DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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June 29, 2004

Fawwaz T. Ulaby, Ph.D.
Vice President for Research
University of Michigan
4080 Fleming Building
503 Thompson Street
Ann Arbor, MI 48109-1340

RE: Human Research Subject Protections Under Federalwide Assurance (FWA) FWA 00004969

Research Project: The Hepatitis C Antiviral Long-Term Treatment Against Cirrhosis (HALT-C) Trial: A Randomized Controlled Trial to Evaluate the Safety and Efficacy of Long-Term Peginterferon Alfa-2a for Treatment of Chronic Hepatitis C in Patients Who Failed to Respond to Previous Interferon Therapy

Principal Investigators: Anna Lok, M.D. and Robert Fontana, M.D.
Protocol Number: 2000-186

Dear Dr. Ulaby:

The Office for Human Research Protections (OHRP) has reviewed the University of Michigan's (UM) June 24, 2003, September 2, 2003, and November 12, 2003 reports submitted in response to OHRP's letter of May 16, 2003 regarding the above-referenced research project.

Based upon its review of UM's reports, OHRP makes the following determinations regarding the above-referenced research:

(1) It was alleged that the informed consent document for the above-referenced research failed to include an adequate description of the reasonably foreseeable risks and discomforts, as required by Department of Health and Human Services (HHS) regulations at 45 CFR 46.116(a)(2). In specific, it was alleged that side effects such as trouble breathing and bloody diarrhea were not described in the informed consent

process. After reviewing the materials provided by UM, OHRP notes that such side effects were described in the institutional review board (IRB)-approved informed consent document. As a result, OHRP finds that this allegation could not be substantiated.

(2) It was alleged that the complainant experienced adverse events as a result of participation in the above-referenced research and the investigators failed to evaluate the subject's complaint when these adverse events were brought to their attention. After reviewing materials provided in UM's reports, it is evident that the investigators arranged to evaluate the subject upon learning of problems being experienced by the subject. As a result, OHRP finds that this allegation could not be substantiated.

(3) HHS regulations at 45 CFR 46.116 prohibit any exculpatory language in informed consent through which the subject is made to waive, or appear to waive, any of the subject's legal rights. OHRP finds the following language in the IRB-approved informed consent document for the above-referenced research to be exculpatory:

> "Your DNA samples might be used to develop commercially valuable medical products. By signing this form, you agree not to seek share of any proceeds that might result; that is, you waive any claim to share in the commercialization of products developed from your DNA samples."

OHRP understands that the above-referenced research is closed to new enrollment and expects that, in the future, informed consent documents will not contain exculpatory language, as required by HHS regulations at 45 CFR 46.116.

At this time OHRP has the following guidance:

(4) HHS regulations at 45 CFR 46.116 require that informed consent information be in language understandable to the subject or the subject's legally authorized representative. IRBs should ensure that medical terms and complex sentences presented in informed consent documents are provided to subjects in simpler language. If the prospective subjects include persons whose primary language is not English or populations with the average of a sixth grade education, the IRB should take special care to ensure that both oral presentations and written consent forms are comprehensible to all subjects. The UM IRB may wish to consult the OHRP guidance at http://www.hhs.gov/ohrp/humansubjects/guidance/ictips.htm and http://www.hhs.gov/ohrp/humansubjects/guidance/ic-non-e.htm for further assistance.

As a result of the above determinations, 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 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 Nowack, Assistant Vice President for Research, UM
Dr. Anna Lok, UM
Dr. Robert Fontana, UM
Dr. Robert Cody, Chair, IRB #1 and #6, UM
Dr. Charles Kowalski, Chair, IRB #2, UM
Mr. John O'Shea, Chair, IRB #3, UM
Dr. Gerald Gardner, Chair, IRB #4, UM
Dr. Suzanne Selig, Chair, IRB #5, UM
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