DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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December 3, 2002

Dr. Michael M. Gottesman
Deputy Director for Intramural Research
National Institutes of Health
Building 1 – Room 114
1 Center Drive
Bethesda, MD 20892

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1000

Research Project: The Effects of Fluoxetine on Measures of Domestic Violence
Principal Investigator: David Ted George, MD
Project Number: 01-AA-0098

Dear Dr. Gottesman:

The Office for Human Research Protections (OHRP) has reviewed your September 20, 2002 report responding to allegations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR Part 46) involving the above-referenced research at the National Institute on Alcohol Abuse and Alcoholism (NIAAA).

The allegations concerned a possible failure to ensure that risks to subjects were minimized by using procedures consistent with sound research design and which do not unnecessarily expose subjects to risk [see 45 CFR 46.111(a)(1)]. Specifically, the complainants alleged that the investigators and the institutional review board (IRB) may have failed to take into account data regarding increased risk of domestic violence with couples counseling, anger management, and administration of Fluoxetine (Prozac).

In reviewing your report, OHRP noted the following:

(1) The NIAAA IRB, and the data safety monitoring board (DSMB) members chosen to review the above research, had the necessary background and expertise to evaluate the research risks to subjects, including perpetrators of domestic violence and significant others (SOs) of perpetrators of domestic violence.

(2) The minutes of the February 6 and December 4, 2001 NIAAA IRB meetings reflect that the IRB debated the research risk of inducing violent conduct, including (1) violence caused by increased anxiety as a potential side effect of fluoxetine, and (2) that the dyadic interaction between perpetrator and spouse or SO, including the discussion of personal and sensitive information, could trigger violent behavior.

(3) Both the NIAAA IRB and the DSMB requested protocol changes designed to minimize the risk of triggering violent behavior in subjects with a history of domestic violence.

As a result, OHRP finds that the above allegations could not be substantiated, and there should be no need for further involvement of OHRP at this time. Of course, OHRP must be notified if new information is identified which might alter this determination.

At this time, OHRP provides the following guidance to the NIAAA:

(4) HHS regulations at 45 CFR 46.116(d) set forth the conditions for IRB approval of a consent procedure which does not include, alters, or waives some or all of the elements of informed consent required by the HHS regulations, including the provision of additional pertinent information after participation. OHRP notes that the use of deception during the consent process would require waiver of certain elements of informed consent.

The Point Subtraction Aggression Paradigm test, the study's primary measure for evaluating the impact of fluoxetine vs. placebo on aggressive behavior in perpetrators, is referenced in the consent form as a "Physical performance test" designed to measure "physical performance and speed." The protocol (p. 16) acknowledges that the test requires deception regarding the existence of a live opponent in a money-acquisition game when, in reality, the "competitor" is a software program that makes pre-controlled decisions. It appears that the IRB did not debate whether the deception as to the nature of the opponent (computer v. human), and as to the true purpose of the test (measuring aggression, not physical dexterity or speed), would require a consent procedure that does not include some elements of informed consent. OHRP notes that the IRB may not have made and documented the required findings to waive or alter informed consent under 45 CFR 46.116(d). OHRP further questions whether debriefing the perpetrator subjects by way of a letter sent to their homes was appropriate, given the potential for domestic violence in this population.

OHRP recommends that NIAAA take steps to inform IRB members of their review responsibilities when conducting research involving deception under 45 CFR 46.116(d).

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,

Carol J. Weil, J.D.
Compliance Oversight Coordinator
Compliance Oversight Division

cc: Dr. Alan L. Sandler, OHSR/NIH
Dr. Ted George, Principal Investigator, NIAAA
Dr. David Goldman, Chair, IRB, NIAAA
Dr. Melody Lin, OHRP
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