gene/environment interaction studies include components that also will contribute relevant information.

NIAAA also is represented in the working group of the upcoming National Children's Study, led by the NICHD, which is following children from before birth to age 21 to assess the impact of environmental influences on their health. The study will include a gene/environment interaction component. In addition, we will encourage collaborations with NICHD, SAMHSA, and other appropriate Institutes and agencies, of longitudinal studies on the impact of gene/environment interactions on alcohol abuse among adolescents.

Item

Medications development for alcoholism treatment – The Committee is aware of advances in the understanding of how genetics and environment influence the response to alcohol. The Committee urges the Institute to encourage studies on the influence of psychological and social factors on the success of treatment, and develop new medications for the treatment of alcoholism and alcohol-related disorders. (p. 39)

Action taken or to be taken

A major new NIAAA initiative will focus on identifying the biological mechanisms that underlie alcohol-use disorders and using this knowledge as the basis for medication development. Components of this kind of research have been ongoing at NIAAA, and we are ready to apply our findings to the next level. The new initiative will provide us with the resources and coordination we need for rational design of medications to sustain recovery. By identifying the biochemical pathways involved in alcohol's actions in the brain and other organs, we will identify potential targets for intervention, and can develop therapeutic compounds accordingly.

Currently, NIAAA's Extramural Program funds several pharmacotherapy grants, from patients with alcohol dependence alone (13 grants) to those with concurrent psychiatric disorders (seven grants) or tobacco dependence (three grants). We also fund three pharmacotherapy trials of adolescents and one of children with fetal alcohol syndrome. Seven NIAAA-funded trials are examining combined medications, and Project Combine is examining the interaction between pharmacological and behavioral therapies. All pharmacotherapy grants include a psychosocial intervention. A clinical trial on treatment of alcohol-induced liver disease also is underway.

Intramural researchers are about to conduct a clinical trial to test efficacy and safety of a medication that targets a biological system, a cannabinoid receptor on nerve cells of the brain, as yet untested for treatment of alcoholism and alcohol craving. Each of several different laboratory approaches implicates it in alcohol's effects. If effective, it will be the first new medication for alcoholism and alcohol craving since the introduction of naltrexone 10 years ago.

In 2002, NIAAA also issued Program Announcements on medications development and treatment of alcoholics with psychiatric comorbidity or tobacco dependence. Others address behavioral therapies. Pending Program Announcements address treatment of alcoholics with substance-use disorders and treatment of adolescents. Grants resulting from a Request for Applications on medication development (for alcoholism and organ damage) will be awarded in 2003.

Item

Multidisciplinary research on fetal alcohol syndrome – The Committee recognizes that fetal alcohol syndrome is among the most common preventable cause of mental impairment. The Committee supports the Institute's efforts to understand the biological mechanisms through which alcohol causes damage to the developing fetus. The Committee also urges the Institute to aggressively pursue research that will lead to effective strategies for the prevention and treatment of fetal alcohol syndrome. (p. 39)

Action taken or to be taken

In 2003, we will award grants from a Request for Applications to conduct studies under a new initiative that will greatly facilitate research on alcohol-induced fetal damage. The Collaborative Initiative on Fetal Alcohol Spectrum Disorders (CIFASD) is intended to speed translation of findings into clinical applications.

Alcohol results in a spectrum of neurological, behavioral, and physical deficits, each of which correlates with the trimester of pregnancy in which the fetus was exposed. Defining when in gestation each of these deficits occurs and discovering the biological mechanisms that lead to it hinge on our ability to integrate information from various fields of study. Likewise, developing treatments for children and adults who sustained alcohol-induced damage while in the womb requires integration of multiple disciplines, from behavior to molecular biology.

We have made significant progress in understanding the mechanisms of alcohol-related fetal damage. The CIFASD will accelerate our research by integrating resources and basic, behavioral, and clinical investigations, and by developing essential new resources. Investigators from outside the alcohol field also will be recruited, resulting in the application of new ideas and technology to fetal-alcohol studies. The CIFASD approach will foster rapid exchange of information that consortium members from various disciplines can integrate into their research.

Children and adults who sustained alcohol-induced damage in the womb often have neurological deficits, but lack the physical symptoms, such as abnormal facial features, by which clinicians traditionally have diagnosed FAS. As a result, FAS sometimes is mistaken for other conditions, such as autism, studied by the NIMH. The NIAAA and the NIMH meet periodically to share findings that will help establish differential diagnoses between FAS and other sources of mental impairment. The last such workshop occurred about 1.5 years ago, and we intend to continue these discussions.

Item

Native Alaskans – The Committee is aware of serious problems with alcohol and substance abuse among Native Alaskans and of the need for translating research into clinical applications for this population. The Committee urges the NIAAA to sponsor a Research to Practice Forum to focus on bridging the gap between researchers and practitioners and translating scientific research into clinical applications, and to support the implementation of any recommendations developed at the forum. (p. 39)

Action taken or to be taken

NIAAA, Center for Substance Abuse Treatment, and representatives of the State of Alaska met on November 19, 2002, in an ongoing discussion of what kind of forum would be most helpful to alcohol- and drug-treatment providers and to the State. We will jointly sponsor such a forum as soon as possible, with a preliminary goal of Spring 2003.

Item

Prevention of alcohol abuse in adolescents –The Committee is very concerned about the increasing number of alcohol-related deaths on college campuses and increasing alcohol use among elementary and secondary school-aged children. The Committee urges the Institute to pursue collaborations with other Institutes, such as the NICHD and NIMH, to study the causes of alcohol abuse among this age group and to devise strategies for effective prevention and intervention. (p. 39)

Action taken or to be taken

A report by NIAAA's Task Force on College Drinking has revealed that the harmful effects of alcohol misuse by college students are more far-reaching than previously known. Included in the report are recommendations for research that will result in practical application of science-based protocols for prevention. The NIAAA has launched an Initiative that implements the Task Force's recommendations.

Outreach is a major component of the Initiative, including partnerships between scientists and college administrators. In 2002, we expanded the Initiative by encouraging the research community to apply for additional grants. The purpose of these grants will be to enable us to implement research protocols for rapid intervention on college campuses that express an urgent need for help with alcohol-related problems. The Consortium for Rapid Response to College Drinking Programs will pair experienced investigators with the requesting school; together, they will design and evaluate interventions that address issues specific to that campus. We have asked the National Highway Traffic Safety Administration, the Department of Education, and the Substance Abuse and Mental Health Services Administration to collaborate. These agencies have expressed preliminary interest, which we will pursue.

At the same time, we are encouraging investigators to apply for grants to study the epidemiology and natural history of alcohol problems among college students and to design and test prevention strategies.

Development and treatment of alcohol dependence have both biological and environmental-behavioral components. We are studying causes and treatment of alcohol problems in children and adolescents from both angles. From the basic-science angle, a major project designed to identify the neurobiological mechanisms of adolescent alcohol abuse is ongoing. Currently, we are encouraging grant applications for use of advanced imaging techniques in nonhuman primates, to examine how brain structure and function respond to alcohol use. These kinds of studies can reveal whether adolescents have unique brain features that protect them from alcohol-induced changes in neurocognitive functions and behaviors, or whether they are vulnerable to damage in unique ways. (Preliminary evidence suggests the latter, for some neurocognitive functions). This project was expanded in 2002 through an announcement requesting additional grant applications.

From the environmental-behavioral angle, fourteen studies on interventions for adolescents with established drinking problems are co-funded by the Center for Substance Abuse Treatment. Additional studies, one of them co-funded by NIMH, address different age ranges, from childhood through adolescence. They are testing prevention strategies, such as school and community programs, individual counseling, and internet websites; assessing environmental factors, such as advertising and family influence, that contribute to initiation and progression of alcohol use; and investigating health services for adolescents in need of treatment. Some focus on special populations, such as poor urban youth, children of alcoholics, and children with high-risk behaviors.

Other collaborative efforts include the Add Health Survey (the National Longitudinal Study on Adolescent Health), of which NICHD is the lead Institute. We contribute funds to this project and have funded several investigators to analyze the data it is generating. The survey is revealing environmental factors that promote unhealthy behaviors among adolescents, including alcohol misuse, or protect them from it. NIAAA also is represented on the Committee on Work and Family Life Initiative coordinated by NICHD. We collaborate with the Office of Behavioral and Social Sciences Research (OBSSR) on a study on preventing abuse in adolescent dating

relationships; with OBSSR and NIMH on an ongoing longitudinal study of youth first interviewed at ages 11-17 in 1976; with OBSSR on an adaptation, for urban youth, of an intervention that was successful in reducing alcohol use by rural youth.

In addition, we collaborate with the NIH Office of AIDS Research on sexual risk-taking, alcohol, and HIV prevention among youth; with the Office of Public Health and Science on a national Hispanic youth initiative; with the NCMHD on a national Native American Youth initiative; and with NICHD in the Leadership Group for the Adolescent Medicine Trials Network.

A 2002 NIAAA announcement encouraged applications for grants that will result in improved behavioral theories for alcoholism treatment, and identified adolescents as one target group.

NATIONAL INSTITUTES OF HEALTH
National Institute on Alcohol Abuse and Alcoholism

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2003 Amount Authorized	2003 Amended President's Budget	2004 Amount Authorized	2004 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite	$405,077,000	Indefinite	$419,955,000
National Institute on Alcohol Abuse and Alcoholism	Section 41B	42§285b	Indefinite		Indefinite	
National Research Service Awards	Section 487(d)	42§288	a/	9,842,000	b/	10,166,000
Total, Budget Authority				414,919,000		430,121,000

a/ Amounts authorized by Section 301 and Title IV of the Public Health Act.
b/ Reauthorizing legislation will be submitted.

NATIONAL INSTITUTES OF HEALTH
National Institute on Alcohol Abuse and Alcoholism

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1995 2/	$182,498,000	$181,328,000	$181,328,000	$181,256,000 3/
Rescission				(0)
1996	185,712,000 2/	198,607,000	183,733,000 2/	198,607,000
Rescission				(195,000)
1997	192,280,000 2/	212,079,000	195,891,000 2/	211,870,000 4/
1998	208,112,000 2/	226,205,000	228,585,000	227,175,000
1999	229,551,000 2/5/	248,778,000	259,747,000	259,747,000
Rescission				(172,000)
2000	248,916,000 2/	265,497,000	265,497,000	293,935,000
Rescission				(1,566,000)
2001	308,661,000 2/	349,216,000	336,848,000	340,678,000
Rescission				(154,000)
2002	381,966,000	379,026,000	390,761,000	384,238
Rescission				(623,000)
2003	415,310,000			
2004	430,121,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.
2/ Excludes funds for HIV/AIDS research activities consolidated in the NIH Office of AIDS Research.
3/ Excludes enacted administrative reductions of $117,000, $4,000 and $68,000.
4/ Excludes enacted administrative reductions of $134,000.
5/ 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 2002 Actual	FY 2003 Amended Pres. Budget	FY 2004 Estimate
Division of Intramural Clinical and Biological Research	106	106	104
Office of the Director	10	10	10
Office of Resource Management	36	36	36
Office of Scientific Affairs	24	23	22
Office of Policy and Public Liaison	7	7	7
Office of Collaborative Research	13	14	14
Division of Clinical and Prevention Research	17	16	16
Division of Basic Research	16	18	17
Division of Biometry and Epidemiology	15	15	15
Total, NIAAA	244	245	241
FTEs supported by funds from Cooperative Research and Development Agreements	(0)	(0)	(0)

FISCAL YEAR	Average GM/GS Grade
2000	11.2
2001	11.6
2002	11.6
2003	11.7
2004	11.5

NATIONAL INSTITUTES OF HEALTH
National Institute on Alcohol Abuse and Alcoholism

Detail of Positions

GRADE	FY 2002 Actual	FY 2003 Amended Pres. Budget	FY 2004 Estimate
ES-6			
ES-5	1	1	1
ES-4			
ES-3	2	2	2
ES-2			
ES-1			
Subtotal	3	3	3
Total - ES Salary	$414,002	$426,836	$435,371
GM/GS-15	27	27	27
GM/GS-14	41	43	42
GM/GS-13	40	40	40
GS-12	30	30	30
GS-11	17	17	17
GS-10	2	2	2
GS-9	21	21	21
GS-8	9	9	8
GS-7	10	10	10
GS-6	6	6	6
GS-5	3	3	3
GS-4	8	8	8
GS-3	0	0	0
GS-2	0	0	0
GS-1	1	1	1
Subtotal	215	217	215
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	1	1	1
Director Grade	1	1	1
Senior Grade	6	6	6
Full Grade			
Senior Assistant Grade			
Assistant Grade			
Subtotal	8	8	8
Ungraded	38	38	38
Total permanent positions	214	212	208
Total positions, end of year	264	265	260
Total full-time equivalent (FTE) employment,end of year	244	245	241
Average ES level	ES-4	ES-4	ES-4
Average ES salary	$138,000	$142,278	$145,124
Average GM/GS grade	11.5	11.5	11.5
Average GM/GS salary	$69,095	$71,237	$72,662