DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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May 10, 2004

John R. Sladek Jr., Ph.D.
Vice Chancellor for Research
University of Colorado Health
Sciences Center
4200 East Ninth Avenue, A095
Denver, CO 80262

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1494 and Federalwide Assurance (FWA) 00005070

Research Project:	**Mapping of Vitiligo Susceptibility Genes**
Project Numbers:	**COMIRB No. 98-693, HHS Project No. AR 45584**
Principal Investigator:	**Dr. Richard Spritz**

Dear Dr. Sladek:

The Office for Human Research Protections (OHRP) has reviewed the University of Colorado Health Sciences Center's (UCHSC) April 17, 2003 and April 19, 2004 reports submitted in response to OHRP's letters of February 3, 2003 and February 11, 2004.

After reviewing UCHSC's reports, OHRP makes the following determinations regarding the above-referenced research:

(1) Department of Health and Human Services (HHS) regulations at 45 CFR 46.103(b)(4)(iii) require that the institutional review board (IRB) review and approve all proposed changes in a research activity, during the period for which IRB approval has already been given, prior to initiation of such changes, except when necessary to eliminate apparent immediate hazards to the subjects. OHRP finds that the following protocol changes were implemented without Colorado Multiple Institutional Review Board (COMIRB) approval:

(a) Dr. Spritz conducted serological tests to detect antibodies to certain autoimmune diseases (thyroid disease, diabetes mellitus, Addison's disease, and celiac disease) without COMIRB approval. The version of the protocol approved by the COMIRB on Dec. 12, 2001 contained the following statement on page 6: "Sera will be assayed for anti-melanocyte antibody activity in the laboratories of Dr. George Eisenbarth and Dr. David Norris at UCHSC." There was no mention of any other serological autoimmune antibody tests to be conducted. `Dr. Spritz revised the protocol and consent documents as part of the IRB-prescribed corrective action in 2002. The revised protocol, stamped "Approved Nov. 22, 2002, COMIRB," contained the following statement: "Sera will be assayed for autoimmune antibody activities and thyroid function in the CLIA-certified laboratories of Dr. George Eisenbarth and E. Chester Ridgway at UCHSC."

Corrective Action: OHRP expressed concern in its February 11, 2004 letter that the protocol did not adequately describe either the rationale for conducting the assays or how the assays will be used. In your April 9, 2004 response, you indicated that COMIRB will require Dr. Spritz to amend the protocol to provide adequate justification for performing the additional serological tests. Your response included the proposed language to be inserted in the protocol. You also stated that the COMIRB reviewer checklist has been revised to prompt the reviewer to verify that the protocol explains the rationale for each procedure.

(b) Two ineligible subjects were enrolled in the above-referenced study. Two of the children enrolled were age 3 and age 5, respectively. However, the protocol states that children six years or older will be included in the study, and the grant application states that children seven years or older will be included.

Corrective Action: OHRP acknowledges UCHSC's statement that Dr. Spritz was unaware that these two ineligible subjects had been enrolled until he received the OHRP letter of Feb. 11, 2004. The costs for the genetic testing of the ineligible subjects have now been returned to the National Institutes of Health grant. Dr. Spritz has instituted biweekly project staff meetings to ensure future

protocol adherence among his research staff. COMIRB has mandated that Dr. Spritz pursue additional educational opportunities to enhance his understanding of his responsibilities in the conduct of human subject research; specifically, Dr. Spritz will be required to complete the PRIM&R course entitled Investigator 101. Dr. Spritz's study staff will be required by COMIRB to complete UCHSC human subjects research training courses by July 1, 2004.

(2) OHRP finds that the informed consent document reviewed and approved by the IRB for the above-referenced research failed to adequately provide a complete description of the procedures to be followed as required by HHS regulations at 45 CFR 46.116(a)(1).

The description of the research procedures in the informed consent documents approved for this study prior to November 22, 2002 did not include any reference to the conduct of serological antibody tests for certain autoimmune diseases (thyroid disease, diabetes mellitus, Addison's disease, and celiac disease). Dr. Spritz has acknowledged that he used the blood samples collected for the research study and conducted these additional serological tests that were not specifically described in the consent form.

Corrective Action: UCHSC's April 17, 2003 report to OHRP stated that Dr. Spritz was asked by COMIRB in August 2002 to revise the consent form and re-consent those subjects on whom he had done the unapproved serological testing. This re-consenting process is ongoing.

(3) HHS regulations at 45 CFR 46.111(a)(7) require that, in order to approve research covered by the regulations, the IRB shall determine that, when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. OHRP finds that the principal investigator failed to maintain the confidentiality of subjects' data.

Corrective Action: OHRP acknowledges UCHSC's statement that Dr. Spritz met in April 2003 with the members of his research group and stressed the need to maintain subject confidentiality, including but not limited to the need to refer to subjects by their coded study identifiers only.

OHRP finds that the corrective actions above adequately address OHRP's concerns and findings and are appropriate under UCHSC's assurance. As a result of these determinations, there should be no need for further involvement of OHRP in this matter. Of course, OHRP must be notified should new information be identified that might alter these determinations.

OHRP appreciates your institution's continued commitment to the protection of human research subjects. Do not hesitate to contact OHRP if you have any questions regarding this matter.

Sincerely,

Karena Cooper, J.D., M.S.W.
Compliance Oversight Coordinator
Office for Human Research Protections

cc: Dr. John Moorhead, Associate Dean for Research, UCHSC
Dr. Adam Rosenberg, IRB Co-Chair, UCHSC
Ms. Lisa Jensen, IRB Director, UCHSC
Dr. Richard Spritz, Principal Investigator, UCHSC
Dr. Lana Skirboll, Director, Office of Science Policy, NIH
Dr. Stephen Katz, Director, NIAMS
Commissioner, FDA
Dr. David Lepay, FDA
Dr. Bernard Schwetz, OHRP
Dr. Melody Lin, OHRP
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