

**Final Recommendations of the NIAAA Extramural Advisory Board
'Developing an NIAAA Plan for HIV-related Biomedical Research'
Oct 4-5, 2006**

Guiding principles:

Alcohol use and alcohol use disorders (AUDS) are prevalent in HIV- infected individuals. Individuals having both HIV and AUDS represent a unique group that merits continued targeted investigation and intervention. Past alcohol-related basic biomedical research has yielded valuable results related to HIV and AIDS which need further development and integration to be translated into prevention and treatment practices for at-risk and HIV+ populations with alcohol use disorders. This work is integral to understanding the AIDS epidemic among different indicated and targeted populations. The following recommendations are focused on the biomedical aspects of the NIAAA-HIV portfolio and are meant to complement behavioral (not replace) science- related efforts to improve the prevention and treatment of HIV/AIDS.

- a) Further research on the interactions between alcohol use disorders, HIV, and other co-morbidities is needed to advance understanding of the epidemiology, natural history, etiology, and pathogenesis (foundational areas) of all these disease endpoints separately and as a whole. In particular, further development of a “bedside” to “bench” approach is needed to assure that basic (foundational) alcohol and HIV research is targeted to the most relevant aspects of HIV infection and progression to AIDS among individuals receiving or in need of care
- b) It is critical that the NIAAA work across institutes to incorporate collection of information on alcohol use and alcohol use disorders in ongoing and new large multi-center, epidemiological and treatment studies and cohorts, including vaccine trials. This includes access to repositories for biological specimens and DNA.
- c) NIAAA should facilitate joint mentoring and training to encourage expertise in HIV and related fields such as expertise in chronic viral infections like hepatitis B and C to be combined with alcohol expertise for the next generation of investigators.

To address these guiding principles, investigations should:

1. Organ and Tissue Injury. Focus on key mechanistic targets for ethanol and HIV-induced injury to identify, measure, and prevent additive and interactive harmful effects at the cellular and organ systems level:

- a) Brain injury and disease, including but not limited to neurocognitive and neuroaffective deficits, peripheral neuropathy, and neural toxicities of HIV and HAART medication regimens.
- b) Anemia, bone marrow dysfunction
- c) Liver disease (attributable to alcohol, hepatotropic viruses, drug toxicities, metabolic

disease)

- d) Cardiopulmonary disease targets
- e) Mitochondrial dysfunction as a common outcome of HIV and ethanol-related cellular injury
- f) Nutritional effects of alcohol, HIV and HIV therapy interactions with a special emphasis on the etiology of wasting

2. Emerging Pharmacotherapies. Examine the pharmaco-kinetic and -dynamic effects of alcohol on current and emerging pharmacotherapies for the treatment of AIDS and alcohol use disorders. In addition identify how alcohol use and its treatment impacts biomedical approaches to the prevention of HIV (e.g., antiretroviral drugs, vaccines, and microbicides, post exposure prophylaxis) and associated co-morbidities (e.g., Hepatitis B and C, drug dependence, mental illness, neurodegeneration, cardiovascular disease, etc.)

3. Targeted Alcohol and HIV/AIDS Populations. Characterize unique aspects of alcohol/HIV interactions among women, children, adolescents and older adults in domestic and international settings and how these are moderated by racial, ethnic, and environmental factors.

- a) Women (e.g., mother-child transmission, prenatal and perinatal alcohol exposure/FASD antiretroviral drug interactions, etc.)
- b) Child, adolescent (e.g., underage exposure and developmental issues, etc.)
- c) Adults, including older adults (e.g., lifespan issues including chronic co-morbid illnesses, medical fragility, etc.)

4. Viral Indices and Disease Dynamics. Examine impact of alcohol on viral indices (e.g. mutation accumulation and resistance), mucosal barriers, blood brain barrier, and immune responses and their impact on susceptibility, progression, and transmission of HIV.

5. Animal Models. Develop cellular, systems-level, and animal models to study mechanisms underlying alcohol/HIV interactions, and to identify effective approaches to translating findings from animal models to human models of alcohol/HIV interactions in the etiology and pathogenesis of AIDS (e.g., imaging in primates, in vitro cellular models of HIV replication, etc.).

6. Complex Patterns of Drinking. Study the effects of longitudinal drinking patterns (including abstinence, withdrawal, and relapse) on HIV disease course (i.e., viral effects and immune effects), co-morbid disease burden, development, and neurocognitive function.

7. Co-infections and Co-factors. Determine mechanisms of alcohol-related immune dysregulation in HIV with and without co-infection (e.g., TB, HCV, etc.) and the impact of other co-morbidities. Consider the effects of cofactors, risk factors, and/or confounders associated with alcohol use disorders and HIV transmission and progression, including but not limited to:

- a) Tobacco
- b) Illicit drugs
- c) Stress
- d) Depression and other co-morbid mental health disorders
- e) Co-occurring infections, including HCV and TB.

- f) Other Chronic medical illnesses
- g) Nutrition (particularly Maternal/ Child and wasting)
- h) Genotypes (viral and host)
- i) Aging

8. Comprehensive Epidemic Modeling. Develop guiding integrative biological models in the areas identified above (areas 1-7) which highlight the multiple impacts of alcohol and to identify overarching complex constructs and processes predicting disease course and outcomes among HIV+ individuals with alcohol use disorders (e.g. frailty, infectivity, rapid progression, etc.). In particular, identify models which can predict the course of the epidemic and help to enhance the quality of care, especially related to the use of medications, and to improve treatment outcomes, including quality of life and survival.