DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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December 20, 2002

Vincent J. Cristofalo, Ph.D.
President
Lankenau Medical Research Center
100 Lancaster Ave.
Wynnewood, PA 19096

RE: Human Subject Research Protections Under Multiple Project Assurance (MPA) M-1554 and Federalwide Assurance FWA-1169

Research Project: Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)
Project Number: F/N-R95-918
Principal Investigator: James Burke, M.D.

Dear Dr. Cristofalo:

The Office for Human Research Protections (OHRP) has reviewed the Main Line Hospitals (MLH) December 16, 2002 report regarding the above-referenced research that was submitted in response to OHRP's November 14, 2002 letter to MLH.

In its November 14, 2002, OHRP made the following determinations regarding the above-referenced research:

> (1) OHRP found that certain unanticipated problems involving risks to subjects or others were not promptly reported to appropriate institutional officials, the institutional review board (IRB), OHRP, or the head of the sponsoring Federal department or agency as required by Department of Health and Human Services (HHS) regulations at 45 CFR 46.103(a) and 46.103(b)(5). OHRP expressed concern that the Adverse Event Policy and Report Form does not define unanticipated problems involving risks to subjects or others and focuses only on "unexpected reactions to biologicals, drugs, or medical devices."
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> **Corrective Action:** OHRP acknowledges that the MLH IRB Adverse Event Reporting Policy and Form have been revised to note that there can be unanticipated problems involving risks to

subjects or others that are unrelated to drugs, biologics and devices (for example, loss of privacy or confidentiality, or suicide attempt after participating in a survey on a sensitive topic) may occur in clinical research.

(2) OHRP found that when reviewing amendments to the above-referenced protocol application, the IRB appeared to lack sufficient information to make the determinations required for approval of research under the HHS regulations at 45 CFR 46.111.

Corrective Action: OHRP acknowledges that the MLH Director of Regulatory Affairs has issued a memorandum to MLH clinical investigators that the MLH IRB should be notified of all changes to research, and approval from the IRB should be obtained before implementing such changes.

OHRP finds that these corrective actions adequately address the above findings and are appropriate under the MLH FWA. As a result, OHRP is closing its investigation and anticipates no need for further involvement in this matter. Of course, OHRP must be notified should new information be identified which might alter this determination.

OHRP appreciates the commitment of your institution to the protection of human 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. Gerald Litwack, Thomas Jefferson University
Dr. Albert A. Keshgegian, Chair, Lankenau Hospital IRB #1
Dr. James Burke, Lankenau Hospital
Dr. Wendy Baldwin, Deputy Director for Extramural Research, NIH
Dr. Claude Lenfant, Director, NHLBI
Dr. Jeffrey A. Cutler, Program Director, NHLBI
Dr. Curt D. Furberg, ALLHAT Steering Committee Chair
Dr. Melody Lin, OHRP
Dr. Michael Carome, OHRP
Mr. George Gasparis, OHRP
Dr. Hal Blatt, OHRP
Mr. Barry Bowman, OHRP
Commissioner, FDA
Dr. David Lepay, FDA