DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852

Telephone: 240-453-8298
FAX: 240-453-6909
E-mail:lisa.buchanan@hhs.gov

November 6, 2009

Kimball C. Atwood, IV, MD
Newton-Wellesley Hospital
2014 Washington St.,
Newton, MA 02462

Robert S. Baratz, MD, DDS, PhD
South Shore Health Center, Inc.
159 Bellevue Street
Newton, MA 02458-1834

Wallace I. Sampson, MD
The Scientific Review of Alternative Medicine
P.O. Box 741
Amherst, NY 14226

Elizabeth Woeckner, AB, MA
Citizens for Responsible Care and Research Inc. (CIRCARE)
10990 Shadow Lane
Columbia, MD 21044

RE: Human Research Protections under Federalwide Assurances FWA-176, FWA-2247, FWA- 9025

Research Project: Trial to Assess Chelation Therapy (TACT)
Principal Investigator: Gervasio A. Lamas, M.D.
HHS Protocol Number: U01-HL-092607

Dear Drs. Atwood, Baratz, Robert, Sampson, Ms. Woeckner:

The Office for Human Research Protections (OHRP) has completed its evaluation of human subject protections in the research referenced above.

Based upon its evaluation, OHRP makes the following determinations relative to protections for human subjects in this research at Mt. Sinai University:

(1) You alleged that the informed consent documents for this study failed to describe accurately and completely all procedures to be followed and to identify any procedures which are experimental as required by HHS regulations at 45 CFR 46.116(a)(1). In specific, you alleged that the informed consent documents falsely imply that the drug being used in the TACT study is approved for treatment of lead toxicity.

We determined that the informed consent documents for this study failed to describe accurately and completely all procedures to be followed and to identify any procedures which are experimental as required by HHS regulations at 45 CFR 46.116(a)(1).

Corrective Action: We acknowledge that the informed consent document was modified to clarify that the disodium EDTA is not the FDA approved agent for chelation therapy in lead toxicity and that the efficacy of this form of EDTA for coronary artery disease (CAD) treatment is being investigated in this study.

(2) You alleged that of the informed consent document for this study failed to include a complete description of any reasonably foreseeable risks and discomforts as required by HHS regulations at 45 CFR 46.116(a)(2). In specific, you alleged that death was not mentioned as a possible adverse event in the list of events that may occur if the test article is infused too quickly.

We determined that the informed consent document for this study failed to include a complete description of the reasonably foreseeable risks and discomforts of the research as required by HHS regulations at 45 CFR 46.116 (a)(2).

Corrective Action: We acknowledge that the informed consent document under Risks and Side Effects was modified to clarify that "death is a rare complication of EDTA infusions."

In addition to the corrective actions above, a "Dear Participant" letter was sent to subjects receiving chelation therapy and the informed consent document was modified to clarify that: 1) the use of disodium EDTA as treatment for heart disease or hardening of the arteries in patients that have suffered a heart attack has never been an approved indication for the drug, and 2) the Food and Drug Administration (FDA) has not approved chelation therapy as an effective treatment for heart disease.

(3) You alleged that the IRB failed to ensure that risks to subjects are minimized and that risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result as required by HHS regulations at 45 CFR 46.111(a)(1) and (2). In specific, you alleged that:

(a) The basis in the protocol for the claim that chelation may be a reasonable treatment for coronary artery disease presented is that removing toxic heavy

metals from the system will treat coronary artery disease. Calcium-sodium EDTA, the form of EDTA used for lead poisoning, would be consistent with that hypothesis and less dangerous than disodium EDTA, but disodium EDTA is the agent used. The use of disodium EDTA in this trial is more consistent with the "decalcification hypothesis" which has been demonstrated to be invalid.

(b) Biochemical literature has demonstrated that the heavy metals hypothesis is implausible and demonstrates that the chelation mixture used in the TACT actually has pro-oxidant effects in vitro.

(c) The trial was begun in the absence of prior supporting laboratory, animal, or human phase 1 or 2 studies, contrary to the usual requirements for a phase 3 trial.

(d) Since the mid-1970's court documents and newspapers have reported at least 30 deaths associated with intravenous disodium EDTA.

In regards to allegations 3(a) through 3(d), the test article used in the TACT study is under an IND issued by the FDA, who may consider the kind of information stated above when issuing an IND. Given this, our office forwarded allegations 3(a) through 3(d) to the FDA for appropriate investigation and/or action.

(e) Several site co-investigators have been disciplined for substandard practices by state medical boards, several have been involved in insurance fraud, and at least three are convicted felons. Most site co-investigators continue to promote chelation while the trial is in progress, even though the intervention has not been shown to be effective.

We note that investigations revealed that several of the TACT study investigators have been accused of substandard practices by state medical boards, involvement in insurance fraud, and three convicted felons. While concerning, these things do not automatically preclude an investigator from participating in research and do not automatically indicate a failure of risks to subjects to be appropriately minimized. The details and circumstances surrounding these incidents must be considered by the IRB when ascertaining the "acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice" as required by HHS regulations at 45 CFR 46.107(b). Based on the information available to us, we determined that, while true, the alleged facts in themselves do not give rise to a violation of 45 CFR 46.

(4) You alleged that the researchers failed to provide subjects with a statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject as required by HHS regulations at 45 CFR 46.116(b)(5) and 46.115(a)(7). In specific, you alleged that subjects should have been informed that the primary agent used in the TACT, is no longer approved for any drug use and have been removed from the market because of safety concerns. (See: http://edocket.access.gpo.gov/2008/pdf/E8-13273.pdf).

We note that the TACT study is testing disodium EDTA for atherosclerosis in post-myocardial infarction subjects and that the use of disodium EDTA in this regard was never an approved indication. Further, in 2008 FDA removed disodium EDTA from the FDA's approved list and withdrew of approval of new drug applications for disodium EDTA. However, the TACT study used disodium EDTA under an FDA issued IND. We determined that subjects should be informed that, disodium EDTA, is not currently indicated to be used for heart disease and that there no reliable evidence of chelation therapy's effectiveness as it may relate to the subject's willingness to continue their participation in this study.

Corrective Action: We acknowledge that the informed consent document was modified to clarify that the research drug, disodium EDTA, is not currently indicated to be used for heart disease and that there no reliable evidence of chelation therapy's effectiveness. This information was included in the "Dear Participant" letter as well.

OHRP has determined that these corrective actions are appropriate under Mt. Sinai University's federal-wide assurance and anticipates no further OHRP involvement in this matter.

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

Sincerely,

Lisa Buchanan, MAOM, CIP
Division of Compliance Oversight

cc:
Dr. Kristina Borror, Director, Division of Compliance Oversight, OHRP