DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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April 11, 2006

Stein Sture, Ph.D.
Vice Chancellor for Research and
Dean of the Graduate School
University of Colorado at Boulder
308 Regent Administrative Center, 26 UCB
Boulder, CO 80309-0026

RE: Human Research Subject Protections Under Federalwide Assurance FWA 3492

Research Project:	**Behavioral Genetic Analyses of Executive Functions**
Principal Investigator:	**John K. Hewitt, Ph.D.**
HHS Project Number:	**R01MH63207**
UC IRB Number:	**0600.01**
Research Project:	**Workshop on Methodology of Twin Studies**
Principal Investigator:	**John K. Hewitt, Ph.D.**
HHS Project Number:	**R25MH019918**
Research Project:	**Heritable Early Indicators of Risk for Drug Dependence; Component 4 of Antisocial Drug Dependence: Genetics and Treatment (CADD-4)**
Principal Investigator:	**John K. Hewitt, Ph.D.**
HHS Project Number:	**P60DA11015**
UC IRB Number:	**0897.09**

Dear Dr. Sture:

The Office for Human Research Protections (OHRP) has reviewed the University of Colorado at Boulder's (UCB) May 5, 2005 report submitted in response to OHRP's March 28, 2005 letter regarding the above-referenced research.

Based on the review of your report, OHRP makes the following determinations regarding the above-referenced research:

(1) Department of Health and Human Services (HHS) regulations at 45 CFR 46.116 state that, except as provided elsewhere in the regulations, no investigator may involve a human being as a subject in research covered by the regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. OHRP finds that the investigator initiated human subject research without meeting this requirement for certain subjects enrolled in both the Executive Functions Study and the CADD-4 Study.

(2) HHS regulations at 45 CFR 46.408(b) require that adequate provisions be made for soliciting the permission of each child's parents or guardian for participation in the research. HHS regulations at 45 CFR 46.408(d) require that permission of parents or guardians be documented in accordance with and to the extent required by HHS regulations at 45 CFR 46.117. In accordance with HHS regulations at 45 CFR 46.115(b), signed parental permission forms must be retained for at least three years after completion of the research.

OHRP notes that the UCB IRB required that permission of parents or guardians be obtained and documented for children involved as subjects in the Executive Functions Study and the CADD-4 Study. OHRP finds that UCB is unable to provide documented evidence of parental permission for certain children involved as subjects in the Executive Functions Study and the CADD-4 Study.

(3) HHS regulations at 45 CFR 46.408(a) require that adequate provisions be made for soliciting the assent of the children enrolling in the research. HHS regulations at 45 CFR 46.408(e) stipulates that when the IRB determines that assent is required, it shall also determine whether and how assent must be documented. In accordance with HHS regulation at 45 CFR 46.115(b), signed assent forms must be retained for at least three years after completion of the research.

OHRP notes that the UCB IRB required that assent of children be obtained and documented for children involved as subjects in the Executive Functions Study and the CADD-4 Study. OHRP finds that UCB is unable to provide documented evidence of assent for certain children involved as subjects in the Executive Functions Study and the CADD-4 Study.

Corrective Actions: OHRP acknowledges that UCB has developed corrective actions to address the above determinations which include the following:

(a) The UCB IRB is requiring the principal investigator to provide a corrective

action plan to address the above issues which would include (i) training of research personnel on obtaining and documenting consent and (ii) ensuring adequate quality assurance reviews.

(b) Data collected from individuals whose consent has not been obtained shall not be used, unless proper documentation is found and presented to the UCB institutional review board (IRB).

(c) The UCB IRB will hire a new QA/Education Coordinator to conduct periodic audits of both high-risk and randomly-selected protocols.

(d) The UCB IRB will develop a standard operating procedure (SOP) to outline its activities during investigations of noncompliance.

(e) In the future, the UCB IRB will inquire into the investigator's plans for quality assurance for large scale protocols.

Required Action: The UCB IRB must submit a report to OHRP on its implementation of these corrective actions. As part of this report, please provide a copy of the principal investigators corrective action plan and a copy of the UCB IRB's new SOP for investigations of noncompliance.

(4) HHS regulations at 45 CFR 46.111(a)(7) require that, where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. OHRP finds that the UCB failed to maintain the confidentiality of certain subjects enrolled in research conducted by the Institute of Behavioral Genetics.

Corrective Action: The UCB has indicated that it will redouble its efforts to protect all confidential information. In addition, the UCB IRB will remind the Office of Legal Counsel of its obligation to protect information about participants in human subjects research.

OHRP finds that this corrective action adequately addresses the above determination and is appropriate under the UCB FWA. However, OHRP recommends that, as part of its ongoing efforts, the UCB should provide education to all institution officials who may utilize information from human subjects research about the need for protecting privacy and maintaining confidentiality of data.

At this time OHRP has the following additional question and guidance:

(5) [Redacted]

[Redacted]

(6) OHRP reminds UCB that HHS regulations at 45 CFR 46.109(e) require that continuing review of research be conducted by the IRB at intervals appropriate to the degree of risk, but not less than once per year. The regulations make no provision for any grace period extending the conduct of the research beyond the expiration date of IRB approval. OHRP notes that for UCB Protocol # 0600.1 the original approval was granted by the IRB on September 1, 2000. The subsequent renewal dates for this protocol were September 17, 2001, September 11, 2002, August 20, 2003, and September 10, 2004.

Please provide your response to the required action and question noted above no later than May 25, 2006.

OHRP appreciates the continued commitment of your institution to the protection of human research subjects. Please do not hesitate to contact me should you have any questions.

Sincerely,

Patrick J. McNeilly, Ph.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Ms. Sheryl Jensen, HRC Executive Secretary, UC
Dr. Margaret Lecompte, Chair, IRB #1, UC
Dr. Thomas Kunstman, Chair, IRB #2, UC
Dr. Bernard Schwetz, OHRP
Dr. Melody H. Lin, OHRP
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Ms. Patricia El-Hinnawy, OHRP

Ms. Janet Fant, OHRP