DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852
Telephone: 301-496-7005
FAX: 301-402-0527

December 23, 2003

Kathryn Handshaw, RN, CIM
Manager, Research Review Committees
and Communications
Lifespan Office of Research Administration
Rhode Island Hospital
593 Eddy Street
Providence, RI 02903

Subject: **Research Protocol Entitled "Alcohol, Sleep and Circadian Rhythms in Young Humans, Study 2 - Effects of Evening Ingestion of Alcohol on Sleep, Circadian Phase, and Performance as a Function of Parental History of Alcohol Abuse/Dependence**

Award Number: **1 R01 AA13252-01**
Principal Investigator **Mary A. Carskadon, Ph.D.**

Dear Ms. Handshaw:

The Department of Health and Human Services (HHS) has completed its review of the above-referenced protocol in accordance with the requirements of the HHS regulations at 45 CFR 46.407 (i.e., research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children).

As you know, in its initial request for review pursuant to 45 CFR 46.407, the Rhode Island Hospital submitted two studies under the larger grant: (1) Study 2 which proposed to study the effects of a small or moderate evening dose of alcohol on sleep, waking performance, and circadian phase in a total of 32 adolescents (15 to 16 years of age) and 32 young adults (21 to 22 years of age), and examine how the effects may differ between individuals who have a parent with a history of alcohol dependence and those who do not; and (2) Study 3, "Effects of Circadian Phase and Sleep/Wake Homeostasis on Alcohol's Effects on Sleep, Performance, Sleepiness, and Mood." Study 3 proposed to alter normal sleep patterns and administer a small or moderate evening dose of alcohol to 24 subjects 18 to 22 years old, in order to study effects of alcohol on the circadian timing mechanism and sleep/wake homeostatic process.

However, the Office for Human Research Protections (OHRP) determined that Study 3 was not eligible for review under the provisions of 45 CFR 46.407 because it involved subjects 18 to 22 years of age and did not involve "children" as defined by HHS regulations and Rhode Island state law. For this reason, a decision by HHS under 46.407 on whether to support the proposed research focused on that portion of Study 2 involving subjects 15 to 16 years of age.

Following consideration of the research protocol, recommendations by experts, comments received from the public, and the deliberations of the of the National Institute on Alcohol Abuse and Alcoholism Special Emphasis Panel, HHS made the two determinations outlined below. For your reference, the HHS decision memorandum is enclosed with this correspondence.

The HHS determinations are as follows:

(1) HHS support of the proposed research, Study 2 involving the enrollment of 15- to 16-year-old subjects is deferred until completion of ongoing IRB-approved studies under grant 1 R01 AA13252 involving the administration of alcohol to subjects 18 years of age or older, and analysis of the resulting data.

(2) This HHS decision is to be made publically available via appropriate methods, such as placement on the OHRP web site.

In addition to deferring HHS support of the proposed research involving the enrollment of 15- to 16-year-old subjects, OHRP provides the following guidance regarding ongoing IRB-approved studies under grant 1 R01 AA13252-01.

(1) The investigators should consider the appointment of a dedicated medical monitor with overall medical oversight for research subjects during the course of the study. It is recommended that this physician be made part of the investigator team and key personnel. In addition to medically clearing the subject for participation in Study 2, the individual would serve as the physician of record during the inpatient alcohol administration studies, and during the follow up of study subjects (see item 2 below). Ideally, this individual would possess experience or certification in addiction medicine.

(2) The investigators should consider incorporating into the experimental protocol a procedure for the medical and psychological follow up of subjects at a defined interval(s) subsequent to the final in-lab study visit. These procedures are intended to assess effects, if any, of study participation on subsequent alcohol or substance use by individual research subjects, and to ensure appropriate medical, psychological, or substance abuse referral.

(3) The investigators should consider revising the assent/permission/consent documents:

   (a) to state more clearly that the study is not likely to present the prospect of direct benefits to individual subjects;
   (b) to avoid implying that the Certificate of Confidentiality may provide more protection than is actually afforded; and

(c) to clearly state the specific amount of alcohol administered in the placebo dose (in milliliters).

(4) The investigators should reconsider the compensation scheme for study subjects to avoid a bonus provided only upon study completion. OHRP is concerned study subjects may feel pressure to complete the alcohol administration study despite experiencing unpleasant side effects from study participation.

Please do not hesitate to contact us with any questions. Thank you for your continuing commitment to the protection of human subjects.

Sincerely,

Irene Stith-Coleman, Ph.D,
Director,
Division of Policy and Assurances
Office for Human Research Protections

Enclosure

cc: Dr. Mary A. Carskadon, Ph.D., E.P. Bradley Hospital
Dr. Lana Skirboll, NIH
Dr. Ellen Witt, NIAAA
Dr. Bernard Schwetz, OHRP
Dr. Melody Lin, OHRP
Dr. Michael Carome, OHRP
Ms. Julie Kaneshiro, OHRP
Ms. Patricia El-Hinnawy, OHRP
Ms. Laura Odwazny, OGC