DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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February 4, 2002

Peter Bond, Ph.D.
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RE: Human Research Subject Protections Under Federal Wide Assurance FWA-149

Dear Dr. Bond:

The Office for Human Research Protections (OHRP) has reviewed your letters dated October 25, 2001, January 2, 2002, and January 29, 2002. OHRP has determined that the corrective actions summarized below appropriately address the findings in OHRP's November 16, 2001 site visit letter and are appropriate under the Brookhaven National Laboratory (BNL) FWA:

(1) OHRP found that the BNL Institutional Review Board (IRB) Chair occasionally used inappropriate expedited review procedures for review of protocol changes that exceed the limit of "minor changes," in contravention of the requirements of Department of Health and Human Services (HHS) regulations at 45 CFR 46.110(b)(2).

Corrective Action: OHRP acknowledges that the BNL IRB Policies and Procedures have been revised to more clearly define the types of protocol addenda that may be reviewed and approved under an expedited review procedure.

(2) HHS regulations at 45 CFR 46.115(a) require that an institution or IRB shall prepare and maintain adequate documentation of IRB activities. OHRP found that, in some 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.

Corrective Action: OHRP acknowledges that the IRB Administrator has reviewed all active protocols to ensure that all required documentation is contained in the files in chronological order, and that improvements to the filing system have been made recently.

(3) OHRP found that the institution did not have written IRB policies and procedures that adequately describe the procedures for ensuring prompt reporting to OHRP of 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, as required by HHS regulations at 45 CFR 46.103(b)(5).

Corrective Action: OHRP acknowledges that the BNL IRB Policies and Procedures have been revised to define the specific reporting requirements under HHS regulations at 45 CFR 46.103(b)(5).

(4) OHRP found that the minutes of BNL IRB meetings failed to document the vote on all IRB actions including the number of members voting for, against, and abstaining, as required by HHS regulations at 45 CFR 46.115(a)(2).

Corrective Action: OHRP acknowledges that the BNL IRB has changed the recording of votes in the minutes of the IRB meetings, in accordance with HHS regulations at 45 CFR 46.115(a)(2).

(5) OHRP was concerned that the IRB Chair occasionally has used an expedited review procedure to approve protocol amendments for which review by or consultations with a physician member of the IRB would have been appropriate because the amendments may have had medical implications for subjects. OHRP strongly recommended that a physician member of the IRB be involved in these reviews.

Corrective Action: OHRP acknowledges that the BNL IRB Policies and Procedures have been revised to clearly require review by the convened IRB of any addendum where the change may have medical implication for the subject to ensure that a physician is involved in the evaluation.

(6) OHRP was concerned that some instances of serious noncompliance were not promptly reported to the BNL IRB and OHRP, as required by HHS regulations at 45 CFR 46.103(b)(5).

Corrective Action: OHRP acknowledges that the BNL IRB Policies and Procedures have been revised to outline the requirements and procedures for reporting instances of serious noncompliance as required by HHS regulations at 45 CFR 46.103(b)(5).

(7) OHRP was concerned that on occasion the IRB approved research contingent upon substantive modifications or clarifications without requiring additional review by the convened IRB. OHRP recommends the following guidelines in such cases: (a) When the convened IRB requests substantive clarifications, protocol modifications, or informed consent document revisions, 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.

Corrective Action: OHRP acknowledges that the BNL IRB Policies and Procedures have been revised to reflect OHRP's guidance on conditional approval of protocols.

As a result, OHRP is closing its investigation and anticipates no need for further involvement in this matter. Of course, OHRP must be notified should new information be identified which might alter this determination.

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 Compliance Oversight

cc: Dr. Peter Paul, Acting Director, BNL
Dr. Thomas Sheridan, Deputy Director, BNL
Ms. Darcy J. Mallon, IRB Administrator, BNL
Ms. Margaret C. Bogosian, IRB Chair, BNL
Dr. Nora Volkow, BNL
Dr. Julia Yang, BNL
Dr. Helene Benvenista, BNL
Dr. Susan L. Rose, DOE
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Dr. David Lepay, FDA
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