DEPARTMENT OF HEALTH & HUMAN SERVICES PUBLIC HEALTH SERVICE

Office for Human Research Protections
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852
Telephone: 301-435-8072
FAX: 301-402-2071
E-mail: borrork@od.nih.gov

July 11, 2002

Maria H. Sjogren, M.D., M.P.H.
Colonel, Medical Corps
Chief, Department of Clinical Investigation
Walter Reed Army Medical Center
6900 Georgia Avenue, N.W.
Washington, DC 20307-5001

RE: Human Research Subject Protections Under Federalwide Assurance FWA-477

Research Project: The Utility of Electron Beam Computed Tomography (EBCT) as a Screening Test for Coronary Artery Disease, and as an Intervention for Risk Factor Modification Among over 40 Active Duty Personnel
Principal Investigator: Allen J. Taylor, M.D.
Work Unit Number: 1215-98

Dear Dr. Sjogren:

The Office for Human Research Protections (OHRP) has reviewed the Walter Reed Army Medical Center (WRAMC) report dated June 19, 2002, submitted in response to OHRP's April 17, 2002 letter regarding the above-referenced research.

Based on its review of WRAMC's March 31, 2000 response, OHRP made the following determination:

(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 found that numerous changes were made and implemented to the above-referenced research protocols prior to IRB review and approval.

In its April 17, 2002 letter, OHRP requested that WRAMC provide further corrective actions to ensure that no WRAMC investigator implements changes to research protocols prior to review and approval by the IRB.

Corrective Action: OHRP acknowledges that WRAMC has taken numerous corrective actions to ensure that no WRAMC investigator implements changes to research protocols prior to review and approval by the IRB. These actions include required training in the ethics and regulatory requirements of human subject research, and reminding investigators of this requirement in approval letters, the WRAMC Principal Investigator Guide, the Memorandum for Clinical Investigation Researchers Regarding Addendum-Guidelines for Changing Protocols, and in a quarterly newsletter. OHRP finds that these corrective actions adequately address the finding and are appropriate under the WRAMC FWA.

In its April 17, 2002 letter, OHRP expressed the following additional questions and concerns regarding the above-referenced research:

(2) In its December 20, 2001 and April 17, 2002 letters, OHRP expressed concerned that the WRAMC IRB may not have any members who are not otherwise affiliated with the institution, in contravention of HHS regulations at 45 CFR 46.107(d).

OHRP acknowledges WRAMC's statement that the Department of Clinical Investigation is actively making inquiries to identify employees of other research-related Federal agencies to serve on the WRAMC IRB.

(3) HHS regulations at 45 CFR 46.116 state that no investigator may involve a human being as a subject in research unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. The draft manuscript entitled "Do Conventional Risk Factors Predict Sub-Clinical Coronary Artery Disease?: Results from the Prospective Army Coronary Calcium Project" stated "[t]hose personnel who did not consent to the study (n=75) were similar to participants with respect to age, gender, education, and cardiovascular risk factors (diabetes mellitus, total cholesterol, and smoking status.)" OHRP expressed concern that the investigators may have obtained identifiable private information about these non-consenting subjects, and that the IRB apparently never found that waiver of informed consent was appropriate.

Corrective Action: OHRP acknowledges that the WRAMC IRB has determined that the collection of non-consenter risk factor information was a protocol violation, and that further use of such information is denied by the IRB. The investigator no longer is collecting any data from non-consenters. OHRP notes that the use of oral consent, as proposed by the IRB for this

study, would require that the IRB make the findings required by HHS regulations at 45 CFR 46.117(c). OHRP finds that this corrective action adequately addresses OHRP's concern and is appropriate under the WRAMC FWA.

As a result, 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,

Kristina C. Borror, Ph.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. James W. Kikendall, WRAMC
Dr. Allen J. Taylor, WRAMC
Dr. Audrey S. Chang, WRAMC
Dr. Greg Koski, OHRP
Dr. Melody H. Lin, OHRP
Mr. George Gasparis, OHRP
Ms. Jan Walden, OHRP
Mr. Barry Bowman, OHRP