DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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August 30, 2005

C. Bradley Moore, Ph.D.
Vice President for Research
Northwestern University
Rebecca Crown Center, 2-223
633 Clark Street
Evanston, Illinois 60208-1108

RE: Human Research Subject Protections Under Federalwide Assurance FWA-1549

Dear Dr. Moore:

The Office for Human Research Protections (OHRP) has reviewed Northwestern University's (NU) August 11, 2005 report that was submitted in response to OHRP's June 29, 2005 letter regarding determinations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human subjects (45 CFR part 46) that were based upon OHRP's May 10-12, 2005 on-site evaluation of human subject protection procedures at NU. OHRP has determined that the corrective actions summarized below adequately address the findings described in OHRP's letter of June 29, 2005, and are appropriate under NU's FWA.

(1) NU has revised its policies and procedures to make it clear that all substantive modifications and clarifications required for approval of proposed research must return to a convened IRB for review and approval. A description of these clarifications was sent to all IRB members and the research community. NU's Office for the Protection of Research Subjects (OPRS) has also modified its reviewer analysis sheet to ensure that IRB review is thorough and consistent with federal regulations and guidance. This new reviewer analysis sheet will be used in the IRB re-review of research protocols #0108-015, #0221-016, #0390-020, #0390-021, and #0542-016.

(2) NU will audit all active research projects involving children to determine the adequacy of previous IRB review. Each research project determined to have had inadequate IRB review will be re-reviewed by October 31, 2005. The re-review of these research projects will include participation by appropriately qualified IRB members or consultants, in accordance with 45 CFR 46.107 and 45 CFR 46, subpart D. To ensure that the appropriate findings are made and documented during this re-review and in the future, OPRS has

developed a specific reviewer analysis checklist for the review of research involving minors.

(3) NU has identified all active research projects involving pregnant women, fetuses, and neonates, and will audit each project to determine the adequacy of previous IRB review. Each research project determined to have had inadequate IRB review will be re-reviewed by October 31, 2005. The re-review of these research projects will include participation by appropriately qualified IRB members or consultants, in accordance with 45 CFR 46.107 and 45 CFR 46, subpart B. To ensure that the appropriate findings are made and documented during this re-review and in the future, OPRS has developed a specific reviewer analysis checklist for the review of research involving these populations.

(4) NU has submitted reports to OHRP of IRB suspensions of approval for research protocols #0141-022, #0141-024, #0141-025, #0141-026, #0141-031, #0141-034, #0141-037, #0165-007, #0947-004, and #1279-005. NU has revised its policies and procedures to include a section on reporting unanticipated problems involving risks to subjects or others, any serious or continuing noncompliance with 45 CFR part 46 or the requirements or determinations of the IRB, and any suspension or termination of IRB approval. This new policy will be communicated to investigators, OPRS staff, and IRB members by September 1, 2005.

(5) NU's IRB has re-reviewed research protocol #0332-006 in accordance with 45 CFR 46, subpart C, and the review was certified to the HHS Secretary. NU now has two prisoner representatives, and a third prisoner representative is currently being trained. In order to preclude IRB review of prisoner research without a voting prisoner representative being present, NU has taken the following actions:

- The senior OPRS staff member in attendance at the convened IRB meeting will complete a quorum checklist that will be verified by the IRB chairperson to ensure the presence of the prisoner representative when applicable.

- An attendance sheet has been developed for convened IRB meetings to record attendance for each IRB member, as well as for OPRS staff and guests.

- An IRB prisoner checklist for reviewers has been developed to document the IRB review and findings in the categories of research permissible under 45 CFR 46, subpart C.

- Training sessions with the OPRS staff and IRB reviewers were held after the incident, and additional training sessions are planned.

(6) OHRP has determined that NU has adequately addressed the concerns raised by OHRP in its letter of June 29, 2005.

As a result, there should be no need for further involvement of OHRP in this matter. However,

OHRP must be notified should new information be identified which might alter this determination.

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

> (7) HHS regulations at 45 CFR 46.108(b) require that, except when an expedited review procedure is used, research be reviewed at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in a nonscientific area. OHRP recommends that the quorum definition stated in sections A.3. and B.5. in NU's revised policy document entitled "Section II: Management, Operations, and Processes of the IRB" be modified to include the requirement that at least one member whose primary concerns are in a nonscientific area be present at convened meetings.

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

Sincerely,

Robert J. Meyer
Compliance Oversight Coordinator
Division of Compliance Oversight

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