DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

FOR US POSTAL SERVICE DELIVERY:
Office for Human Research Protections
6100 Executive Boulevard, Suite 3B01
National Institutes of Health (MSC 7507)
Rockville, Maryland 20892-7507

FOR HAND DELIVERY OR EXPRESS MAIL:
Office for Human Research Protections
6100 Executive Boulevard, Suite 3B01
Rockville, Maryland 20852

Telephone: 301-435-5654
FAX: 301-402-0527
E-mail: sandy_leikin@nih.gov

January 22, 2001

Dr. Robert L. Barchi
Provost
110 College Hall
University of Pennsylvania
Philadelphia, PA 19104

Ms. Mary Chatterton, J.D.
Secretary
Monell Chemical Senses Center
3500 Market Street
Philadelphia, PA 19104-3308

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M1025

Research Project: Perception of Acetone; IRB Numbers 1921-1
Principal Investigator: Charles J. Wysocki;
HHS Project Numbers: RO1 DC-00298; P50 DC00214; F32 DC-00197

Dear Dr. Barchi and Ms. Chatterton:

The Office for Human Research Protections (OHRP) has reviewed your September 29, 2000 report regarding the above referenced research that was submitted in response to OHRP's August 23, 2000 letter.

Based upon its review of your report, OHRP makes the following determinations regarding the actions required by OHRP in its August 23, 2000 letter:

(1) OHRP has determined that the corrective actions summarized below appropriately address the following OHRP findings:

(a) OHRP Finding: The above referenced research underwent initial and continuing review by the University of Pennsylvania (UP) Institutional Review Board (IRB) under an expedited review procedure even though it did not meet the criteria for expedited review, and as a result, did not receive adequate IRB review.

Corrective Actions: (i) UP has implemented training of IRB members and staff in the Office of Regulatory Affairs as to the categories of expedited review. (ii) Only the Executive IRB Chair, or in his absence one of the IRB Chairs designated by the Executive Chair, has authority to perform an expedited review of research. (iii) UP has implemented a procedure whereby all IRB members are notified of all research approved under an expedited review procedure.

(b) OHRP Finding: When the UP IRB conducted its initial and continuing review of the above referenced research, it failed to receive or request from the investigators sufficient information to make the determinations required by Department of Health and Human Services (HHS) regulations at 45 CFR 46.111(a)(1) and (2).

Corrective Actions: (i) Monell Chemical Senses Center (MCSC) has developed an internal working group to review the safety and consent issues related to their research and has worked with the UP IRB to strengthen the IRB's knowledge base regarding the context of research design and risks associated with MCSC's research studies. (ii) UP has engaged outside expert consultants to review the operations of the UP IRB and improve the performance of the IRB. (iii) MCSC now includes full chemical exposure calculations for all protocols similar to the above referenced research that are being submitted to the UP IRB.

(c) OHRP Finding: Informed consent documents approved by the UP IRB for the above referenced research to varying degrees failed to adequately address or include all of the elements required by HHS regulations at 45 CFR 46.116(a).

Corrective Actions: (i) See corrective actions cited for (b) above. (ii) MCSC has revised its sample informed consent document to include all elements of informed consent required under applicable HHS regulations. (iii) One MCSC staff member has been assigned responsibility for reviewing all proposed informed consent documents to ensure that all required elements of informed consent are included.

As a result, OHRP finds that UP and MCSC have adequately implemented Action 1 required by OHRP in its August 23, 2000 letter.

(2) OHRP finds that UP and MCSC have failed to adequately implement Action 2 required by OHRP. In particular, documentation that the proposed debriefing plan provided with your report was reviewed and approved by the UP IRB was not provided to OHRP. Furthermore, OHRP has the following concerns regarding the proposed debriefing documents:

(a) The documents do not appear to describe the concentration of chemicals to which the subjects were exposed during their participation in the research.

(b) The language employed in the documents is highly complex and technical and is unlikely to be understandable to most of the subjects.

Action 1 - Required: The University of Pennsylvania IRB, with input from the research investigators, must develop and forward to OHRP a revised plan, including both the means and the content, for contacting the subjects who participated in the above referenced research and adequately informing them of the nature of the research and its potential risks. OHRP anticipates that any proposed debriefing text would summarize (i) the names and concentrations of the chemicals to which the subjects were exposed; (ii) the exposure safety limits for each chemical; and (iii) the known side effects of each chemical for the range of concentrations at which subjects were exposed. Please submit a written report regarding the IRB's determinations and plan for this matter and the documentation underlying these determinations, including relevant IRB minutes and the proposed text for debriefing the subjects. Please forward your report so that OHRP receives it no later than February 16, 2001.

(3) OHRP finds that UP and MCSC have implemented action 3 required by OHRP in its August 23, 2000 letter.

(4) Regarding Action 4 required by OHRP in its August 23, 2000 letter, OHRP acknowledges that the Executive Chair of the UP IRB now receives and reviews Federal grant applications proposing research involving human subjects. **UP must ensure that such reviews have occurred for all active Federally supported research projects involving human subjects being conducted by UP.**

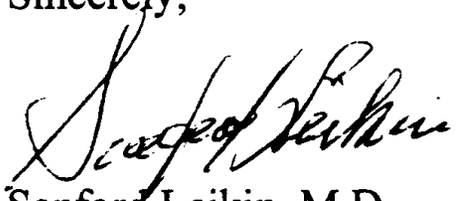
(5) Regarding Action 5 required by OHRP in its August 23, 2000 letter, OHRP finds that revised written IRB policies and procedures were not provided with your report. OHRP acknowledges the extensive efforts being taken by UP to develop new written IRB policies and procedures. According to the time line provided with your report, a draft of the new IRB policies and procedures was expected to be completed by January 15, 2001.

Action 2 - Required: By February 16, 2001, UP must provide OHRP with the current draft of its draft revised written IRB policies and procedures that include an adequate description of all procedures required by HHS regulations at 45 CFR 46.103(b)(4) and (5).

Regarding the issue of Assurances with respect to MCSC, OHRP strongly recommends that MCSC submit to OHRP for approval a new Federalwide Assurance of Protection for Human Subjects. Please see OHRP's website at http://ohrp.osophs.dhhs.gov/irbasur.htm for instructions on submission of a Federalwide Assurance to OHRP.

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

Sincerely,



Sanford Leikin, M.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Greg Koski, OHRP
Dr. Melody Lin, OHRP
Dr. Michael Carome, OHRP
Dr. Katherine Duncan, OHRP
Ms. Roslyn A. Edson, OHRP
Dr. Jeff Cohen, OHRP
Mr. Barry Bowman, OHRP
Dr. Joseph Sherwin, Director of Regulatory Affairs, University of Pennsylvania
Dr. Nicholas Kefalides, IRB Chair, University of Pennsylvania
Dr. David Lepay, FDA
Commissioner, FDA
Dr. James F. McCormack, FDA