DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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April 25, 2006

Richard Homan, M.D.
Philadelphia Health and Education Corporation
(Drexel University College of Medicine)
245 N. 15th Street
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Philadelphia, PA 19102-1192

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1532 and Federalwide Assurance FWA-5917

Research Publication: Brannagan TH, et al. High-dose cyclophosphamide without stem-cell rescue for refractory CIPD. Neurology 58: 1856-58.

Research Project: "High-dose Cyclophosphamide for the Treatment of Severe Aplastic Anemia, Paroxysmal Nocturnal Hemoglobinuria and Refractory Autoimmune Disease, Felty's Syndrome and Pseudo-Felty's Syndrome"

Project Number: 60733

Principal Investigator: Isadore Brodsky, M.D.

Dear Dr. Homan:

The Office for Human Research Protections (OHRP) has reviewed Drexel University College of Medicine's (DUCM) April 10, 2006 response to OHRP's February 24, 2006 letter.

In its February 24, 2006 letter, OHRP asked DUCM to provide additional explanations for the following findings regarding the above-referenced research:

(1) OHRP found that there is little evidence that the IRB determined that the selection of subjects was equitable, as required by 45 CFR 46.111(a)(3).

OHRP acknowledged the corrective actions set forth in DUCM's January 11, 2006 response. However, DUCM was asked to explain the procedures by which the IRB will assess whether the selection of subjects is equitable and free of coercion, both explicit and implied.

Corrective Actions: DUCM stated in its April 10, 2006 response that the following additional actions had been taken:

- Presentation of educational materials to the IRB regarding equitable selection of participants.
- Discussion of the need for the IRB to pay greater attention to this issue.
- Modification of the IRB submission form to require investigators to describe the procedures to be used to ensure that selection of subjects is equitable.
- Modification of the IRB submission form to solicit information on the recruitment process to be used.
- Modification of the IRB reviewer checklist to include questions related to equitable selection.

(2) OHRP found that DUCM IRB failed to adequately review the materials presented at continuing review for the above-referenced research when it failed to detect discrepancies in enrollment numbers, in contravention of HHS regulations at 45 CFR 46.111.

OHRP acknowledged the corrective actions set forth in DUCM's January 11, 2006 response. However, DUCM was asked to develop a corrective action plan to specifically address the fact that the discrepancies in enrollment numbers were not detected from continuing review to continuing review.

Corrective Actions: DUCM stated in its April 10, 2006 response that the following additional actions had been taken:

- Modification of the continuing review form to require investigators to provide the exact number of subjects the IRB approved to enroll and the number enrolled at continuing review.
- The IRB will review whether the number of subjects enrolled corresponds to the number of subjects approved to be enrolled at initial review.

OHRP finds that the corrective actions expressed above adequately address OHRP's findings, questions, and concerns.

(3) It was alleged that researchers initiated human subjects research described in the above-referenced research publication without obtaining legally effective informed consent of the subject or the subject's legally authorized representative, as required in HHS regulations at 45 CFR 46.116.

In its October 27, 2005 letter, OHRP found that the above-referenced protocol approved by the DUCM IRB did not contemplate the enrollment of subjects with CIDP and, as a result, the enrollment of four subjects with chronic inflammatory demyelinating polyneuropathy (CIDP) constituted the conduct of nonexempt human subjects research without IRB review and approval as well as the implementation of a protocol change without prior IRB review and approval. In light of this finding, OHRP declines to make another finding regarding the allegation above.

(4) It was alleged that the IRB failed to report serious or continuing noncompliance to OHRP, as required by HHS regulations at 45 CFR 46.103(a) and (b)(5), when the IRB became aware of a Phase I trial described in the above-referenced research publication that was conducted without IRB review. As stated above, OHRP has already made a finding regarding the enrollment of four subjects with CIDP. OHRP declines to make another finding regarding the allegation above.

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.

OHRP appreciates your institution's continued commitment to the protection of human research subjects. Do not hesitate to contact OHRP if you have any questions regarding this matter.

Sincerely,

Karena Cooper, J.D., M.S.W.
Compliance Oversight Coordinator
Office for Human Research Protections

cc: Dr. Sreekant Murthy, HPA & Vice Provost for Research Compliance, DUCM
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