DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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October 10, 2002

Thomas R. Frieden, M.D., M.P.H.
New York City Department of Health and Mental Hygiene
225 Broadway, 23rd Floor
New York, NY 10007

RE: Human Research Protections Under Multiple Project Assurance (MPA) M-1541

Dear Dr. Frieden:

The Office for Human Research Protections (OHRP) has reviewed your August 12, 2002 report regarding the above-referenced research conducted at the New York City Department of Health and Mental Hygiene (NYCDOH) that was submitted in response to OHRP's July 1, 2002 letter.

Based on its review of your February 21, 2002 and June 5, 2002 reports, OHRP made the following determinations:

(1) Department of Health and Human Services (HHS) regulations at 45 CFR 46.110(b)(1) limit the use of expedited review procedures to specific research categories published in the Federal Register at 63 FR 60364-60367. Generally, if research did not qualify for expedited review at the time of initial review, it does not qualify for expedited review at the time of continuing review, except in limited circumstances described by expedited review categories (8) and (9) at 63 FR 60364-60367.

OHRP found that the NYCDOH Institutional Review Board (IRB) inappropriately used an expedited review procedure for continuing review of some research.

Corrective Action: OHRP acknowledged NYCDOH's statement that the IRB is aware that research qualifies for expedited review only under certain circumstances, and that the NYCDOH is complying with this requirement. In its July 1, 2002 letter, OHRP expressed concern that the NYCDOH IRB still was not implementing appropriately the regulatory provisions for expedited review. OHRP acknowledges that the acting chair of the IRB has a thorough understanding of the requirements pertaining to expedited review and that IRB members are being educated as to expedited review (such as when it may be appropriate and

what documentation may be required). The IRB has been notified that where HHS regulations require an IRB to make specific findings, the findings must be documented by the IRB chair or designated member in the IRB record and that the category qualifying the study for expedited review must be documented. These corrective actions appear to adequately address the above finding and are appropriate under the NYCDOH MPA.

(2) HHS regulations at 45 CFR 46.103(f) require that an institution with an approved assurance shall certify that each *application* for research has been reviewed and approved by the IRB. OHRP found that the NYCDOH IRB fails to review grant applications.

Required Action: Please provide a corrective action to address this finding. In its July 1, 2002 letter, OHRP acknowledged NYCDOH's concern that reviewing every grant application prior to actual funding presents a number of problems. OHRP noted that many of these problems can be addressed. In addition, OHRP notes that HHS regulations at 45 CFR 46.118 state that certain types of applications for grants, cooperative agreements, or contracts are submitted to departments or agencies with the knowledge that subjects may be involved within the period of support, but definite plans would not normally be set forth in the application or proposal. These include activities such as institutional type grants when selection of specific projects is the institution's responsibility; research training grants in which the activities involving subjects remain to be selected; and projects in which human subjects' involvement will depend upon completion of instruments, prior animal studies, or purification of compounds. These applications need not be reviewed by an IRB before an award may be made. However, except for research exempted or waived under §46.101 (b) or (i), no human subjects may be involved in any project supported by these awards until the project has been reviewed and approved by the IRB, as provided in this policy, and certification submitted, by the institution, to the Department or Agency.

In addition, NYCDOH stated that the materials submitted in most grant applications bear little resemblance to those that are ultimately incorporated in the final protocol. In your corrective action plan, please include a description of procedures that will be followed to ensure that all discrepancies between the grant application and any IRB protocol application are resolved completely.

Based on its review of NYCDOH's February 21, 2002, June 5, 2002, and August 12, 2002 reports, OHRP makes the following additional determinations:

(3) 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 IRB files examined by OHRP, it was difficult to reconstruct a complete history of all IRB actions related to the review and approval of the protocol. For example, items in the file did not appear to be in chronological order, meeting minutes and other important records were often missing, and dates of review were often not noted.

Corrective Actions: OHRP acknowledges that the new IRB administration has been working to improve the maintenance of IRB files. In addition, the IRB office has been moved to the NYCDOH headquarters building and the files have been placed into secure storage. The new IRB administration has also created an interactive relational database that can track the complete history and all current and future actions on all protocols submitted to the IRB since 1994. These corrective actions appear to adequately address the above finding and are appropriate under the NYCDOH MPA.

(4) In its April 17, and July 1, 2002 letters to NYCDOH, OHRP expressed concern that the NYCDOH IRB is not sufficiently qualified through the experience and expertise of its members, and the diversity of its members, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects, and as a result of this lack of expertise would not have been able to determine that the risks to subjects would be minimized by using procedures which are consistent with sound research design, as required by HHS regulations at 45 CFR 46.107 and 46.111(a)(1). When members of the IRB recognized the IRB's lack of expertise, there appeared to have been some perception by other members that this expertise was not necessary. OHRP noted that HHS regulations at 45 CFR 46.107(f) stipulate that an IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the IRB.

Corrective Action: OHRP acknowledges that the current board has expertise in many areas of research it commonly reviews and that the IRB retains consultants to assist it with review of applications, progress reports, or adverse event reports that require additional or specialty expertise. These corrective actions appear to adequately address the above concern and are appropriate under the NYCDOH MPA.

(5) OHRP finds that the institution does not appear to have written IRB policies and procedures that adequately describe the following activities, as required by HHS regulations at 45 CFR 46.103(a) and 46.103(b)(4) and (5):

> (a) The procedures which the IRB will follow (i) for determining which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review; and (ii) for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.
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> (b) The procedures for ensuring prompt reporting to appropriate institutional officials and OHRP of (i) any unanticipated problems involving risks to subjects or others or any

serious or continuing noncompliance with 45 CFR Part 46 or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval.

Required Action: Please provide OHRP with copies of revised written procedures to address these findings. Please note that while the NYCDOH IRB procedures do mention some of the above-referenced procedures, there is no description of the operational details for the implementation of these procedures. Please see OHRP guidance on written IRB procedures at http://ohrp.osophs.dhhs.gov/humansubjects/guidance/irbgd702.htm for assistance in developing appropriate written IRB procedures.

Please submit to OHRP your response to the above determinations, concerns, and questions no later than November 15, 2002. If upon further review of the concerns and questions, NYCDOH identifies instances of noncompliance with the HHS regulations for protection of human subjects, please include detailed corrective action plans to address the noncompliance.

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

Sincerely,

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

cc: Dr. Benjamin Mojica, Deputy Commissioner, NYCDOH
Dr. Lucia Torian, NYCDOH IRB Chair
Mr. Wilfredo Lopez, NYCDOH, OGC
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