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Testimony of Peter M. Monti, Ph. D.
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President Shapiro, Members of the Scientific Resource Management Board of NIH: I am Dr. Peter Monti, Professor of Medical Science at Brown University, a member of the National Advisory Council for NIAAA, and President of the Research Society on Alcoholism (RSA). The RSA was established in 1976 to serve as a meeting ground for scientists working in all fields of alcoholism and alcohol-related problems. Our society represents over 1,600 scientists who are committed to understanding and intervening in the consequences of alcohol through basic research, clinical protocols and epidemiological studies. The task that you have before you, to recommend whether to consider a merger of NIAAA and NIDA, has been visited by other committees and groups over the past two decades. In my testimony, I hope to convince you of the importance of NIAAA as a distinct Institute focused on the scientific inquiry of the manifold public health consequences of alcohol use.

As a globally unique institution created by the American people, the NIH continues to demonstrate its critical role in advancing human health through scientific discovery and the applications of science to patient care and disease prevention. Before considering major structural changes in a successful organization, it is incumbent on the advocates of change to identify problems that were not addressed because of the present structure, and how proposed changes in the structure would improve performance without creating a new set of problems.

As the premier scientific organization in the alcohol field, RSA believes that there has been no significant mandate of alcohol research that could not be addressed with the present structure of NIH. Further, we believe that a merger of NIAAA with NIDA would impede scientific progress and create serious problems. Prior to the creation of NIAAA, the field of alcohol research had labored in a climate of public denial that alcoholism was even a problem. There was a widespread lack of attention among health professionals to the need for finding ways to treat and prevent alcoholism and alcohol-related illness. NIAAA's emergence as an Institute brought the importance of alcohol problems to national attention. It also signaled to researchers outside the community that alcohol research was an important area of scientific inquiry and thus attracted the best and brightest investigators to the field.

Alcohol and the Public Health: NIAAA is one of the smallest Institutes at NIH addressing

one of the most significant public health problems. Because of its ubiquity in the environment and its contribution to health, disease and public safety risks throughout the life cycle, alcohol research has a very broad scientific agenda. Toxic in high doses and over time, alcohol can have damaging effects on multiple organ systems, including the liver, pancreas, other endocrine organs, the immune system, heart, muscle, and the peripheral, and central nervous systems. Alcohol is also a risk factor for certain cancers. Both directly, and through its effects on nutritional status, alcohol related toxicities account for more than 30% of admissions to hospitals in the US. Excessive drinking contributes to over one-third of automobile-related deaths and is associated with non-motor vehicle trauma, occupational injuries, criminal violence, suicide, family violence, as well as many chronic health problems. Over 1,400 students in American colleges and universities died in alcohol-related unintentional injuries in addition to 500,000 full time four-year university students who were injured while under the influence of alcohol. These are America's future leaders. In aggregate, the cost of alcohol abuse to this country is estimated to be \$185 billion, due to lost productivity, health care expenditures, criminal justice system costs and costs related to alcohol related motor vehicle crashes. The public health needs related to alcohol misuse, abuse, and dependence are self-evident, and underline the imperative for preserving NIAAA as an independent Institute at NIH dedicated to research on alcohol-related health problems.

Alcohol is Unique Among Drugs of Abuse:

Alcohol is unique among all drugs of abuse. Non-prescription use of most drugs of abuse is prohibited by law. The use of tobacco, while legal, results in severe injury to multiple organ systems and has no health benefits. Therefore, prevention and cessation of use is the public health goal for all illicit drugs and tobacco. In contrast, alcohol is legal, socially acceptable, and used responsibly by 100 million Americans, to their social and medical betterment. There is convincing evidence that moderate alcohol use reduces the risk of heart disease and stroke. However, some individuals who are unable to limit their drinking experience the protean medical, psychological, and social consequences of alcohol abuse and alcoholism. Research is required to explore both the beneficial aspects of moderate alcohol use and the factors that govern the transition from moderate to harmful drinking. Because alcohol is widely available, heavily advertised, socially sanctioned, and has potential health benefits, understanding the development of alcohol abuse and alcoholism poses special challenges. We believe the strategic planning and funding in support of alcohol research would be diluted and unfocused in a merged institute with a primary focus on addiction.

The implicit and explicit message of the research supported by NIDA (and its Director) must be the prevention of use and abstinence from illicit drug use, while the implicit and explicit message of NIAAA-supported research must be the prevention of alcohol-related problems and harm reduction. This leads to the possibility of competing and unworkable institutional goals within any combined substance abuse institute. Any attempt to bring together NIAAA and NIDA would be disastrous for our national drug control policy and its focused message as well as the critical research into the medical consequences of alcohol toxicity.

The Challenges and Successes of Prevention Research in the Alcohol Field:
Epidemiologists have determined that those who begin drinking before the age of 15 have four times the likelihood of becoming alcoholic at some point in life than do those who begin drinking later. There is a solid scientific basis for prevention of alcohol problems that extends much further than school-based education (the primary prevention strategy for illicit drugs). The challenge of prevention research has been to develop and test effective ways to teach responsible and safe drinking and to inform the general public as well as high risk individuals about the potential for harm associated with heavy drinking in high risk situations. These strategies are directed at lowering the risk of harm associated with alcohol. Epidemiological research has suggested the potential of alcohol to lower the risk of heart disease. More prevention research is essential to determine the most effective approaches to assist people in finding the best and safest drinking style for them. NIAAA-funded prevention research highlights the uniqueness of alcohol among drugs of abuse, and the incompatibility of the harm reduction/moderate drinking message with the abstinence message that is tied to illegal use of drugs and the health related consequences of smoking.

NIAAA Sponsored Research and Public Policy

Alcohol is the third leading cause of preventable death in the United States and yet is legally used and enjoyed by over 100 million Americans. Our public policies regarding limiting the harmful effects of alcohol have been greatly impacted by NIAAA supported research. Examples include studies on minimum drinking age, responsible beverage service training, and research on the elimination of wine and spirits retail monopolies. NIAAA sponsored research has helped to inform the policy debate and to evaluate the effects of policy implementation. Research by NIAAA sponsored scientists was used in public discussions in the U.S. Congress in requiring that all states establish at least a .08 BAC limit as well as providing incentives for states to pass “Zero Tolerance” laws for young drivers. A good example of a government-sponsored effort to evaluate all available research on a policy topic was the U.S. Government Accounting Office review of minimum alcohol purchase age research. This study, which was commissioned by the U.S. Congress, reviewed all published research, most of which had been supported directly by NIAAA, accounted for their differences in methods and quality, and reached a policy conclusion that there was clear evidence that higher minimum drinking ages yielded reduced alcohol-involved traffic crashes for young people.

The Breadth of NIAAA-Supported Research:

In addition to research related to prevention and public policy (cited above), NIAAA supports all areas of research relevant to alcohol, alcohol-related problems, alcohol-related toxicity, and alcohol abuse and dependence. The following is a very brief summary of some research accomplishments with more detail provided in the appendix to this testimony:

Genetic Research: Results of epidemiological genetic studies conducted over decades have revealed that about half the risk of alcoholism is genetic. The Collaborative Study on the Genetics of Alcoholism (COGA) has identified several chromosomal regions likely to contain some of these genes and serves as a human reference library for the mechanistic approaches of behavioral genetic studies in animal models.

- Neuroscience Research:** Using animal models, including targeting specific genes, investigators have been able to observe the molecular and cellular pathways of alcohol-related behaviors. Recent research has found specific components of nerve cells act as a “front door” access of alcohol into neural function. These findings provide new targets for intervention.
- Liver Disease:** NIAAA-funded research has revealed a complex chain of alcohol-induced molecular events that begin in the gut and follow the bloodstream to the liver, where components of the immune system then trigger production of damaging free radicals and inflammation. NIAAA-funded investigations have strong evidence that treatment with antioxidants attenuates this alcohol-induced liver damage.
- Fetal Alcohol Syndrome:** Significant progress has been made in understanding the biological mechanisms through which maternal drinking during pregnancy damages the developing nervous system and underlies the leading preventable cause of mental retardation in the Western Hemisphere. This research is the foundation for developing treatments that promote recovery and normal brain function.
- Treatment Research:** NIAAA-funded clinical trials have produced two new medications approved by FDA for the treatment of alcoholism, and evaluated dozens of other promising formulations. Additional clinical trials revealed the synergistic effects of brief behavioral intervention with pharmacotherapy in a primary care setting providing a basis for widely-available treatment approaches.
- Interdisciplinary Research:** Only an Institute dedicated to alcohol research can focus resources on the multiple causes, consequences, and elements of recovery that define alcohol related problems, toxicities and dependence. These are all influenced by multiple host susceptibility factors (e.g. personality, metabolism, genetic variations in responses to alcohol); by multiple environmental factors that promote or deter excessive alcohol consumption (e.g., availability, peer relationships, religiousness); and by the unique pharmacology of alcohol. It is necessary to support collaborative research designs that span from the molecular to the behavioral and social sciences and provide the knowledge for ever-more efficacious treatment and prevention strategies
- Lifespan Research:** Understanding of the environmental, bio-behavioral and genetic factors that promote early initiation of alcohol drinking and transition into harmful use/abuse and dependence (alcoholism), as well as the factors that promote remission and abatement of alcohol problems in untreated populations.
- Military** Early drinking has significance for our military as well as our civilian population. Of the 180,000 young adults ages 17-24 who enter the military annually, 75% are drinkers at the time of entry, and of these 28% of males and 13% of females report drinking patterns that are defined as heavy, high risk drinking. Age of drinking initiation and amount of heavy drinking as a teen are directly related to a continuation of drinking while in military service. Heavy drinking in the military poses a vital threat to military preparedness and to the defense of our nation.
- Special Populations** Understanding of the interplay of biological factors (genetics, metabolic, age, sex), cultural/ethnic background, and socio-economic status as risk factors for the development of, and the course of, different kinds of health and social problems associated with alcohol use and abuse across the lifespan.

Summary:

In summary, the RSA believes that alcoholism research is poised to capitalize on our past 40 years of NIAAA supported research and change existing paradigms for the prevention and treatment of alcohol-induced disease states and alcohol dependence within the decade. Some of the nation's most vulnerable and venerable sectors (the unborn, victims of childhood trauma, adolescents, college and military) are waiting for these advancements. In the absence of an Institute focused on alcohol and alcoholism, alcohol research will fail to reach this imperative public health goal.

The advocates of change have not identified deficiencies in the present structure and have not shown how proposed changes in the NIH structure would improve performance without creating a new set of problems. In contrast, we believe that a merger of NIAAA with NIDA would damage our national drug control message, while also harming alcohol specific research efforts. If you examine the NIAAA portfolio carefully, you will note that it does not fall within any possible cluster of another Institute's mission statement. In addition, the merger is unnecessary as there are no major barriers to collaborative efforts between NIAAA and NIDA on matters of addiction. However, a merger of NIAAA with NIDA would almost certainly decrease the comprehensive approach to alcohol-related health disorders that includes, but is not limited to, studies of addictive behavior and brain disease. Finally, when NIAAA was part of the ADAMHA cluster, it was never able to attract an active scientific leader to the helm. NIAAA has benefited over the past decades from the leadership of highly distinguished physician-scientists who report directly to the NIH Director and Congress regarding the impact, prevention and treatment of alcohol abuse and alcoholism on our public's health.

Any plan to merge multiple NIH institutes must take into account the costs and benefits. RSA believes that the considerable disruptions associated with any merger are not counterbalanced by the loss of focus on the entire NIAAA portfolio. There is no compelling reason for raising the question of merger at this time. Moreover, in the absence of a Secretary of HHS, a permanent NIH Director, and a permanent Director of NIAAA, the timing of this examination of the organization of NIAAA and NIDA is mystifying and risks damaging NIAAA and discouraging the best candidates from applying for the currently vacant position of NIAAA Director.

Thank you very much for this opportunity to testify before your Committee.

Appendix

NIAAA Research Accomplishments

The Breadth of NIAAA-Supported Research:

NIAAA supports all areas of research relevant to alcohol, alcohol-related problems, alcohol-related toxicity, alcohol abuse and alcohol dependence. The following is a brief summary of some research accomplishments that illustrate the breadth of research funded by the NIAAA.

Genetic Research: Results of epidemiological genetic studies conducted over decades have revealed that about half the risk of alcoholism is genetic. Finding the multiple genes that underlie this risk has been one of the highest priorities of NIAAA. The Collaborative Study on the Genetics of Alcoholism (COGA) has identified several chromosomal regions likely to contain some of these genes. More recently, investigators strengthened these findings by replicating them in two of these chromosomal regions.

Neuroscience Research: In recent years, neuroscience research has increasingly been shaped by research in molecular genetics. Genes that underlie alcoholism produce proteins that regulate the functions of the nervous system. Alcohol interferes with brain function and behavior through its effects on these proteins. With chronic high dose alcohol exposure, the brain undergoes molecular adaptations that result in alcoholism. Much of the research on mechanisms of alcohol dependence relies heavily on animal models, including gene knock-outs or knock-ins, in which a specific gene's activity can be eliminated or enhanced. These models enable investigators to observe the effects of genetic change on alcohol-related behaviors. This research has provided very strong evidence that specific components of specific proteins on nerve cells act as binding sites for alcohol molecules, that components of proteins that regulate appetite for food also probably play a role in propensity for alcohol, and that alcohol disrupts the function of several protein components that act as chemical messages within the nervous system. The latter effects of alcohol disrupt molecular activities crucial to normal nerve-cell function and, thus, brain function and behavior.

Liver Disease: NIAAA-funded research has revealed a complex chain of alcohol-induced molecular events that begin in the gut and follow the bloodstream to the liver, where components of the immune system then trigger production of damaging free radicals and inflammation. NIAAA-funded investigations have strong evidence that treatment with antioxidants attenuates this alcohol-induced liver damage.

Fetal Alcohol Syndrome: Alcohol also damages the developing nervous systems and other organs of unborn children whose mothers drink during pregnancy, often resulting in the life-long deficits of fetal alcohol syndrome (FAS). FAS is the leading cause of preventable mental retardation in the United States. At present, there are no treatments that will prevent the damage of FAS or ameliorate it once it has occurred. However, significant progress has been made in understanding the biological mechanisms through which this damage occurs, laying the foundation for the development of treatments that target specific molecular sites. For example, NIAAA-funded researchers have uncovered the role that alcohol-induced free radicals play in fetal tissue damage, and, *in vitro*, the ability of antioxidants to neutralize these destructive molecules and attenuate their devastating effects. They have developed a clearer picture of the mechanisms through which alcohol interferes with the normal life-and-death cycles of developing fetal cells and their differentiation into the specialized tissues of the body. They have also shown,

for the first time in a living mammal model, that genetic manipulations that increase production of nerve-growth factor protect a fetal brain region normally sensitive to damage from alcohol. Nerve-growth factor is among the substances that regulate survival of fetal brain cells and their differentiation into specialized cells of the nervous system. Importantly, NIAAA-funded researchers have demonstrated that it is possible to attenuate alcohol-induced damage *after* birth by administering choline, an essential nutrient in humans. Choline is among the substances in the nervous system that enable nerve cells to send electrical and chemical messages to and from each other and their environments, to trigger and regulate crucial biological activities.

Treatment Research:

NIAAA has led the way in the development and testing of promising medications and non-pharmacological treatments of alcoholism. NIAAA-funded clinical trials produced the first new medication approved by FDA for the treatment of alcoholism in more than four decades. The research has demonstrated that, naltrexone is very effective in preventing relapse in some recovering alcoholics. Once neuroscience research provides a more complete picture of how specific protein sites interact with alcohol and how the chronic effects of this interaction can be modified, medications can be developed to alter the pathophysiological mechanisms of alcohol dependence. In the behavioral arena, NIAAA funded Project MATCH which determined that three types of treatment -- cognitive-behavioral, motivational enhancement, and 12-step programs -- are equally effective in treating alcoholism and Project COMBINE which studied combinations of behavioral therapies with pharmacotherapies. Investigators continue to study which of many treatment modalities are most cost-effective.

Prevention Research: Prevention research supported by NIAAA over the past 20 years has established the basis for science-based prevention programs and approaches for every U.S. community and state. In addition to its contribution to public policy concerning BAC limits for youth and the underage drinking laws, recent advances in NIAAA prevention research include a series of community prevention trials which have shown significant effectiveness in reducing underage drinking initiation as well as drinking levels (Project Northland and Communities Mobilizing for Change on Alcohol) and alcohol-involved trauma (Community Trials in California and South Carolina). NIAAA sponsored research is currently undertaking extensive prevention effectiveness trials of comprehensive campus and community interventions to reduce college student high risk drinking and associated injury and death.