Final Recommendations of the NIAAA Extramural Advisory Board
'Mechanisms of Alcohol Addiction (MAAIT II)'
June 6-7, 2006

All recommendations are to be taken in the context of a translational, feasible approach to understanding aspects of the transition from controlled to uncontrolled drinking. Prospective human studies that include genetics were recommended as likely to be particularly useful. In addition, efforts should be made to foster applications of new technologies and innovative approaches to address specific hypotheses regarding uncontrolled drinking and dependence. Attention to quantity and frequency of alcohol exposure and concentration of alcohol at relevant sites is important. Discovering mechanisms involved in the transition to compulsive alcohol misuse will reveal factors common to other addictions and compulsions, as well as unique alcohol actions that are manifested in distinct characteristics of alcohol dependence. The specific recommendations for priorities are:

1. Learning and Tolerance Mechanisms.
Explore learning, cognitive and tolerance mechanisms that facilitate or inhibit the escalation of drinking (within and across drinking bouts) in human and animal paradigms, and identify actions in relevant molecular and neural systems supporting these mechanisms.

Specific areas of emphasis:
- Thorough assessment of ethanol tolerance in human laboratory studies.
- Interrelationships between cellular, molecular, behavioral manifestations of tolerance as they relate to controlled and compulsive drinking and examine the influence of opponent processes.
- Neural plasticity mechanisms involved in development of compulsive alcohol drinking as they relate to ethanol tolerance and the transfer of control between neural systems supporting instrumental behavior, information processing and motivation.

2. Endophenotypes (risk and genetics)
Identify physiological, temperamental, and cognitive traits and responses to alcohol associated with risk for or protection from developing alcohol dependence and study mechanistically-based hypotheses in animal and human laboratory paradigms.

Specific areas of emphasis:
- Effects of ethanol on measures of impulsivity, motor and emotional response, and physiological measures in controlled studies in humans.
- Hypothesis-driven experiments using animal modeling approaches that adequately capture traits and responses associated with risk for alcohol dependence in humans and incorporating measures of stress-response, subjective/interoceptive effects of ethanol, and imaging. Models should be relevant to important features of the human condition.

3. Adolescent to Adult transitions

Study alcohol's actions upon and interactions with genetic, physiological, hormonal, temperamental, neurocognitive, and social-affective factors associated with transitions into adolescence and adulthood that establish drinking patterns leading to uncontrolled drinking and examine the role of gender and early life events on this trajectory.

4. Epigenetics

Determine the mechanisms and examine the role of epigenetic modifications in the etiology or progression of alcoholism and alcohol-relevant behaviors, examining the influence of alcohol exposure at various life-stages and interactions with stressors and other internal and external moderators.