DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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March 27, 2006

Arthur C. Vailas, Ph.D.
Vice President for Research
University of Houston
4800 Calhoun
316 East Cullen
Houston, TX 77204-2015

RE: Human Research Subject Protections Under Federalwide Assurance FWA-5994

(1) Research Project: Investigation of Variables Involved in the Behavioral Treatment of Children with Autism
Project Number: 03-097
Principal Investigator: Gerald Harris, Ph.D.

(2) TYAP Project: Acquisition of ABA Treatment Skills: In-Vivo vs. Video Modeling

(3) Research Project: Generalization of Parent Training: A Comparison Study
Principal Investigator: Gerald Harris, Ph.D.

(4) Research Project: Training and Generalizing Interaction Skills with Siblings of Children with Autism
Principal Investigator: Gerald Harris, Ph.D.

(5) Research Project: The Relationship of Parental Stress to Autism Treatment Type and Duration
Principal Investigator: Gerald Harris, Ph.D.

Dear Dr. Vailas:

The Office of Human Research Protections has reviewed the University of Houston's (UH) March 2, 2006 and January 27, 2005 reports regarding the above referenced research and OHRP's inquiry regarding allegations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects involving the above-referenced research.

(1) In its January 25, 2006 letter, OHRP made the following determination:

HHS regulations at 45 CFR 46.103(a), 46.103(b)(4)(ii) and 46.103(b)(5) require that institutions have written institutional review board (IRB) procedures that adequately describe IRB operations with respect to:

> (a) determining which projects require review more often than annually and which need verification from sources other than the investigators that no material changes have occurred since previous IRB review, and
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> (b) ensuring prompt reporting to the IRB, appropriate institutional officials, any Department or Agency head, and OHRP of (a) any unanticipated problems involving risks to subjects or others; (b) any serious or continuing noncompliance with 45 CFR Part 46 or the requirements or determinations of the IRB; and (c) any suspension or termination of IRB approval.

OHRP found that the UH IRB Policies and Procedures supplied to OHRP do not contain specific procedures for how the IRB conducts these activities.

Corrective Action: OHRP acknowledges that UH's IRB Policies and Procedures have now been revised to describe IRB operations adequately with respect to the above requirements under HHS regulations at 45 CFR 46.103(a), 46.103(b)(4)(ii), and 46.103(b)(5).

OHRP makes the following additional findings about the above-referenced research and projects:

(2) HHS regulations at 45 CFR 46.109(a) require institutional review boards (IRBs) to review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by the HHS regulations. With respect to allegations that research was conducted without IRB review and approval and without legally effective informed consent, OHRP finds that this allegation cannot be substantiated. OHRP acknowledges UH's statements that (a) the IRB-approved study # 03-097 titled "*Investigation of Variables Involved in the Behavioral Treatment of Children with Autism*" involves the collection of data from the clinical files of the investigator's private clients at the Texas Young Autism Project; (b) the second referenced project (hereinafter referred to as "TYAP Project") is a presentation of activities conducted by TYAP and was not subject to UH IRB review or approval, and (c) the last three projects (two presentations and one poster) were not based on independent research, but utilized a subset of the research database created under the first, IRB-approved research project.

(3) HHS regulations at 45 CFR 46.116 require investigators to obtain legally effective informed consent prior to the initiation of research. For research involving children, HHS regulations at 45 CFR 46.408 require IRBs to determine that adequate provisions are made for soliciting the assent of children and the permission of each child's parents or

guardian. OHRP finds that when the UH IRB approved study #03-097, it reviewed and approved a parental permission form which contained all of the required elements of informed consent set forth under 45 CFR 46.116. OHRP notes that there is no evidence in the IRB file to determine whether the UH IRB considered, as required by 45 CFR 46.408(a), whether the child subjects involved in study #03-097 were capable of providing assent; however, OHRP acknowledges that UH IRB Policies and Procedures require assent from children capable of providing it, and describe appropriate criteria to include in assent forms.

(4) HHS regulations at 45 CFR 46.111(a)(1)(i) state that, in order to approve research covered by the regulations, the IRB shall determine that risks to subjects are minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk. OHRP questioned whether the UH IRB, in reviewing project #03-097, obtained sufficient information from the investigator regarding data recording technique and statistical method to determine that these regulatory requirements were satisfied.

Corrective Action: OHRP acknowledges that IRB project #03-097 involved only the collection of pre-existing data from TYAP files, and that the UH IRB identified the only significant risk of this research to be the possible loss of confidentiality. OHRP further acknowledges that UH modified its "IRB Application To Conduct Research Using Human Subjects" form to request that investigators include a description of date recording techniques and/or statistical methods to be employed in the research.

(5) HHS regulations at 45 CFR 46.110(c) require IRBs that use expedited review procedures to keep all IRB members advised of research proposals which have been approved via expedited review.

OHRP finds that the UH IRB did not keep all IRB members advised of the approval of project # 03-097, as required by 45 CFR 46.110.

Corrective Action: The UH IRB has modified its reporting procedures to ensure that the minutes for the expedited review subcommittee reflect subcommittee decisions regarding the research proposals it reviews under an expedited review procedure, and that these minutes are presented to the full IRB by one of the reviewing subcommittee members.

(6) HHS regulations at 45 CFR 46.404-407 (subpart D) require specific findings on the part of the IRB for approval of research involving children. OHRP expressed concern that the UH IRB file for project #03-097 provides no evidence that the IRB made the required Subpart D findings.

Corrective Action: OHRP acknowledges UH's statement that, as a matter of policy and practice, the IRB reviews the requirements of subpart D for all research activities involving children. OHRP notes that UH initiated the following changes to address OHRP's concern in this and future research activities: (a) the IRB application form now

requires investigators seeking approval for research involving children to designate what they believe to be the category of the research under HHS regulations (45 CFR 46.404, 46.405, or 46.406) and to explain how the regulatory criteria are met by the study; (b) a new reviewer's worksheet has been developed to require reviewers to identify the appropriate regulatory category for involvement of children in research and to ensure that child assent is obtained if appropriate, and (c) the regulatory category for involvement of children in research will now be noted in IRB meeting minutes.

OHRP finds that the above corrective actions are adequate and appropriate under UH's FWA. As a result, there should be no need for further OHRP involvement in this matter, although you should notify OHRP if new information becomes available which might alter this determination.

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,

Carol J. Weil, J.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Ms. Debra Comeaux, Research Compliance Specialist, U Houston
Dr. Merrill Hiscock, IRB Chair, U Houston IRB #2A and 2B
Dr. Gerald Harris, U Houston
Dr. Bernard Schwetz, OHRP
Dr. Melody H. Lin, OHRP
Dr. Michael Carome, OHRP
Dr. Kristina Borror, OHRP
Ms. Shirley Hicks, OHRP
Dr. Irene Stith-Coleman, OHRP
Ms. Pat El-Hinnawy, OHRP
Ms. Janet Fant, OHRP