

## FOREWORD

This meeting is the first review of the biomedical aspects of the NIAAA portfolio and will serve to guide future directions in developing NIAAA research goals in the Alcohol and HIV areas. This area of research represents within and across-Institute collaboration involving both behavioral and biomedical research. Such collaboration reflects the broader need to develop effective transdisciplinary teams. As AIDS becomes a chronic “relapsing” disease with effective treatment, long term comorbidities such as alcohol use disorders and their impact on medication adherence and medical complications need to be understood over the course of the disease. It is critical that this plan be responsive to the new discoveries in both the alcohol and HIV/AIDS research communities. The recent XVI conference in Toronto Canada identified five “tracks” of research comprising over 13,000 abstracts and hundreds of presentations. The overall theme of the conference, “Time to Deliver,” highlighted critical developing modes of prevention (vaccines and microbicides) as well as distribution of treatment regimens into resource-poor areas where the highest incidence and prevalence of HIV infection are found.

The five tracks, all of which are relevant to alcohol and AIDS research, focus on A) etiology and pathogenesis, which encompass all aspects of HIV-1 biology and host response. Areas include genetics, viral fitness (structure and function), the progression of HIV disease, and both adaptive and innate immune responses that increase host susceptibility (measured in both human and animal models). Preclinical research on vaccines and microbicides acted as the focus for many discussions. The second track (B) targets clinical research, treatment and care. This track underscores the complexities of studying HIV/AIDS in human populations and the controversies related to diagnosis and treatment of HIV infection. A wide range of issues regarding antiretroviral therapies, access, and treatment failure were discussed. These issues included substance use comorbidities, the development of new therapies, pharmacokinetics, drug-drug interactions, adherence, short and long term adverse events, and roles of specific viral clade types in developing drug resistance. Approaches to care among women and children, marginalized groups such as substance abusers, and provision of care in resource limited settings were also addressed. In addition to these first two tracks there were discussions of the role of (C) epidemiology in guiding prevention activities; (D) social, behavioral and economic issues, and (E) the impact of policy on care provision and discrimination. Many of the research issues, particularly those outlined in the first two track areas of the XVI International AIDS Conference are relevant to the current NIAAA EAB review meeting.

Overall 300+ abstracts from the conference include references to alcohol as a cofactor. These abstract topics range from liver failure to cost of illegal alcohol production. This number is quite impressive since the meeting in general did not focus on the issue of substance abuse (particularly alcohol use) as a cofactor. For example, one abstract describes the finding that among providers of HIV care in resource-poor settings, approximately one third reported problem alcohol use themselves (as measured by the AUDIT). The author pointed to the devastating nature of the task of caring for AIDS

patients with inadequate medical resources as the explanation for the levels of drinking and the susceptibility of these workers themselves to becoming infected.

Many individuals have contributed to the vitality of the NIAAA alcohol research portfolio. Research in this area is a difficult endeavor because of the dual expertise required in both the alcohol and HIV areas for development of successful applications. The current EAB meeting brings individuals on the Extramural Advisory Board of NIAAA together with AIDS experts who have an appreciation for alcohol research and with individuals who have developed some of the major AIDS research. Other individuals from within NIAAA have given generously of their time to help guide this document by describing current and future potential areas of research. I thank each of them for their thoughtful participation in this project and wish to acknowledge their help in making this document a useful tool for promoting alcohol and AIDS research in the future.

We believe that, through this planning opportunity made possible by senior staff of NIAAA, we will be able to identify critical directions for research that represent the best opportunities for improving patient outcomes in this time of increasing fiscal constraint. It must be noted that our current effort is set against the backdrop of a need for increasingly effective prevention research to develop vaccines and microbicides. The goals of our combined efforts in both the biological and behavioral areas are to help control the ongoing pandemic, to prevent new infections, and to provide effective care for those infected with HIV, many of whom have coexisting alcohol use disorders.

Kendall Bryant, Ph.D., AIDS Coordinator, NIAAA

## **ACKNOWLEDGEMENT**

I would also like to acknowledge Leslie Isaki, Ph.D., whose hard work in the area of alcohol immunology early in the epidemic helped NIAAA develop many important grant applications and attract new researchers in the basic biological alcohol and AIDS field of research.

## MANDATE AND MEETING GOALS

The National Institute on Alcohol Abuse and Alcoholism (NIAAA), part of the National Institutes of Health (US Department of Health and Human Services), is the primary source of funds for alcohol and HIV/AIDS research and supports a continuing and expanding program of domestic and international research. NIAAA seeks to fulfill multiple goals identified in the *National Institutes of Health Plan for HIV-Related Research* through a broad range of research and collaborative activities focused on HIV/AIDS prevention and treatment among alcohol using, abusing, and dependent populations.

The past decade of NIAAA research funding has demonstrated the complexity of alcohol and HIV/AIDS relationships within both biomedical and behavioral research and the need to continue the effort to understand these relationships. Currently NIAAA receives approximately 27 million dollars annually for support of this research through the Office of AIDS Research, NIH. Annual plans are developed and submitted to the Office of AIDS Research for current, expanded, and new initiatives in the AIDS research area. The overall legislative mandate under the National Institutes of Health Revitalization Act (Public Law 103-43) provides for the development of HIV/AIDS plans in conjunction with outside experts for research in both the basic and applied areas of biomedical and social sciences.

### Meeting Goals

This meeting focuses on briefly reviewing some of the major basic biological and related biomedical treatment research issues and priorities in the area of HIV/AIDS and alcohol. The primary goal of this review and subsequent discussion is to provide a framework for continuing and expanding existing lines of research, as well as suggesting new alcohol-related initiatives for the prevention and treatment of HIV/AIDS. Because of the scope of ongoing research in the NIAAA portfolio, **we decided that this meeting would not directly address behavioral or social issues, particularly in the area of behavioral prevention.** The areas of behavioral prevention and prevention sciences (combining both behavioral and biological research) will be addressed in part within the high priority topic of vaccines and in subsequent meetings. Specific basic biological and biomedical topics will be treated in greater depth based on current findings and program priorities in the FY2005 and FY2006 portfolios. The current meeting is focused on achieving some of the broader strategic goals outlined below. (Portions of text are highlighted for emphasis.)

- (1) Evaluate the impact of research on biological mechanisms and biomedical patient-focused research in identifying the role of alcohol in **tissue and organ injury** and identifying **mechanisms of action underlying accelerated** morbidity and mortality in co-occurring alcohol use disorders and HIV/AIDS.
- (2) Assess progress in identifying the impact of alcohol use on **susceptibility to infection and early progression (set points and trajectories) of HIV/AIDS-related** morbidity and mortality, and the implications of bench and clinical research in this area for prevention and treatment of HIV/AIDS in domestic and applicable international contexts.
- (3) Discuss methods for and progress in targeting new research to the areas of clinical health **most relevant** to future improvements in **early diagnosis and treatment of HIV+ individuals with alcohol use disorders**.
- (4) Identify and integrate significant **emerging research** areas (e.g. **Biomarkers, Rapid Testing, Viral Genetics, and Vaccine Development**) that appear especially important to the alcohol and AIDS mission of NIAAA.
- (5) Identify ways to improve patient-focused health research through improved measurement of alcohol use and analysis of relevant data, identification of **current and new biomedical indices related to alcohol and AIDS illnesses, and development of models for measuring provider care and patient-relevant quality of life outcomes**.
- (6) Discuss the use of this research to inform and target new opportunities for biomedical and biological research, including **advancing understanding of the epidemic through simulation studies and informed statistical modeling**.
- (7) Evaluate ongoing activities and suggest future program activities to **increase the use of NIAAA research resources and findings** for preventing and reducing illness and injuries, including expansion of applied biological and biomedical research in domestic and international populations at-risk due to alcohol use.
- (8) **Integrate biological and clinical/behavioral approaches and teams of researchers** to address complex biobehavioral problems such as “Prevention for Positives”, which may include issues in medications adherence, toxicity, failure, and computer assisted clinical decision-making paradigms, and interventions to reduce transmission.
- (9) Understand the more efficient **use of existing datasets and available HIV/AIDS** cohorts to conduct research, including clinical trials for vaccines and therapeutics and epidemiological studies of comorbid disorders.

## Content of EAB Document

Presented in this document are some of the selected areas of biological and biomedical research within a broader NIH framework for effective action. These brief sections comprise reviews of both past and ongoing research highlighting promising findings, and discussion of areas of research critical to HIV and AIDS prevention and treatment. Opportunities for continuing, expanding, and developing new initiatives are discussed. Of particular importance are findings providing further evidence that alcohol use and misuse increases the morbidity and mortality of HIV+ alcohol users who may or may not be receiving treatment. While the impact of alcohol or HIV/AIDS on morbidity and mortality may be independently explained by additive effects, it is the interactive (synergistic) effects that are of greatest interest to basic research, and that are indicators of underlying shared or interactive mechanisms of action. For this reason general methodological issues need to be addressed in the measurement of alcohol and HIV/AIDS conjoint characteristics at the individual and population levels. As research continues to illustrate, it is the pattern of alcohol use relative to HIV disease course, including early infection, treatment initiation, and failure, which determines the complex multiple effects on individual survival and quality of life.

Understanding how basic biological and biomedical research may be strengthened requires an understanding of current NIAAA activities in these areas. Two broad areas of focus characterize NIH/NIAAA biomedical research: 1) **Etiology and Pathogenesis**; and 2) **Epidemiology and Natural History**. Within the area of Etiology and Pathogenesis are a variety of issues concerning both host-virus relationship and the clinical manifestations of HIV disease. These topics broadly cover NIAAA interests in immune function and neurological impairment.

## **Contributors to Document**

### **AIDS Epidemic Overview and Introduction**

Kendall J. Bryant, Ph.D.  
AIDS Coordinator, NIAAA-NIH  
Division of Epidemiology and Prevention Research

### **NIAAA Alcohol and HIV/AIDS Biomedical Research**

Kendall J. Bryant, Ph.D.  
AIDS Coordinator, NIAAA-NIH  
Division of Epidemiology and Prevention Research

Deidra Roach, M.D.  
Program Officer  
Division of Treatment and Recovery Research

### **Strategic Plan Area: Natural History and Epidemiology**

Samir Zakhari, Ph.D.  
Director  
Division of Metabolism and Health Effects

Diane Lucas, PhD  
Program Officer  
Division of Metabolism and Health Effects

Deidra Roach, M.D.  
Program Officer  
Division of Treatment and Recovery Research

Kendall J. Bryant, Ph.D.  
AIDS Coordinator, NIAAA-NIH  
Division of Epidemiology and Prevention Research

## **Strategic Plan Area: Etiology and Pathogenesis**

Diane Lucas, PhD  
Program Officer  
Division of Metabolism and Health Effects

Roger Sorensen, Ph.D.  
Program Officer  
Division of Neurological and Behavioral Research

Ellen Witt, Ph.D.  
Program Officer  
Division of Neurological and Behavioral Research

## **Strategic Plan Area: Prevention Science: Vaccines**

Kendall J. Bryant, Ph.D.  
AIDS Coordinator, NIAAAA-NIH  
Division of Epidemiology and Prevention Research

Maria Miquez, M.D.  
Research Faculty  
University of Miami

### Editing and Organization

Deidra Roach, M.D.  
Kendall J. Bryant, Ph.D.  
Susan Maier, Ph.D.

### Additional Comments and Scientific Review

Kenneth Warren, Ph.D.  
Howard Moss, M.D.  
Abraham Bautista, Ph.D.