DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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September 29, 2003

Thomas J. Rosol, D.V.M., Ph.D.
Interim Vice President for Research
The Ohio State University
Office of Research
208 Bricker Hall
190 North Oval Mall
Columbus, OH 43210-1321

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1238

Research Publication: **Charcot-Marie Tooth Neuropathy Gene Mutation and Their Role in Pathogenesis**
Principal Investigator: **Zarife Sahenk, M.D.**

Dear Dr. Rosol:

The Office for Human Research Protections (OHRP) has reviewed the Ohio State University's (OSU) September 18, 2003 report in response to OHRP's letter of August 4, 2003 which described additional concerns related to the protection of human subjects enrolled in the above-referenced research. These additional concerns were raised when additional material was provided to the OHRP by the complainant.

Based on its review of OSU's report, OHRP makes the following determinations:

(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 major protocol changes were implemented without IRB approval:

(a) The inclusion of healthy control subjects in the study. These healthy control subjects underwent sural nerve biopsy as part of the research procedures.

(b) The inclusion of remuneration for control subjects.

(2) HHS regulations at 45 CFR 46.103(a) and (b)(5) require prompt reporting to the IRB, appropriate institutional officials, the Department of Agency head and OHRP of any suspension or termination of IRB approval. OHRP notes that the IRB approval for the above-referenced research, as well as all other human subjects research conducted by this investigator, was suspended as noted in an April 18, 2003 letter to the investigator. To date, OHRP has not received any report, other than OSU's September 18, 2003 report, describing the suspension of this investigator's research. OHRP finds that OSU failed to promptly report the suspension of the investigator's human subjects research as required by HHS regulations.

Required Action: OSU must provide to OHRP a corrective action plan which adequately addresses the determinations in items (1) and (2) above. In addition, OHRP requests that you provide all records relating to the review of the above-referenced research by the IRB investigative subcommittee. This should include the following:

(a) Copies of minutes (or transcripts) of any meeting of the IRB investigative subcommittee.

(b) Copies of the documents reviewed by the IRB investigative subcommittee.

(c) Copies of all correspondence between the investigator and the IRB.

(d) A copy of any report of the IRB investigative subcommittee submitted to the full IRB or any other OSU official.

(e) Copies of the minutes of any IRB meeting where the above-referenced research was discussed or reported on.

(f) Copies of the informed consent documents (redacted) signed by the healthy control subjects referenced in the OSU September 18, 2003 report.

(g) Any other pertinent information.

Please provide your report and corrective actions no later than October 24, 2003.

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

Sincerely,

Patrick J. McNeilly, Ph.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Judith Neidig, Director, Office of Responsible Research Practices, OSU
Dr. Arthur F. Hefti, Chair, Biomedical Sciences IRB, OSU
Dr. Thomas E. Nygren, Chair, Behavioral and Social Science IRB, OSU
Dr. William E. Carston, III, Chair, Cancer IRB, OSU
Dr. Bernard Schwetz, OHRP
Dr. Melody H. Lin, OHRP
Dr. Michael Carome, OHRP
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Ms. Yvonne Higgins, OHRP
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Ms. Patricia E-Hinnawy, OHRP
Ms. Melinda Hill, OHRP