DEPARTMENT OF HEALTH & HUMAN SERVICES

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December 11, 2000

Joseph M. Moerschbaecher, PhD
Vice Chancellor for Academic Affairs
Louisiana State University Medical Center of New Orleans
433 Bolivar Street
New Orleans, LA 70112

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1130

Dear Dr. Moerschbaecher:

The Office for Human Research Protections(OHRP), formerly the Office for Protection from Research Risks (OPRR), has reviewed your April 4, 2000 report responding to concerns that were raised by OPRR as a result of the December 3, 1999 Food and Drug Administration (FDA) Warning Letter that was issued to the Louisiana State University Medical Center (LSUMC).

Based upon its review of your report, OHRP has determined that LSUMC has taken appropriate corrective actions that adequately address the concerns cited in OPRR's February 15, 2000 letter. In particular, OHRP acknowledges that (i) LSUMC has revised and expanded its written Institutional Review Board (IRB) policies and procedures; (ii) the IRB has implemented improved procedures for conducting continuing review at least annually; (iii) minutes of IRB meetings now document the details required by Department of Health and Human Services (HHS) regulations at 45 CFR 46.115(a)(2); (iv) investigators are informed in writing of all IRB decisions to approve or disapprove proposed research activities; and (v) expedited review of research by the IRB is limited to the specific categories of research stipulated by HHS regulations (see 63 FR 60364).

As a result of the above determination, there should be no need for further OHRP involvement in this matter. Of course, OHRP should be notified of any new information which might alter this determination.

At this time, OHRP would like to provide the following additional guidance:

(1) 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. Materials should include the full protocol, a proposed informed consent document, any relevant grant applications, the investigator's brochure (if one exists), and any advertising intended to be seen or heard by potential subjects. Unless a primary reviewer system is used, all members should receive a copy of the complete documentation. These materials should be received by members sufficiently in advance of the meeting date to allow review of this material.

(2) If the IRB uses a primary reviewer system, the primary reviewer(s) should do an in-depth review of all pertinent documentation (see (1) above). All other IRB members should at least receive and review a protocol summary (of sufficient detail to make the determinations required under HHS regulations at 45 CFR 46.111), the proposed informed consent document, and any advertising material. In addition, the complete documentation should be available to all members for review.

(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 (see OPRR Reports 95-01 at http://ohrp.osophs.dhhs.gov/humansubjects/guidance/hsdc95-01.htm). Furthermore, the minutes of IRB meetings should document separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB.

When conducting research under an expedited review procedure, the IRB Chair (or designated IRB member(s)) should receive and review all of the above referenced documentation.

The LSUMC IRB Re-approval Form should be expanded to include a request for the following information: a summary of recent relevant literature, a description of changes to the research since the last review, and a description of any subject complaints.

(4) The written IRB policies and procedures should be expanded to include the operational details for LSUMC procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, any supporting Department or Agency head, and OHRP **any unanticipated problems involving risks to subjects or others**, as required by HHS regulations at 45 CFR 46.103(b)(5).

(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.

(6) IRBs must determine which protocols require continuing review more often than annually, as appropriate to the degree of risk [see 45 CFR 46.103(b)(4) and 46.109(e)]. OHRP recommends that the minutes of IRB meetings clearly reflect these determinations regarding risk and approval period (review interval).

(7) OHRP recommends that IRBs affix the approval and expiration dates to all approved informed consent documents and stipulate that copies of these dated documents must be used in obtaining consent. This procedure helps ensure that only the current, IRB-approved informed consent documents are presented to subjects and serves as a reminder to the investigators of the need for continuing review.

OHRP appreciates your institution's continued commitment to the protection of human research subjects. Do not hesitate to contact me if you have any questions regarding this matter.

Sincerely,

Kristina C. Borror, Ph.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. M. Wayne Hurst, IRB Chair, LSU
Commissioner, FDA
Dr. David Lepay, FDA
Dr. James F. McCormack, FDA
Dr. John Mather, ORCA, Department of Veterans Affairs
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