Dr. Ting-Kai Li’s  
Former Director, NIAAA  
Responses to the Substance Use, Abuse and Addiction Working Group

Question 1

- Does current NIH organizational structure of substance use, abuse and addiction research:
  - Facilitate the progress of science in these areas?

Yes, the inclusion of NIAAA and NIDA in the NIH as separate Institutes has been beneficial for research on both alcohol and drugs. NIAAA, NIDA and NIMH were transferred from ADAMHA to NIH in 1992 in recognition that the scientific domains that these entities support addressed important health issues. Notably, each was established as an independent Institute within the NIH. This organizational restructuring that integrated NIAAA, NIDA and NIMH into the NIH has facilitated increased opportunities for collaborative and integrative approaches to address common problems across the NIH, not limited to alcohol and addiction, while the existence of each as an independent Institute has facilitated research in the scientific domains most relevant to each.

With respect to alcohol, the substance itself and its metabolic products (acetaldehyde and acetate) affect virtually every organ of the body leading to and contributing to severity of a large variety of life-threatening and health impairing disorders including alcohol addiction (alcoholism) and liver cirrhosis, cardiomyopathy, liver and GI cancers, fetal alcohol syndrome, and metabolic syndrome. NIAAA-supported research encompasses all of these areas and their integration where appropriate. Since becoming part of the NIH, NIAAA has established productive collaborative efforts with NIDDK, NHLBI, NCI, NIAID, and other NIH Institutes to further understand how alcohol use, not just alcoholism, affects the heart, the liver, and the brain, to cause and/or to significantly contribute to major disease and illnesses and to extend this knowledge to health care providers at large, not just addiction specialists. We now know that high-risk drinking (5+ drinks daily) increases the risk for several cancers, pancreatitis, ischemic stroke and other major diseases by 50% and we are well on the way toward developing biomarkers of alcohol use that will help physicians identify high-risk drinking patients in the same manner that they now identify patients at high risk for hypertension or diabetes. Had NIAAA limited its focus to only the addiction-related aspects of alcohol use, this progress in understanding and addressing the consequences of a substance used by 65% of the U.S. adult population likely would not have occurred.
Foster and/or promote gains in public health?

Yes, the current organization fosters/promotes gains in public health. It is important to note that the placement of NIAAA within the National Institutes of Health sends a different and important message to the public at large. NIAAA was created by the Comprehensive Alcohol Abuse and Alcoholism Prevention, Treatment and Rehabilitation Act of 1970 to establish a federal research program on the full range of medical and health issues related to alcohol, a legal, widely used, and widely available substance. This singular focus has allowed the Institute the flexibility to develop a systems model to understand the complex links between biology and behavior that are a part of why some people drink in high-risk patterns endangering themselves and others and to move the science more firmly into the realm of biomedical science with its traditional links to clinical practice and to the at-risk patient.

As a result, the way we approach prevention as well as screen for, diagnose, and treat alcohol problems is changing dramatically. For example, research over the last decade has shown clearly that alcohol addiction/alcoholism presents not just in middle aged populations as was previously thought, but actually occurs more commonly among young adults. Furthermore, we began to uncover the genetic and environmental risks that begin to emerge in childhood or adolescence. In response, the public health focus has shifted to younger age groups and emphasizes the risks of binge drinking (5+/4+ in 2 hours) for alcohol abuse, and of frequent heavy drinking (5+ drinks per day) for organ pathology and alcoholism. This is an important paradigm shift in our public health message in primary prevention and the identification of high risk persons for secondary intervention through screening and brief intervention.

In addition, evidence-based screening and brief intervention, funded and nurtured by NIAAA is rapidly moving from the specialty sector to the primary care sector broadening the public health response to harmful alcohol use, including but not limited to alcohol use disorders, and related health problems. Just as health care providers counsel their patients about diet and exercise wherever they are on the continuum from normal weight to obese, NIAAA is facilitating the dialog between clinicians and their patients about the risks associated with various levels of alcohol consumption. The effectiveness of ALCOHOL screening and brief intervention in primary care settings is well-established in the scientific literature. The widespread inclusion of this practice in primary care will ensure that individuals who would otherwise be unlikely to seek help to change harmful drinking behaviors will recognize, acknowledge and receive help thereby improving their health and well-being.
Question 2

- Are there areas of substance use, abuse and addiction research:
  - Not currently addressed by NIAAA – NIDA that warrant attention?

From the alcohol research perspective, my answer is NO. The NIAAA rolling 5-year strategic plan provides annually a comprehensive update of scientific discoveries, research opportunities and gaps. The limitation is budgetary.

- That would benefit from a trans-Agency approach?

That depends on your definition of trans-Agency approach. Certainly science as a whole benefits from cross-pollination of ideas and transdisciplinary approaches and alcohol research is no different. Alcohol use disorders have multiple genetic and environmental risk factors which emerge across the life span and vary by age, sex, social clusters and ethnic/racial groups. Alcohol research intersects with many different areas of interest to other NIH Institutes and Centers including NIDA, NCI, NHLBI, NIDDK, NIMH, and NICHD. There are areas which already benefit from collaborations/interactions between NIAAA and other ICs. In additional areas that might benefit from an enhanced trans-NIH approach, implementing a Roadmap-type activity involving the relevant ICs could provide the necessary flexibility and focus to achieve this goal. For example NIAAA is very supportive of the Science of Behavioral Change activity that attempts to integrate the science and perspectives of a number of ICs interested in what underlies motivation to change harmful behaviors and how to incorporate them to create more effective interventions. Other scientific areas might also benefit from this type of cross-pollination such as studies on mechanisms of tissue injury, including oxidative stress, energy metabolism (example: glucose and ethanol-derived acetate metabolism) and nutrient imbalance and how injury in one organ negatively impacts other organs in the body.

Question 3

- Given the entire NIH portfolio on Addiction:
  - Do NIAAA and NIDA collaborate with each other or with other Institutes and Centers regarding addiction research?
Yes. NIAAA and NIDA collaborate on a number of large projects such as the National Epidemiological Survey on Alcohol and Related Conditions (NESARC), the Collaborative Study On The Genetics of alcoholism (COGA), and with NIDA and NCI in the Transdisciplinary Tobacco Use Research Center (TTURC) program. The one that has been the most successful in terms of translational impact, public health, significance and publications has been the NESARC which is a 43,000 person general population sample of alcohol, drug, psychiatric and related health disorders.

○ **If so, how effective are these collaborations and what metrics are used to assess effectiveness?**

It is important to establish guidelines on metrics to assess effectiveness (I presume this means translation to the community?)

*This is a question that I can only give an answer based on the example of NESARC. NIAAA should be able to provide details, e.g. publications, public health significance, etc.*

○ **Are there areas of addiction research not currently addressed by NIH that warrant attention (e.g., gambling)?**

If the SUAA is considering enlarging the scope of addiction to include habituating activities such as gambling, computer and internet use, exercising, eating (esp., sugar, fats, and chocolates) even drinking coffee that become compulsive despite negative consequences (as defined above), the answer is **YES**. For example, pathological gambling is accepted as an addiction disorder, yet no NIH Institute/Center funds gambling research unless it is studied in the context of a comorbidity, e.g. alcohol abuse and gambling, or drug addiction and gambling. With respect to the other behaviors listed above, many of which are currently addressed by NIH, they have as much to do with mental health, obesity, cancer, hypertension, and diabetes as they do with addiction. The question then is whether merging NIAAA and NIDA ultimately accomplishes the overall charge to the SUAAA, and in turn the SMRB, to determine if the current structure of the NIH advances the science of addiction. I would posit that the current structure (i.e., NIAAA, NIDA) is but a piece of the larger picture and that the science of addiction can only be further advanced by bringing together the numerous perspectives about addiction from the broad range of ICs that address these behaviors and their health consequences into a Roadmap-type initiative, thereby providing the flexibility to address addiction in a meaningful way. The NIH needs to collectively decide on the priorities of addiction research, based on prevalence of use, misuse and addictive use and the health disabilities arising from them (e.g. estimation of Disability Adjusted Life-Years lost).
Question 4

- Do you think that organizational change within the agency, regarding Institutes and Centers with addiction-related research portfolios, could address any of these concerns?

If change refers to the merging of Institutes, as noted in my answer to Question 3, the answer is an unqualified NO. Rather, the rationale for integrative and collaborative research across multiple ICs is compelling and has the potential for greater returns than simply merging two ICs. The boundaries of addiction research extend far beyond alcohol which is socially acceptable, and drugs that are illicit (opoids, stimulants), and those that are legal but socially unacceptable (nicotine). Importantly, potentially addictive ingesta with high taste appeal, e.g., sugar and fats, have tremendous negative consequences as evidenced by the “epidemic” of obesity and Type II diabetes. Understanding the science of behavioral change is key to forging effective messages to combat these rising public health problems. Facilitating an addiction-focused effort within NIH has little to do with changing organizational structure and much to do with furthering the cause of transdisciplinary research with meaningful involvement from all ICs with an element of addictive science embedded in a broader portfolio. A wholesale reorganization of all components of all ICs with a focus on some element of the addictive process, even if such a re-structuring were achievable, is not practical and may not reflect the state of the science in the future. Much more promising is the development of several meaningful transdisciplinary initiatives based either on roadmap or other paradigms.

  - What are potential options for organizational change (structural or functional)?

Merging NIDA and NIAAA is a major structural change that is neither necessary nor sufficient. Both are addressing their priorities within their legislated mandates and missions, as described in their strategic plan documents. The argument is specious that the two institutes should merge because the science is the same. The science is not the same even for the drugs that NIDA studies. The most obvious are the contrasting mechanisms of actions of stimulants, depressants, and opioid analgesics. Both the common and unique properties of alcohol as compared with other licit and illicit drugs have been presented by numerous scientists before the SUAA and SMRB.

By contrast, functional change within NIH that brings together under a joint effort all ICs with a vested interest in addiction be it food, drugs, alcohol, internet, gambling, etc., should have broad appeal because of the missions of the various ICs that would be affected: by population (NICHD, NIA, NCMHD) profession (NINR), organ pathology (NIDDK, NCI, NIAID, NHLBI). NIMH, in particular, should be involved because of the role of underlying
comorbid mental disorders such as the mood and anxiety disorders, schizophrenia, ASPD, and PTSD, etc, etc, in the development of addictive behavior.

- What are the pros and cons of these options?

The arguments against structural trans-Agency organizational change in terms of a merger between NIAAA and NIDA have been summarized above as have the arguments in favor of functional change to create an initiative that spans multiple ICs. I see no gain and much pain in structural reorganization. Apart from the usual negative toll accompanying mergers on staff, time and cost, there will be critical loss of focus in the translation of research findings to the community, especially in NIAAA’s underage and college drinking initiatives, screening and brief intervention efforts and medications development program.

To maximize functional integration, I would favor adopting a model as suggested by SUAA to develop a new initiative for NIH Addiction Sciences. This would be a translational companion to the Basic Behavioral Sciences Opp-Net. As a new Trans – NIH initiative, it would need a strategic plan to be formulated. A mechanism might be the formation of a NIH Addiction Sciences Steering Committee that would recommend priority initiatives, the funding model to accomplish these goals (e.g. the Roadmap – Common Fund and the Neuroscience Blueprint or an admixture). Most importantly, the Committee would establish metrics for programmatic success and monitor the progress of this bold and exciting initiative.
Definitions on Substance Use, Abuse and Addiction

**Substance** – includes drugs, both legal and illegal, naturally occurring and synthetic.

*Should also include ingesta that have high reinforcing properties (e.g. sugar) or contain a naturally occurring drug (e.g. coffee).*

**Abuse** – Use in excessive or contraindicated amount and frequency causing harm to self, others and society.

**Addiction** –

1. A compulsive physiological and psychological need for and acquisition by self-administration, of a habit-forming substance.

2. A chronically relapsing disorder that is characterized by:
   a.) compulsion to seek and take the drug
   b.) loss of control in limiting intake in spite of impairment of health or social functioning
   c.) emergence of a negative emotional state when access is denied.
   (Koob and Volkow Neuropharmacology Reviews 35: 217-238, 2010)

The four major classes of psychoactive substances that have the greatest economic impact on society and cause, or contribute to, many life-threatening disorders, including liver cirrhosis, heart disease, HIV/AIDS, and cancer are:

- Nicotine
- Alcohol
- Opioids
- Stimulants