DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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May 13, 2002

William Pinsky, M.D.
Executive Vice President/Chief Academic Officer
Ochsner Clinical Foundation
1516 Jefferson Highway
New Orleans, LA 70121

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1046 and Federalwide Assurance (FWA) 00002050

FDA Warning Letter Dated March 5, 2002

Dear Dr. Pinsky:

The Office for Human Research Protections (OHRP) has reviewed the reports from the Ochsner Clinical Foundation (OCF) dated March 22, 2002 and April 29, 2002 that were submitted in response to OHRP's letter of March 8, 2002 regarding the above-referenced Food and Drug Administration (FDA) warning letter. OHRP acknowledges the commitment of OCF to the protection of human subjects in its letter of March 20, 2002.

OHRP acknowledges the following corrective actions taken by the OCF in response to OHRP's March 8, 2002 letter:

(1) OCF has (i) suspended all federally sponsored research which had not had appropriate continuing review; and (ii) initiated a procedure for appropriate continuing review of all suspended protocols.

(2) OCF has reorganized its Institutional Review Board (IRB) including the appointment of a new IRB chair.

(3) OCF has provided new space to house the IRB staff and conduct protocol reviews.

(4) OCF has revised the standard Operating Procedures (SOP) of the OCF IRB.

(5) OCF has conducted training for IRB members, staff and investigators. Additionally, new SOPs require that training be conducted at least twice a year.

(6) OCF has modified the minutes of IRB meetings to meet HHS regulations at 45 CFR 46.115(a)(2).

OHRP makes the following determinations:

(1) OHRP finds that the OCF IRB failed to conduct substantive and meaningful continuing review of research in accordance with HHS regulations at 45 CFR 46.109(e). However, OHRP finds that the corrective actions noted above adequately address this finding and are appropriate under the OCF FWA.

(2) OHRP finds that OCF has adequately responded to the additional concerns raised in OHRP's March 8, 2002 letter.

As a result of the above determinations, 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:

(3) OHRP notes that the OCF Guideline for Consent Form Corrections states "[t]he investigator will make the required changes to the consent form, and return the corrected consent form to the panel for confirmation. The confirmation may be made by the Chair or by an assigned expedited reviewer. If the changes are complicated or substantial, the Chair or expedited reviewer has the authority to require that the corrections be confirmed at the next full Panel meeting." OHRP recommends that the following guidelines in such cases: (a) When the convened IRB requests substantive clarifications or modifications regarding the protocol or informed consent documents that are directly relevant to the determinations required by the IRB under HHS regulations at 45 CFR 46.111, IRB approval of the proposed research should 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.

(4) OHRP notes that the OCF guideline for Consent Forms - Required Signature Lines states "[t]he IRB does not require a witness signature line, but will approve consent forms that have one when they are submitted." HHS regulations at 45 CFR 46.117(b)(2) allow for the approval of a short form written consent stating that the elements of informed consent required by HHS regulations at 45 CFR 46.116 have been presented orally to the subject or the subject's legally authorized representative. When such a method is used, there shall be a witness to the oral presentation and the witness shall sign the short form and a copy of the summary. OHRP recommends that the OCF written procedures be revised to address this requirement.

(5) OHRP notes that the OCF informed consent document template asks the investigator to list free medication, laboratory studies and physical examination among the benefits of the research. Although these provisions should be presented to the prospective subject, OHRP believes it is more appropriate to consider the provision of free medical care to be an incentive to participation in a research study and should not be considered a benefit to be gained from the research.

(6) OHRP has the following guidance regarding the OCF Clinical Research Handbook:

(a) The section on Reporting Adverse Events (page 34) makes no mention of the requirements of reporting unanticipated problems involving risks to subjects or others as required by HHS regulations at 45 CFR 46.103(b)(5). OHRP would like to point out that there may be unanticipated problems involving risks to subjects which may not be characterized as an adverse event. For example, the theft of a research computer containing private identifiable information about subjects could be considered an unanticipated problem involving risks to subjects which is reportable to OHRP under the HHS regulations but not under FDA regulations.

(b) The section on Informed Consent Waivers (page 42) references 45 CFR 46.117. OHRP wishes to point out that this regulation only waives the requirement for obtaining a signed consent document. The IRB may only waive informed consent if it finds and documents the criteria at 45 CFR 46.116(c) or (d).

(c) To ensure that investigators at OCF are aware of the HHS regulations for the protection of human subjects OHRP recommends, where appropriate, that HHS regulations related to specific topics be referenced along with those of FDA.

OHRP appreciates the commitment of your institution to the protection of human subjects of research. Please contact me if you have any questions regarding this matter.

Sincerely,

Patrick J. McNeilly, Ph.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Richard Re, OCF
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