DEPARTMENT OF HEALTH & HUMAN SERVICES

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Office of Public Health and Science

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February 22, 2001

Dr. Alison F. Richard
Provost
Yale University
P.O. Box 208236
New Haven, CT 06520-8236

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1452

Research Project: Delaying or Preventing Psychosis: A Clinical Trial of Olanzapine in Persons Prodromal to Psychosis
Principal Investigator: Thomas H. McGlashan
Yale Protocol Number: HIC 9253
HHS Project Number: K05 MH01654

Dear Dr. Richard:

The Office for Human Research Protections (OHRP) has reviewed your report of January 26, 2001 regarding the above referenced research project, that was submitted in response to OHRP's December 12, 2000 letter.

Based upon its review, OHRP makes the following additional determinations regarding the above referenced research conducted at Yale:

(1) Department of Health and Human Services (HHS) regulations at 45 CFR 46.111(b) require that the Yale Institutional Review Board (IRB) ensure that additional safeguards have been included in research to protect the rights and welfare of vulnerable subjects. OHRP finds that the IRB records provided with your report failed to demonstrate that the Yale IRB considered such safeguards for the subjects in this project, some of whom the investigators stated would develop psychoses in the course of the research.

Corrective Action: OHRP acknowledges the additional safeguards that Yale has since instituted, such as capacity assessment by a psychiatrist not associated with the research

and referring those judged not to have the capacity to consent to a clinic or doctor for treatment. OHRP has determined that these corrective actions are appropriate under the Yale Multiple Project Assurance (MPA).

(2) OHRP finds that the informed consent documents reviewed and approved by the IRB for this research project failed to include an adequate description of the reasonably foreseeable risks and discomforts, as required by HHS regulations at 45 CFR 46.116(a)(2).

Corrective Action: OHRP acknowledges that the Yale IRB has required the principal investigator to revise the informed consent documents to address the concerns in (6b-e) of OHRP's December 12, 2000 letter. OHRP has determined that these corrective actions are appropriate under the Yale MPA.

(3) OHRP finds that your January 26, 2001 letter adequately addresses all other concerns and questions raised by OHRP in its December 12, 2000 letter.

As a result of the above determinations, OHRP has closed its compliance oversight evaluation of the above-referenced research and anticipates no further OHRP involvement in this matter.

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

Sincerely,

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

cc: Mr. Allen Brown, CEO, The APT Foundation
Mr. James Jerrell, President, Community Consultation Board, Inc.
Dr. Selby C. Jacobs, Director, Connecticut Mental Health Center
Mr. Philip E. Rubin, Vice President, Haskins Laboratories
Mr. Lawrence E. Marks, Director, John B. Peirce Laboratory, Inc.
Ms. Sarah Cohn, Director Legal Affairs/Risk Management, Yale-New Haven Hospital
Dr. Marianne Lafrance, Chair, IRB-01, Yale
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Mr. Barry Bowman, OHRP