

WRITTEN STATEMENT

SUBMITTED BY

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ON BEHALF OF THE

AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

ALEXANDRIA VA

TO THE

SCIENTIFIC MANAGEMENT REVIEW BOARD

OF THE

NATIONAL INSTITUTES OF HEALTH

BETHESDA, MD

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Chairman Augustine and Members of the Board:

Thank you for the opportunity to present written testimony to you today. We are most grateful for the willingness of the Board to hear from those of us who work in the field and to read the genuine concerns that many of us in the scientific research community have with the path that is being considered here today.

My name is Scott Friedman, MD. I am the Fishberg Professor of Medicine and the Chief of Liver Diseases in the Division of Medicine at Mount Sinai School of Medicine in New York City. In addition, I am the current President of the American Association for the Study of Liver Diseases, based in Alexandria, Virginia and on whose behalf Dr. Szabo and I are submitting this testimony.

My name is Gyongyi Szabo, MD, PhD. I am a Professor and Associate Dean for Clinical and Translational Research, as well as the Director of the Hepatology and Liver Center in the Department of Medicine at the University of Massachusetts Medical School. In addition, I am the Chair of the NIH Liaison Committee of the American Association for the Study of Liver Diseases (AASLD).

The AASLD is the leading organization in the world representing researchers and clinicians in liver disease and liver wellness. We are unalterably opposed to the SMRB moving forward with the consideration of a merger between the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the National Institute on Drug Abuse (NIDA).

Let us be very clear about what we just said. AASLD is not just opposed to merging these two institutes. We are opposed to the SMRB even *considering* the merger of these two institutes and we will explain the scientific implications of such action by this Board – both on research that benefits our patients and on the investigator community – in our statement.

We fully understand that this issue will be addressed by the SMRB in terms of its impact on science and we believe that is appropriate. This should not be about individual research portfolios, nor should it be about bureaucratic convenience. But, underlying all the analysis that must be done is a fundamental fact: **Any action taken by this Board – and by any of us – must be action taken to benefit patients. We don't do research for research's sake – we do it to keep healthy people well and to make sick people better. If consideration of merging these two institutes impairs that mission – and we strongly believe it does – then it should not go forward.**

Liver Disease and the NIH

For the Board to fully understand our position, it is critical that it fully understand the larger picture of the distribution of liver disease-related research throughout the National Institutes of Health (NIH).

According to the Action Plan on Liver Disease Research published by the NIH in December 2004, 18 Institutes, Centers, and Offices currently support and collaborate on liver and biliary disease research. That research portfolio is coordinated by the Liver Disease Subcommittee of the Digestive Diseases Interagency Coordinating Committee (DDICC). Far from being a detriment to liver research, the diversity of scientific opportunities presented by this wide-ranging structure has served to invigorate the science, promote opportunity and competition, and therefore advance the wellness of the public.

The wide variety of Institutes and Centers addressing liver disease and liver wellness is a strength of the NIH system, not a weakness, and it needs to be recognized as such.

Consideration of a Merger: The Impact on Science

As the SMRB deliberates the question of whether or not to consider a merger of NIAAA and NIDA, there is no immediate question that is more important than the impact that such consideration will have on science and therefore on health. **It is the position of the AASLD that the impact of such consideration will slow scientific progress in a field that is critically important today and is growing in importance as we speak.**

Please consider the following points relevant to extramural research as you deliberate:

- It is currently estimated that more than 2 million Americans suffer from alcohol-related liver disease. While in 2001 there were 27,035 deaths from alcohol related chronic liver disease and cirrhosis, the impact of alcohol use on liver diseases extends beyond this population. Alcohol use together with hepatitis C virus (HCV) and hepatitis B virus (HBV) infection accounts for 70-90% of all cases of chronic liver diseases in the western world. Up to 44% of individuals with chronic HCV infection has a history of alcohol abuse, and alcohol abuse has been identified as an independent risk factor for liver cirrhosis and development of hepatocellular cancer.
- NIAAA is the primary source of extramural NIH funding for alcohol-related liver research. Although NIDDK's liver research portfolio is six times larger than NIAAA, alcohol-related liver studies are supported only by NIAAA. As a result of this focused effort of research funding and research direction from NIAAA, there have been significant milestones reached in alcohol-related liver research that have directly benefitted patients in the United States and throughout the world.
- NIAAA-supported research has lead to seminal discoveries in liver diseases in general, not limited solely to alcohol-related liver disease. For example, discovery of the concept of liver inflammation as a result of gut-derived pathogens in alcohol-related liver disease was seminal, and impacted the entire field of hepatology by unearthing a critical

pathogenic mechanism common to liver diseases of any origin. In addition, mitochondrial dysfunction, which was first discovered in alcohol-related liver disease research, applies to all kinds of liver disease.

- Similarly, the “multiple hit hypothesis” originally discovered in alcohol-related liver disease, has become the central element of the pathogenesis of non-alcoholic fatty liver disease (NAFLD). NAFLD has a major impact on the society and liver diseases in the United States, and many of the discoveries in NAFLD were made by investigators supported by NIAAA funds.
- In addition, NIAAA-funded alcohol research paved the way to discoveries in obesity and metabolic syndrome research, thus advancing the science in two research fields that are critical to public health.
- Again, as a result of NIAAA supported research, we now know that gut-derived microbes due to either increased gut permeability or impaired detoxification in the liver, contribute to disease progression in NAFLD, HCV and HIV-related liver damage, diseases that afflict millions of Americans.
- Discoveries in alcohol-related liver research directly lead to the progress made in the understanding of NAFLD, the most common liver disease in the US. Pioneering work in signal transduction pathways and nuclear receptors in alcohol-related liver injury tremendously benefited research in NAFLD.
- It has been long known that alcohol use is a cofactor in progression of chronic infection with HCV or HBV. **NIAAA is the only NIH institute that supports research on the combined effects of alcohol with other liver insults.**

In addition to the impact on extramural investigation, it is important that the Board carefully consider the likely deleterious impact on the intramural research program at NIAAA, as well:

- The NIAAA intramural research portfolio supports very high quality liver-related research. Within the intramural component of NIAAA, the research program of four of the 19 principal investigators is focused either exclusively or predominantly on liver biology.
- Breakthrough research on metabolic syndrome has led to recognition of the role of the liver as both a source and target for endocannabinoids. This led to a new path in research that has resulted in the founding of a new biotech company to develop compounds that have now been patented. These compounds effectively reduce weight and hepatic steatosis, improve glucose tolerance and dyslipidemias without causing depression or anxiety, a major improvement for patients.

Because the extramural research program in these institutes – and throughout the NIH – tends to be substantially larger and more geographically dispersed, there is a tendency to overlook the important work done intramurally at NIH. But, just these two examples point to the important role played and successes that have occurred under the current structure.

Consideration of the Merger: The Impact on Investigators

Beyond the scientific impact that the deconstruction of the NIAAA alcohol-related liver focus would have, it is important that consideration also be given to the likely impact on the investigator community. Established investigators who are either considering mid-career moves and potential young investigators are likely to be negatively impacted by consideration of merging these two institutes.

Both these classes of investigators take years to develop. The pipeline is a long and laborious one, not a spigot that can be turned on and off and on again. Nothing scares potential scientific researchers from the field they are considering faster than uncertainty. And, the process of undergoing a review by the SMRB is the definition of uncertainty.

By the time the SMRB goes through its public processes and private deliberations, the Director of NIH reviews the recommendation, the Secretary reviews the Director's recommendation, and the issue is referred to Congress for a six month waiting period during which the Congress could prevent its implementation, uncertainty about the future of alcohol-related research will prevail. This could be devastating to the alcohol-related liver research community. Potential investigators could easily decide to look into other aspects of liver disease.

NIDDK's liver research budget is six times larger than NIAAA's. NIAID's is more than twice as large; NCI is also about double that of NIAAA. There are plenty of other opportunities in liver research. But for the two million or more Americans who suffer from alcohol-related liver disease, they do not get to switch to another disease when the researchers are switching to another specialty.

Conclusion

On behalf of the AASLD, we want to thank the SMRB for the opportunity to present our views here today. We very appreciate the difficult and complicated job you have before you and wish to make a positive and constructive contribution to this debate.

To summarize, AASLD believes that to consider merging NIAAA and NIDA will:

- Negatively impact the science of alcohol-related liver research and thus negatively impact on the health and well-being of the public; and,

- Negatively impact the recruitment and training of new researchers in the field.

We certainly understand the surface appeal of a suggestion to merge these two institutes. But, we believe that a careful analysis of the impact that consideration of such a proposal will have on the science – both today and in the future – belies that superficial appeal. Rather, it clearly demonstrates that the negative impact on the science – and therefore on the public's health and well-being – far outweighs the minor benefit to NIH administrators of having one less institute with which to deal.

Again, we want to thank you for having the opportunity to present this testimony to you and we welcome the opportunity to participate in this dialogue.