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: 301-435-0668
FAX: 301-402-2071
E-mail: pmcneilly@osophs.dhhs.gov

December 11, 2001

William Tasman, M.D.
Ophthalmologist-in-Chief
Wills Eye Hospital
900 Walnut Street
Philadelphia, PA 19107

Gerald Litwack, Ph.D.
Associate Dean for Scientific Affairs
Thomas Jefferson University
1020 Locust Street, M-5
Philadelphia, PA 19107-6799

D. McWilliams Kessler
Executive Director
Wills Eye Hospital
900 Walnut Street
Philadelphia, PA 19107

Thomas J. Lewis
President and Chief Executive Officer
Thomas Jefferson University Hospital, Inc.
111 South 11th Street
Philadelphia, PA 19107

RE: Human Research Subject Protections Under Multiple Project Assurances (MPA) — M-1231 and M-1115

Research Project: Phase I Dose Escalation Study of Multiple Fraction Stereotactic Radiotherapy for the Treatment of Intracranial Arteriovenous Malformations
Principal Investigator: David W. Andrews

Dear Dr. Tasman, Mr. Kessler, Dr. Litwack and Mr. Lewis:

The Office for Human Research Protections (OHRP) has reviewed the Thomas Jefferson University (TJU) reports dated June 6, 2001and November 21, 2001, as well as the Wills Eye Hospital (WEH) reports dated June 7, 2001 and November 19, 2001. Based on the documents provided in your

reports and subsequent discussion during a telephone conference call with OHRP on November 2, 2001, OHRP acknowledges the following corrective actions taken by TJU and WEH:

(1) TJU and WEH have developed a satisfactory plan to contact all subjects of the above referenced research. The text of the draft letters intended to inform the subjects appropriately describes their unwitting participation in the research, the risks associated with the research, and the nature of the investigators noncompliance.

OHRP finds that the proposed procedure for contacting and debriefing subjects which was approved by the TJU and WEH IRBs is acceptable. OHRP concurs with this procedure. OHRP requests that TJU provide OHRP with a copy of a representative letter submitted to the study subjects (with redaction of name and address) once the initial contact letters have been issued.

(2) TJU and WEH have conducted a campus-wide audit of all research involving human subjects to ensure that all studies had undergone IRB review and approval and have appropriately suspended all research studies which had not had proper Institutional Review Board (IRB) approval.

(3) TJU and WEH have developed an adequate plan to educate all research investigators, IRB members, and all IRB staff on an ongoing basis about the ethical principles and regulatory requirements for the protection of human subjects.

(4) TJU and WEH have provided written procedures and documents which adequately address the additional findings raised in OHRP's April 23, 2001 letter. OHRP acknowledges the increase in staffing for the IRB, the new policies and procedures for the conduct of IRB meetings, review of protocols, and procedures for obtaining informed consent for at WEH. OHRP also acknowledges the efforts by TJU to strengthen its system for the protection of human subjects including expansion of IRB staffing, appointment of a full time Executive Secretary, increasing the quality of its IRB minutes and revising IRB templates for informed consent documents.

(5) TJU has suspended all research involving human subjects which had previously undergone continuing review during the period of October 2000 through October 2001. In addition, TJU has conducted a substantive and meaningful review of those protocols which were suspended. OHRP acknowledges that, as of November 21, 2001, of the 268 protocols which were suspended, 233 were reapproved, 6 remain conditionally approved and 29 were disapproved.

(6) The TJU IRBs have approved a new Standard Operating Procedure for the review of protocol amendments.

(7) The workload of the TJU IRBs has been split and each IRB no longer acts and votes on the research that is reviewed by the other IRB. Separate minutes are now recorded for each IRB which document the discussion and vote for each continuing review and protocol amendment.

OHRP finds that the corrective actions listed above adequately address the issues raised in its April 23, 2001 and October 15, 2001 letters to TJU and WEH. Based on this determination and under the presumption of full implementation of the debriefing plan referenced in item (1) above, there should be no further involvement of OHRP relating to this matter.

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. David G. Brock, Chairperson, IRB-01, TJU
Dr. Stephen P. Weinstein, Chairperson, IRB-02, TJU
Dr. Gregory Mokrynski, Chairperson, IRB-03XB, TJU
Dr. Larry Donoso, IRB Administrator, WEH
Dr. Carl Regillo, Chairperson, IRB, WEH
Dr. David Andrews, TJU
Commissioner, FDA
Dr. David Lepay, FDA
Dr. James F. McCormack, FDA
Dr. John Mather, Veterans Health Administration, Department of Veterans Affairs
Dr. Greg Koski, OHRP
Dr. Melody Lin, OHRP
Dr. Michael Carome, OHRP
Mr. Harold Blatt, OHRP
Mr. George Gasparis, OHRP
Dr. Jeffrey Cohen, OHRP
Mr. Barry Bowman, OHRP