DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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April 11, 2006

Robert E. Burke
Managing Director
Research Foundation for Mental Hygiene, Inc.
New York Psychiatric Institute Division
44 Holland Avenue
Albany, NY 12229

RE: Human Research Subject Protections Under Federalwide Assurance FWA 6105

Research Project:	**Brain Imaging and Treatment of Persistent Lyme Encephalopathy**
Principal Investigator:	**Brian Fallon, M.D.**
Protocol Number:	**3613**
Research Project:	**An Open Label Study of the Effects of Zoloft (Sertraline) on the Prevention of Post-Stroke Central Pain and/or Depression Following Lateral Medullary and/or Thalamic Stroke (Wallenberg Syndrome)**
Principal Investigator:	**Jay Mohr, M.D.**
Protocol Number:	**3844**
Research Project:	**Monitoring Safety of PET Radiotracers**
Principal Investigator:	**Mark Laruelle, M.D.**
Protocol Number:	**4481**
Research Project:	**Sleep and Circadian Rhythms after Pineal Resections**
Principal Investigator:	**Marianna Mila Macchi, Ph.D.**
Protocol Number:	**4485**
Research Project:	**Functional and Neural Mechanisms of the Interval Time Sense in Humans**
Principal Investigator:	**Chariklia Malapani, M.D.**

Protocol Number:	**4579R**
Research Project:	**Evaluation of Evidence Based Trauma Treatment for Child and Youth Affected by September 11 Terrorist Attack (CATS)**
Principal Investigator:	**Jennifer Havens, M.D.**
Protocol Number:	**4643**
Research Project:	**PET Study of Cocaine**
Principal Investigator:	**Eric Rubin, M.D.**
Protocol Number:	**4692**

Dear Mr. Burke:

The Office for Human Research Protections (OHRP) has reviewed the Research Foundation for Mental Hygiene, Inc.'s (RFMH) July 19, 2005 report submitted in response to OHRP's March 24, 2005 letter regarding the above-referenced research.

Based on the review of your report, OHRP makes the following determinations regarding the above-referenced research:

(1) It was alleged that investigators in Protocols 3613, 3844, 4485, 4579R, and 4643 failed to obtain the legally effective informed consent of one or more subjects. OHRP notes that the RFMH report indicated that there were a number of documentation lapses on the part of the investigators in these studies, including failure of the investigator to sign or date the informed consent document. However, OHRP finds that there was one instance where screening was initiated prior to obtaining signing the informed consent document for Protocol 4485.

(2) It was alleged that investigators failed to obtain the legally effective informed consent of a subject under circumstances that provide sufficient opportunity to consider whether or not to participate in Protocol 3613. The complaint alleged that one subject described being rushed through the informed consent process for the study. The RFMH response indicated that this subject had raised the issue of being rushed through the informed consent process with the institutional review board (IRB) chair after experiencing an adverse event. After further investigation, it appears that the subject had numerous interactions with the study investigators and at one point refused participation in another aspect of the study (i.e., lumbar puncture). It appears that the subject may have had ample time to consider whether or not to participate in the study. Therefore, OHRP is unable to make a determination regarding this allegation.

(3) It was alleged that there was a failure to ensure prompt reporting to the New York State Psychiatric Institute (NYSPI) IRB (RFMH's designated IRB), appropriate institutional officials, the head of the sponsoring Federal department or agency, and OHRP of any unanticipated problem involving risks to subjects or others and any serious

or continuing noncompliance, as required by HHS regulations at 45 CFR 46.103(a) and 46.103(b)(5). The complaint alleged that adverse events related to thrombus development after PICC-line insertion in Protocol 3613 were not reported to the IRB. The RFMH report indicates that these incidents were reported and discussed by the NYSPI IRB and these events were reported to OHRP. As a result, OHRP finds that this allegation could not be substantiated.

(4) It was alleged that investigators failed to obtain informed consent using a written consent form approved by the IRB, as required by HHS regulations at 45 CFR 46.117(a). OHRP finds that there was one instance where an investigator used an outdated consent form to obtain consent.

(5) It was alleged that investigators failed to solicit the assent of a child involved in Protocol 4643, in contravention of HHS regulations at 45 CFR 46.408(a). The complaint alleged that the assent for a child enrolled in Protocol 4643 was not signed prior to enrollment in the research. The RFMH report indicated that the subject's mother wanted more time to think about participation in the study but returned one week later, at which time the informed consent and assent documents were signed. Therefore, OHRP is unable to make a determination regarding this allegation.

(6) It was alleged that subjects participating in the Protocol # 4692 were not informed of the results of HIV testing, as required by U.S. Public Health Service Policy (See OPRR Reports 6/10/88). The RFMH report indicates that discussing the results of HIV testing was part of the IRB-approved protocol and described in the informed consent document. The principal investigator has confirmed that he provided HIV test counseling to all subjects enrolled in the study. As a result, OHRP find this allegation could not be substantiated.

Corrective actions: OHRP notes the following corrective actions taken by RFMH:

(1) The NYSPI has increased support for its IRB including increased staff, IRB office space and an IRB database.

(2) Dual IRB review by the NYSPI and the Columbia University Medical Center has been eliminated to ensure a smoother approval process.

(3) The NYSPI IRB has provided training to investigators to ensure that regulatory requirements are followed for research conducted at NYSPI. This training included instruction on appropriate practices for obtaining and documenting informed consent of subjects.

(4) The NYSPI research monitoring process was reviewed by an outside consultant. The NYSPI has revised certain monitoring policies and is developing an updated monitoring database.

OHRP finds that these corrective action adequately address the above determinations and are appropriate under the institution's assurance.

After reviewing documents contained in your report, OHRP has the following additional concern:

[Redacted]

Please provide OHRP with your response to the above concern no later than May 25, 2006.

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. Abel Lajtha, President, RFMH
Ms. Susan J. Delano, Deputy Managing Director, RFMH

Mr. Frank Mucha, Deputy Director of Administration, RFMH
Dr. David Strauss, Chair, IRB #1, NYSPI
Commissioner, FDA
Dr. Lana Skirboll, NIH
Dr. Bernard Schwetz, OHRP
Dr. Melody H. Lin, OHRP
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Dr. Kristina Borror, OHRP
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Ms. Patricia El-Hinnawy, OHRP
Ms. Janet Fant, OHRP