DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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December 14, 2001

David Dunlap
Chief Executive Officer
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2700 Napoleon Avenue
New Orleans, Louisiana 70115

RE: Human Subject Protections Under Cooperative Project Assurance (CPA) T-3744

Dear Mr. Dunlap:

The Office for Human Research Protections (OHRP) has reviewed your October 31, 2001 report that was submitted in response to the findings and concerns cited in OHRP's September 4, 2001 letter.

Based upon its review, OHRP has determined that Memorial Medical Center (MMC) has implemented or proposed appropriate corrective actions to address OHRP's findings and concerns. In particular, OHRP notes the following:

(1) The minutes of MMC Institutional Review Board (IRB) meeting now include all details required by Department of Health and Human Services (HHS) regulations at 45 CFR 46.115(a)(2).

(2) The minutes of MMC IRB meetings now document that substantive review of research takes place at convened meetings.

(3) The MMC IRB policies and procedures have been expanded to include additional operational details for initial review and the IRB is developing additional written policies and procedures required under HHS regulations at 45 CFR 46.103(b)(4) and (5).

(4) MMC has adequately addressed OHRP's concerns regarding the NSABP 28 protocol.

As a result of the above determination, 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 additional guidance:

(1) The MMC IRB written policies and procedures should be revised to include additional operational details of the following procedures:

(a) The procedures which the IRB follows for conducting its continuing review of research.

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

(c) 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.

(d) The procedure which the IRB follows for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.

(e) The procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and Department or Agency head of each of the following

(i) Any unanticipated problems involving risks to subjects or others.

(ii) Any serious or continuing noncompliance with 45 CFR Part 46 or the requirements or determinations of the IRB.

(iii) Any suspension or termination of IRB approval.

(2) Continuing reviews of research must be conducted by the convened IRB, except where expedited review is appropriate under HHS regulations at 45 CFR 46.110(b)(1) for the

categories of research listed in the Federal Register of November 9, 1998 (63 FR 60364-60367).

(3) 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. Furthermore, the minutes of IRB meetings should document separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB.**

(4) Please note that when the convened IRB approves research contingent upon specific revisions requiring simple concurrence by the investigator, only the IRB Chair or another IRB member designated by the Chair may review and approve the revised research protocol on behalf of the IRB under an expedited review procedure. Furthermore, all IRB members must be advised of such approval actions in accordance with HHS regulations at 45 CFR 46.110(c).

(5) Where HHS regulations require specific findings on the part of the IRB, such as (a) approving a procedure which alters or waives the requirements for informed consent [see 45 CFR 46.116(d)]; (b) approving a procedure which waives the requirement for obtaining a signed consent form [see 45 CFR 46.117(c)]; (c) approving research involving prisoners (see 45 CFR 46.305-306); or (d) approving research involving children (see 45 CFR 46.404-407), the IRB should document such findings. OHRP strongly recommends that all required findings be fully documented in the IRB minutes, including protocol-specific information justifying each IRB finding.

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: Dr. Barry F. Faust, Chair, IRB, MMC
Ms. Joan Mauer, NCI, CTEP
Commissioner, FDA
Dr. David Lepay, FDA
Dr. James F. McCormack, FDA
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