DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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January 29, 2002

Ronald S. Newbower, Ph.D.
Senior Vice President for Research and Technology
50 Staniford Street, Suite 1001
Massachusetts General Hospital
Boston, MA 02114

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1331

Research Project: Ventilation with Lower Tidal Volumes as Compared with Traditional Tidal Volumes for Acute Lung Injury and the Acute Respiratory Distress Syndrome (N. Engl J Med 2000;342:1301-8)
HHS Project Number: N01-HR46064

Dear Dr. Newbower:

The Office for Human Research Protections (OHRP) has your September 26, 2000 report responding to allegations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR Part 46) that were presented in OHRP's August 3, 2000 letter regarding the above-referenced research.

The allegations involved the following:

(1) Failure of the investigators to obtain the legally effective informed consent from the subjects or legally authorized representatives of the subjects in contravention of the requirements of HHS regulations at 45 CFR 46.116.

(2) The Institutional Review Board (IRB) may have approved waiver of the requirement for obtaining informed consent of some subjects when the research did not satisfy the criteria for such a waiver under HHS regulations at 45 CFR 46.116(d). In specific, it is alleged that the

research involved greater than minimal risk and did not satisfy the required criterion at 45 CFR 46.116(d)(1).

Based upon its review of your report, OHRP acknowledges the following:

(1) Massachusetts General Hospital (MGH) was the coordinating center for the above referenced multi-center trial.

(2) As the coordinating center, the MGH collected data from other sites and provided data analysis. MGH did not enroll or interact with subjects, and thus did not participate in the informed consent process or determine whether a waiver of such consent was appropriate.

As a result, OHRP finds that the above-referenced allegations were not substantiated with respect to MGH's involvement in the research, and 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.

At this time, OHRP provides the following feedback regarding MGH's written IRB policies and procedures:

(1) OHRP commends MGH for having written IRB policies and procedures that overall are very detailed and substantive.

(2) MGH's written IRB policies and procedures should be expanded to provide the additional operational details for each of the following procedures required by HHS regulations at 45 CFR 46.103(b)(4) and (5):

(a) The procedures which the IRB follows for determining which projects require review more often than annually.

(b) The procedures which the IRB follows for determining which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review.

(c) The procedures for ensuring prompt reporting to OHRP of any unanticipated problems involving risks to subjects or others.

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,

Michael A. Carome, M.D.
Director, Division of Compliance Oversight

cc: Mr. Harold J. DeMonaco, Chairperson, IRB, MGH
Commissioner, FDA
Dr. David Lepay, FDA
Dr. James F. McCormack, FDA
Dr. Melody H. Lin, OHRP
Mr. George Gasparis, OHRP
Dr. Jeffrey Cohen, OHRP
Ms. Yvonne Higgins, OHRP
Mr. Barry Bowman, OHRP