DEPARTMENT OF HEALTH & HUMAN SERVICES

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August 28, 2001

Francisco Cigarroa, M.D.
President
The University of Texas Health Science Center at San Antonio
7703 Floyd Curl Drive
San Antonio, Texas 78229-3900

Frank F. Ledford, Jr., M.D., F.A.C.S.
President
Southwest Foundation for Biomedical Research
P.O. Box 760549
San Antonio, Texas 78245-0549

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1403

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. Cigarroa and Dr. Ledford:

The Office for Human Research Protections (OHRP) has reviewed your November 20, 2000 report regarding the above-referenced research that was submitted in response to OHRP's October 24, 2000 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) define 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 Texas Health Science Center at San Antonio (UTHSC) and Southwest Foundation for Biomedical Research (SFBR) MPA (see Part 1, section II.B) require that all research involving human subjects that is not exempt be reviewed and approved by the UTHSC 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 no evidence that the above-referenced human subject research conducted by investigators at UTHSC and SFBR was reviewed and approved by the UTHSC IRB. 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.

(3) HHS regulations at 45 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 MPA M-1403 (see Part 2, section I.E) stipulated that your institutions were responsible for ensuring that no affiliates cooperating in the conduct of federally sponsored research for which MPA M-1403 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, UTHSC and SFBR must submit to OHRP a satisfactory corrective action plan to address the above findings.

<u>Action 2 - Required</u>: By October 12, 2001, UTHSC and SFBR must submit to OHRP a list

of all other institutions engaged in the conduct of the above-referenced research.

<u>Action 3 - Required</u>: UTHSC and SFBR, in conjunction with all of their investigators 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 th UTHSC IRB. UTHSC and SFBR must suspend immediately any nonexempt research involving human subjects that has not been reviewed and approved by the UTHSC IRB. 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. Wayne P. Pierson, Director, IRB, UTHSC
Mr. Jose R. Coronado, Director, South Texas Veterans Health Care System
Dr. Charles A. Coltman, Jr., Medical Director, CTRC Research Foundation
Dr. Helen Hazuda, Chairperson, IRB, UTHSC
Dr. Michael Escamilla, UTHSC
Dr. John Mather, Director, Office of Research Compliance and Assurance, Department of Veterans Affairs
Dr. Greg Koski, OHRP
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Dr. Clifford C. Scharke, OHRP
Mr. Barry Bowman, OHRP