DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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March 24, 2003

William F. Streck, M.D.
President and CEO
The Mary Imogene Bassett Hospital
One Atwell Road
Cooperstown, NY 13326

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1151

Research Publication: Effective Treatment of Cobalamin Deficiency with Oral Cobalamin, Kuzminski, A.M., *et al*, Blood, 94(2):1191-8 (1998).

Dear Dr. Streck:

The Office for Human Research Protections (OHRP) has reviewed the Mary Imogene Bassett Hospital's (MIBH) November 9, 2001 response to allegations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human subjects (45 CFR Part 46) that were presented in OHRP's October 3, 2001 letter regarding the above-referenced publication.

The allegations involved the following:

(1) Failure to ensure that risks to subjects were minimized as required by HHS regulations at 45 CFR 46.111(a)(1). Specifically, it was alleged that some subjects enrolled in the above-referenced research were not adequately treated for B_{12} deficiency, as per the protocol, placing the subjects at risk of developing irreversible neurologic damage.

(2) Failure to report unanticipated problems involving risks to subjects or others in accordance with the requirements of 45 CFR 46.103(a) and (b)(5). In specific, it was alleged that the MIBH failed to ensure prompt reporting of the unanticipated problems related to inadequate treatment of B_{12} deficiency in some subjects to the institutional review board (IRB), appropriate institutional officials and OHRP.

Based upon its review of your report, OHRP finds no evidence to substantiate the above allegations. In particular, OHRP could find (i) no evidence that subjects were not adequately treated for B_{12} deficiency as part of the protocol; and (ii) no evidence of unanticipated problems involving risks to subjects or others which required reporting to the IRB, institutional officials, the appropriate Department of Agency head, or OHRP as required under the HHS regulations.

As a result of the above determination, 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.

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

(1) OHRP notes that Appendix 2 of the MIBH Application for Research Project Involving Human Subjects lists the research activities which may be reviewed through expedited review procedures. Please note that this list of categories was updated by OPRR and FDA on November 9, 1998 at 63 FR 60364. The list is available on the OHRP web site at http://ohrp.osophs.dhhs.gov/humansubjects/guidance/expedited98.htm.

(2) OHRP notes that Appendix 4 of the MIBH Application for Research Project Involving Human Subjects indicates that informed consent must include a description of any benefits to the subject which may reasonably be expected from the research as required by HHS regulations at 45 CFR 46.116(a)(3). The document goes on to state "Monetary payment to subject is a benefit." OHRP believes it is more appropriate to consider the monetary payment to be an incentive to participation in a research study and should not be considered a benefit to be gained from the research.

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,

Patrick J. McNeilly, Ph.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Roberta G. Reed, Chair, MIBH IRB
Dr. Bernard Schwetz, OHRP
Dr. Melody Lin, OHRP
Dr. Michael A. Carome, OHRP
Dr. Kristina Borror

Ms. Shirley Hicks, OHRP
Mr. George Gasparis, OHRP
Ms. Yvonne Higgins, OHRP
Ms. Melinda Hill, OHRP