DEPARTMENT OF HEALTH & HUMAN SERVICES

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August 28, 2000

Ms. Peggy McGill
Office of Research Administration-Lifespan
The Miriam Hospital
164 Summit Avenue
Providence, RI 02906

**RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1369**
**Research Projects Involving Prisoners**

Dear Ms. McGill:

The Office for Human Research Protections (OHRP), formerly the Office for Protection from Research Risks (OPRR), has reviewed The Miriam Hospital's (TMH's) January 28, 2000 report regarding research involving prisoners as subjects, as well as the February 17, 2000 addendum to this report.

Based upon its review of this report, OHRP makes the following determinations:

(1) OHRP finds that a prisoner, or a prisoner representative was not routinely in attendance as a voting member when the Institutional Review Board (IRB) at THM reviewed and approved research involving prisoners as subjects (including initial review, continuing review, review of protocol modifications, and review of unanticipated problems involving risks to subjects or others), as required by Department of Health and Human Services (HHS) regulations at 45 CFR 46.304(b).

Corrective Action: OHRP finds that TMH has taken appropriate corrective actions to address the above finding, including (a) suspending all research involving prisoners as subjects; (b) requiring that the IRB re-review all such research with a prisoner representative participating at the convened IRB meeting as a voting member; and (c) implementing a new IRB policy requiring that the prisoner representative member be present as a voting member at all IRB meetings at which research involving prisoners as subjects is to be reviewed.

(2) OHRP finds that prior to February 2000, TMH failed to certify to OHRP, acting on behalf of the Secretary of HHS, that the IRB had fulfilled all its duties stipulated under 45 CFR 46.305(a) when reviewing and approving HHS-supported research involving prisoners as subjects, as required by HHS regulations at 45 CFR.46.305(c) and 46.306(a)(1).

Corrective Action: OHRP finds that TMH has taken appropriate corrective actions to address the above finding, including (a) submitting to OHRP the certification required by HHS regulations at 45 CFR 46.305(c) and 46.306(a)(1) for all current HHS-supported research involving prisoners as subjects; and (b) implementing a new IRB policy requiring TMH to obtain confirmation that OHRP, acting on behalf of the Secretary of HHS, has judged each HHS-supported research protocol involving prisoners as subjects to involve solely one or more of the permissible categories of research stipulated by HHS regulations at 45 CFR 46.306(a)(2)(A)-(D) prior to the enrollment of prisoner subjects in such research.

(3) HHS regulations at 45 CFR 46.115(a)(2) require that the minutes of IRB meetings document the vote on all IRB actions including the number of members voting for, against, and abstaining. Based upon its review of minutes of recent IRB meetings, OHRP finds that the IRB fails to consistently satisfy this requirement.

In order to document the continued existence of a quorum, OPRR strongly recommends that votes be recorded in the minutes using the following format: Total = 15; Vote: For-14, Opposed-0, Abstained-1 (NAME).

(4) OHRP finds that the institution does not have written IRB policies and procedures that adequately describe the following activities, as required by HHS regulations at 45 CFR 46.103(b)(4) and (5):

(a) The procedures which the IRB will follow for determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review.

(b) The procedures for ensuring prompt reporting to appropriate institutional officials, any supporting Department or Agency head, and OHRP of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with 45 CFR Part 46 or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval.

(5) Continuing IRB review of research must be substantive and meaningful. In conducting continuing review of research not eligible for expedited review, all IRB members should at least receive and review a protocol summary and a status report on the progress of the research, including (a) the number of subjects accrued; (b) a description of any adverse

events or unanticipated problems involving risks to subjects or others and of any withdrawal of subjects from the research or complaints about the research; (c) a summary of any recent literature, findings obtained thus far, amendments or modifications to the research since the last review, reports on multi-center trials and any other relevant information, especially information about risks associated with the research; and (d) a copy of the current informed consent document. Primary reviewer systems may be employed, so long as the full IRB receives the above information. Primary reviewers should also receive a copy of the complete protocol including any modifications previously approved by the IRB (see OPRR Reports 95-01). Furthermore, the minutes of IRB meetings should document separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB.

Regarding the description of the continuing review procedure in the TMH IRB Policies and Procedures, OHRP is concerned that continuing review of research by the IRB may fail to satisfy all of the above requirements. In specific, OHRP is concerned that all IRB members do not receive copies of progress reports and informed consent documents prior to the convened meetings.

As a result of the above determinations, and assuming that TMH will implement additional corrective actions to appropriately address findings (3)-(5) above, there should be no need for further involvment of OHRP's Compliance Oversight Branch in 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,

Sanford Leikin, M.D.
Compliance Oversight Coordinator
Division of Human Subject Protections

Enclosure: OPRR Reports 95-01

cc: Dr. Melody Lin, OHRP
Dr. Michael Carome, OHRP
Dr. J. Thomas Puglisi, OHRP
Ms. Freda Yoder, OHRP
Ms. Carol J. Weil, OHRP
Dr. Katherine Duncan, OHRP
Dr. Jeffrey Cohen, OHRP
Dr. Roger Griffith, Chairperson, TMH
Ms. Kathryn E. Handshaw, TMH

Commissioner, FDA
Dr. David Lepay; FDA
Dr. James F. McCormack, FDA