DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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October 19, 2000

Paul E. Stanton, Jr., M.D.
President
East Tennessee State University
P.O. Box 70,734
Johnson City, Tennessee 37614-0734

Carl J. Gerber, M.D., Ph.D.
Medical Center Director
Veterans Affairs Medical Center
Mountain Home, Tennessee 37684

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1194

Research Project: Study of prevalence of reflux esophagitis and Barrett's epithelium in developmentally delayed patients without classic symptoms of reflux
Investigators: P. Goenka, et al

Dear Dr. Stanton and Dr. Gerber:

The Office for Human Research Protections (OHRP) has reviewed Dr. Michael Woodruff's October 10, 2000 report responding to an allegation of noncompliance with Department of Health and Human Services (HHS) regulations for protection of human subjects involving the above referenced research project.

OHRP acknowledges Dr. Woodruff's report that the above referenced research involved a retrospective review of medical records in which data was collected and recorded in such a manner that subjects could not be identified. Based upon this information, OHRP concurs with the assessment that the research was exempt under HHS regulations at 45 CFR 46.101(b)(2) and, as such, informed consent of the subjects or legally authorized representatives of the subjects was not required.

As a result of the above determination, there should be no need for further involvement of OHRP in this matter. Of course, OHRP must be notified should new information be identified which might alter this determination.

OHRP commends East Tennessee State University (ETSU) and the James H. Quillen Veterans Affairs Medical Center (VAMC) for the overall high quality of their written IRB policies and procedures.

At this time, OHRP would like to provide the following guidance regarding your Institutional Review Board (IRB) policies and procedures:

(1) Regarding the Guidelines for the IRB, page 10, fourth paragraph, it appears that the IRB coordinator, a non-voting member of the IRB, may review and approve non-substantive changes stipulated by the IRB. Please note that protocol changes required by the IRB as a condition for approval must be reviewed and approved either by the convened IRB when changes are substantive, or by the IRB Chair (or another voting member designated by the Chair) when the changes are specific and require simple concurrence by the principal investigator.

(2) Where HHS regulations require specific findings on the part of the IRB, such as (a) approving a procedure which alters or waives the requirements for informed consent [see 45 CFR 46.116(d)]; (b) approving a procedure which waives the requirement for obtaining a signed consent form [see 45 CFR 46.117(c)]; (c) approving research involving prisoners (see 45 CFR 46.305-306); or (d) approving research involving children (see 45 CFR 46.404-407), the IRB should document such findings. OHRP strongly recommends that all required findings be fully documented in the IRB minutes, including protocol-specific information justifying each IRB finding.

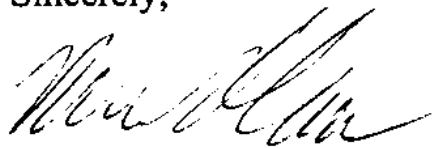
(3) OHRP recommends that ETSU expand its IRB application form and narrative to ensure that the IRB receives sufficient information to make all of the determinations required for approval of research under HHS regulations at 45 CFR 46.111, as well as the additional determination required under 45 CFR Part 46, Subpart B, C, and D. For example, the IRB application should solicit additional information regarding (a) minimization of research risks; (b) subject recruitment and enrollment procedures; (c) the equitable selection of subjects; (d) provisions to protect the privacy of subjects and maintain the confidentiality of data; and (e) additional safeguards to protect the rights and welfare of subjects who are likely to be vulnerable. Furthermore, for research proposing involvement of prisoners or children, investigators should be prompted to provide specific information justifying the inclusion of such subjects in order to satisfy the requirements of Subparts C and D, respectively.

(4) Regarding the POSSIBLE BENEFITS section of the sample informed consent document, OHRP recommends that subject payments not be listed as a benefit of research.

(5) Regarding the sample informed consent document for prisoners, OHRP recommends that a section on alternative treatments or procedures be added.

OHRP appreciates the commitment of your institutions to the protection of human subjects. Please feel free to contact me if you have any questions regarding this matter.

Sincerely,



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

cc: Dr. Michael L. Woodruff, Associate Vice President for Research, ETSU
Dr. David N. Walters, M.D., Chairperson, IRB, ETSU/VAMC
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. J. Thomas Puglisi, OHRP
Mr. George Gasparis, OHRP
Dr. Katherine Duncan, OHRP
Dr. Clifford C. Scharke, OHRP
Dr. Jeffrey Cohen, OHRP
Mr. Barry Bowman, OHRP