DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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January 29, 2009

Jonathan J. Oviatt, J.D.
General Counsel
Mayo Clinic
Siebens 9
200 First Street SW
Rochester, MN 55905

RE: Human Research Subject Protections Under Federalwide Assurance FWA– 5001

Dear Mr. Oviatt:

Thank you for your January 8, 2009 letter in response to our December 4, 2008 letter regarding research conducted under the above-referenced Federalwide Assurance (FWA).

A. Determinations

In our December 4, 2008 letter we made the following determination, among others:

> HHS regulations at 45 CFR 46.115(a) require that the institution prepare and maintain adequate documentation of IRB activities. In numerous instances among the 11 IRB files that were examined, it was difficult to reconstruct a complete history of all IRB actions related to the review and approval of the protocol. In some instances, we could not determine what the IRB actually approved. Given this, we determined that for, some research protocols, the Mayo Clinic failed to prepare and maintain adequate documentation of IRB activities as required by Department of Health and Human Services (HHS) regulations at 45 CFR 46.115(a).

Resolution: We acknowledge your statement that it was unclear whether certain documents related to specific protocols were inadvertently not included in the initial submission of paper files to our office, or if they were difficult to locate due to the very large volumes of documents that were sent. We note your conclusion that the Mayo Clinic's electronic IRB system maintains adequate documentation of IRB actions in accordance with 45 CFR 46.115. This conclusion was based on the fact that all versions of each protocol that were requested by our office were easily

located within the electronic IRB system. Mayo believes that any difficulties associated with adequate documentation of IRB actions arise from the limitations in representing an electronic system by providing paper. We appreciate this explanation, and, given this new information, we rescind our former determination that your institution was in violation of 45 CFR 46.115(a) through its recordkeeping practices.

B. Recommendations

We note that you provided the following information in the January 8, 2009 report:

> "Mayo Clinic notes that the IRB files begin with page 86 of the grant because the first 85 pages contained grant information not reviewed by the IRB. This includes financial information, biographical sketches, and the like. Information describing the specific research proposal began on page 86."

HHS regulations at 45 CFR 46.103(f) require that an institution with an approved assurance shall certify that each application or proposal for research covered by the assurance has been reviewed and approved by an IRB designated under the institution's federalwide assurance. Please note that our guidance document entitled *IRB Review of Applications for HHS Support*, available at http://www.hhs.gov/ohrp/humansubjects/guidance/aplrev.htm, states that the awardee institution for any grant, contract, or cooperative agreement should retain a copy of the entire HHS application or proposal (exclusive of appendices) among IRB records and make such application/proposal available to any IRB member who may wish to review it. The document also indicates that it is important for designated IRB reviewers to have ready access to the entire application or proposal (exclusive of appendices) because information related to the protection of human subjects sometimes appears only in seemingly peripheral sections. Examples include information about (i) the number and qualifications of collaborating investigators and other members of the research team; (ii) cooperating institutions or performance sites that may require separate or additional IRB review or an Assurance of Compliance; (iii) characteristics of proposed research facilities that may affect subject safety or the confidentiality of data; (iv) the feasibility of financial commitments made to subjects; and (v) the cost of proposed subject protection measures, such as consent monitors or translators. This guidance document represents our current thinking regarding why the IRB should have access to the entire grant application, as we have interpreted 45 CFR 46.103(f) to require that the IRB review all of the information in the grant application relating to the specific research proposal at issue. Therefore, we recommend that you revise your policy regarding IRB review of HHS grant applications or proposals for research accordingly.

We acknowledge the remaining response to the question/concern in our December 4, 2008 letter which was provided in your January 8, 2009 letter.

At this time, there should be no need for further involvement by our office in this matter. Please notify us if you identify new information which might alter this determination.

We appreciate your institution's continued commitment to the protection of human research subjects.

Sincerely,

Lisa A. Rooney, J.D.
Compliance Oversight Coordinator

cc: Ms. Marcia Andresen-Reid, Administrator, IRBs, Mayo Clinic
Dr. Bart L. Clarke, Chair, Mayo Foundation IRB #1 and #5
Dr. Joseph K. Lobl, Chair, Mayo Foundation IRB #2
Dr. Randall K. Pearson, Chair, Mayo Foundation IRB #3
Dr. Joseph Rubin, Chair, Mayo Foundation IRB #4
Dr. R. Scott Wright, Chair, Mayo Foundation IRB #6
Acting Food and Drug Administration (FDA) Commissioner
Dr. Joanne R. Less, FDA
Dr. Sherry Mills, Office of Extramural Research (OER), National Institutes of Health (NIH)
Mr. Joe Ellis, OER, NIH