DEPARTMENT OF HEALTH & HUMAN SERVICES

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Office of Public Health and Science

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August 27, 2001

Zach Hall, Ph.D.
Executive Vice Chancellor
513 Parnassus Avenue
Room S-101
University of California
San Francisco, CA 94143-0407

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1169 and Federalwide Assurance (FWA) 000068

Research Project: M. A. Escamilla, et al. A minimalist approach to gene mapping: locating the gene for Acheiropodia, by homozygosity analysis. ***Am J Hum Genet*** **66:1995-2000; 2000.**
NIH Project Numbers: K01 MH01453, R01 MH49499, and K02 MH01375

Dear Dr. Hall:

The Office for Human Research Protections (OHRP) has reviewed your January 16, 2001 report regarding the above-referenced research that was submitted in response to OHRP's October 24, 2001 letter.

Based upon its 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 46.102(d) define research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for the purposes of the Federal Regulations at 45 CFR Part 46 whether or not they are conducted or supported under a program which is considered research for other purposes. HHS regulations at 45 CFR 46.102(f) defines human subject as a living individual about whom an investigator conducting research obtains (i) data through intervention or interaction with the individual; or (ii) identifiable private information.

OHRP finds that the activities described in the above-referenced *Am J Hum Genet* article constituted research involving human subjects as defined by HHS regulations.

(2) HHS regulations at 45 CFR 46.109(a) and the University of California San Francisco (UCSF) MPA (see Part 1, section II.B) require that all research involving human subjects that is not exempt be reviewed and approved by the UCSF Institutional Review Board (IRB).

(a) OHRP finds that the above-referenced human subject research did not satisfy the criteria for any category of exempt research under HHS regulations at 45 CFR 46.101(b). In particular, the research did not satisfy the criteria for exemption under HHS regulations at 45 CFR 46.101(b)(4) since (i) the DNA samples obtained by the research team (i.e., the authors of the above referenced *Am J Hum Genet* article) were not existing pathological or diagnostic specimens; and (ii) the information was recorded by the research investigators in a manner that subjects could be identified.

(b) OHRP finds that the above-referenced human subject research was conducted without UCSF IRB review and approval. As a result, there is no evidence that the research satisfied the criteria for IRB approval stipulated by HHS regulations at 45 CFR 46.111. In particular, there is no evidence that the investigators obtained and documented the legally effective informed consent of the subjects in accordance with the requirements of HHS regulations at 45 CFR 46.116 and 46.117, respectively.

(3) HHS regulations at CFR 46.103 require that each institution engaged in human subject research covered by HHS regulations at 45 CFR Part 46 provide OHRP with a satisfactory written assurance that it will comply with the requirements of the HHS regulations. Furthermore, the UCSF MPA (see Part 2, section I.E) stipulated that UCSF was responsible for ensuring that no affiliates cooperating in the conduct of federally sponsored research for which the USCF MPA applied did so without an appropriate assurance of compliance.

OHRP finds that not all institutions engaged in the above-referenced human subject research supported by HHS held an applicable OHRP-approved Assurance.

<u>Action 1 - Required</u>: By October 12, 2001, UCSF must submit to OHRP a satisfactory corrective action plan to address the above findings.

<u>Action 2 - Required</u>: One of the UCSF IRBs, in conjunction with the investigators for the above-referenced research, must assess the adequacy of the informed consent process for the subjects who participated in the research. At a minimum, this assessment should include a review of the informed consent documents used for this research. Following this

assessment, the UCSF IRB must determine whether or not it would be appropriate to develop a plan to contact the subjects and provide them with additional information about their participation in the research. By October 12, 2001, UCSF must submit to OHRP a report on the outcome of this review and assessment by the IRB.

<u>Action 3 - Required</u>: By October 12, 2001, UCSF must submit to OHRP a list of all other institutions engaged in the conduct of the above-referenced research.

<u>Action 4 - Required</u>: UCSF, in conjunction with all of its investigators and and relevant administrators, must audit and identify all ongoing research projects involving human subjects that are not exempt under HHS regulations at 45 CFR 46.101(b) and confirm that all such research has been reviewed and approved by one of the UCSF IRBs. UCSF must suspend immediately any nonexempt research involving human subjects that has not been reviewed and approved by one of the UCSF IRBs. By October 12, 2001, please provide OHRP with a report on the results of this audit and a list of any research activities that have been suspended as a result of this audit.

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

Sincerely,

Michael A. Carome, M.D.
Director, Division of Compliance Oversight

cc Dr. Reese T. Jones, Chairperson, IRB #1, UCSF
Dr. Jay H. Tureen, Chairperson, IRB #2, UCSF
Ms. Sharon Friend, Director, Committee on Human Research, UCSF
Dr. Michael Escamilla, University of Texas Health Science Center
Dr. John Mather, Director, Office of Research Compliance and Assurance, Veterans Health Administration
Commissioner, FDA
Dr. David Lepay, FDA
Dr. James F. McCormack, FDA
Dr. Greg Koski, OHRP
Dr. Melody H. Lin, OHRP
Dr. George Gasparis, OHRP
Dr. Jeffrey Cohen, OHRP
Dr. Kamal Mittal, OHRP
Mr. Barry Bowman, OHRP