DEPARTMENT OF HEALTH & HUMAN SERVICES

OFFICE OF THE SECRETARY
OFFICE OF PUBLIC HEALTH AND SCIENCE

FOR US POSTAL SERVICE DELIVERY:
Office for Human Research Protections
6100 Executive Boulevard, Suite 3B01
National Institutes of Health (MSC 7507)
Rockville, Maryland 20892-7507

FOR HAND DELIVERY OR EXPRESS MAIL:
Office for Human Research Protections
6100 Executive Boulevard, Suite 3B01
Rockville, Maryland 20852

Telephone: 301-435-0062
FAX: 301-402-2071
E-mail: weilc@od.nih.gov

February 15, 2001

Dr. James W. Patrick
Dean and Vice President of Research
Baylor College of Medicine
12090 Moursund Street
Houston, TX 77030

Re: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1060

Dear Dr. Patrick:

The Office for Human Research Protections (OHRP) has reviewed the information submitted by Dr. Paul Meyers on January 2, 2001, describing recent developments in the human subject protection program at Baylor College of Medicine (BCM).

Based upon its review, OHRP has determined that the BCM institutional review board's (IRB's) modified initial and continuing review procedures are in compliance with the Department of Health and Human Services (HHS) regulations governing the protection of human research subjects.

As a result, 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.

OHRP Guidance

At this time, OHRP provides the following additional guidance to BCM:

(1) Section IV(B)(2) of BCM's document entitled "Narrative Description – Initial and Continuing Review Procedures at Baylor College of Medicine and Related Documents" describes the BCM IRB's procedures for approving protocols with modifications. The description appears to indicate that the IRB approves protocols contingent upon the investigator making substantive changes not dictated expressly by the IRB, without requiring additional review by the convened IRB. OHRP recommends the following guidelines in such cases: (a) When the convened IRB requests substantive clarifications, protocol modifications, or informed consent document revisions, IRB approval of the

proposed research must be **deferred**, pending subsequent review by the convened IRB of responsive material. (b) Only when the convened IRB stipulates specific revisions requiring simple concurrence by the investigator may the IRB Chair or another IRB member designated by the Chair subsequently approve the revised research protocol on behalf of the IRB under an expedited review procedure.

(2) Section (IV(B)(5) of BCM's document entitled "Narrative Description – Initial and Continuing Review Procedures at Baylor College of Medicine and Related Documents" indicates that abstention from voting by an IRB member results in "no procedural changes." OHRP notes that Department of Health and human Services (HHS) regulations at 45 CFR 46.107(e) stipulate that no IRB member may participate in the IRB's initial or continuing review of a project in which the member has a conflicting interest, except to provide information requested by the IRB. OHRP strongly recommends that IRB members absent themselves from the meeting room when the IRB votes on research in which they have a conflicting interest, and such absence should be noted in the IRB meeting minutes. OHRP emphasizes that in accordance with HHS regulations at 45 CFR 46.108, should the quorum fail anytime during a convened IRB meeting (e.g., those with conflicts being excused, early departures, loss of a nonscientist), binding actions and votes cannot be taken until the quorum is restored.

(3) In conducting the initial review of proposed research, IRBs must obtain information in sufficient detail to make the determinations required under HHS regulations at 45 CFR 46.111. The BCM IRB's Human Protocol Summary Form submitted to OHRP requests that investigators limit information provided on the form to three (3) pages. OHRP is concerned that this page limitation may discourage investigators from providing to the IRB information necessary for it to make required determinations under HHS regulations at 45 CFR 46.111. OHRP acknowledges BCM's statement that the page limitation is not enforced, and that BCM intends to eliminate the page restriction on its Human Subject Protocol Form.

(4) A BCM document entitled "Chart Review Protocol Summary Information" in Appendix L: Information Packet for Investigators states that if a chart review is within an investigator's private clinical practice, IRB review and approval is not required. Please note that HHS regulations at 45 CFR 46.101(b)(4) exempt from IRB review research involving the study of patients' medical records if (a) the records already exist at the time the research is proposed, and (b) the information obtained is recorded in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. OHRP recommends that BCM evaluate its policy regarding chart reviews to ensure that all human subject research covered by the BCM MPA which involves review of patient medical records that does not satisfy the criteria for exemption under HHS regulations at 45 CFR 46.101(b)(4) is reviewed and approved by the BCM IRB.

(5) On page 3 of BCM's Policy and Procedures Handbook for IRB members, there is a definition for Implied Consent. OHRP notes that the HHS human subject protection

regulations do not recognize this concept. Under 45 CFR 46.116, obtaining legally effective informed consent is a prerequisite to involving human subjects in research. Under HHS regulations at 45 CFR 46.116(d), an IRB may alter or waive some or all of the elements of informed consent if the IRB makes and documents four specific findings. Under HHS regulations at 45 CFR 46.117, informed consent is to be documented by the use of a written and signed consent form, unless the IRB waives this documentation requirement after making the specific findings required under HHS regulations at 45 CFR 46.117(c).

(6) 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.

(7) Page 9 of BCM's Policy and Procedures Handbook contains a section entitled Compassionate/Emergency Approval which authorizes circumvention of the normal IRB review process where there are unforeseeable, urgent clinical needs or opportunities in individual patients. HHS regulations at 45 CFR 46.116(f) clarify that the HHS human subject protection regulations are not intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable Federal, State, or local law. However, OHRP notes that when emergency medical care is initiated pursuant to a research protocol but without prior IRB review, the patient may not be considered a research subject. Such emergency care may not be claimed as research, nor may any data regarding such care be included in any report of a research activity.

OHRP appreciates the continued commitment of BCM to the protection of human research subjects. Please do not hesitate to contact me should you have any questions.

Sincerely,

Carol J. Weil, J.D.
Division of Compliance Oversight

cc: Dr. Kathleen J. Motil, BCM
Dr. Addison A. Taylor, BCM
Dr. Paul E. Meyers, BCM
Dr. Michael Carome, OHRP
Dr. Kristina Borror, OHRP
Dr. Jeffrey Cohen, OHRP
Dr. George Gasparis, OHRP
Mr. Barry Bowman, OHRP
Commissioner, FDA
Dr. David Lepay, FDA
Dr. James F. McCormack, FDA
Dr. John Mather, ORCA
Dr. Elizabeth Horigan, NIAID/NIH