DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

FOR US POSTAL SERVICE DELIVERY:
Office for Human Research Protections
6100 Executive Boulevard, Suite 3B01
National Institutes of Health (MSC 7507)
Rockville, Maryland 20892-7507

FOR HAND DELIVERY OR EXPRESS MAIL:
Office for Human Research Protections
6100 Executive Boulevard, Suite 3B01
Rockville, Maryland 20852

Telephone: 301-402-5567
FAX: 301-402-2071
E-mail: mc2a@nih.gov

October 27, 2000

Christopher T. Hill, Ph.D.
Vice Provost for Research
Professor of Public Policy and Technology
George Mason University
Mail Stop 3A2
Fairfax, Virginia 22030-4444

RE: Human Research Subject Protections Under Single Project Assurances (SPA) Designated S-5276

Dear Dr. Hill:

The Office for Human Research Protections (OHRP), formerly the Office for Protection from Research Risks (OPRR), has reviewed your November 23, 1999 report regarding human subject protections for research conducted under the above referenced OPRR-approved Assurances.

Your report indicated that, as of November 1999, there were three active research projects involving human subjects that were being conducted by investigators at George Mason University (GMU) and were supported by the Department of Health and Human Services (HHS). One of these three projects (*Nonlinear Dynamics of Neuronal Ensembles*) was judged to be exempt under HHS regulations at 45 CFR 46.101(b)(4). Based upon its review of relevant documents provided with your report, OHRP finds that GMU's designation of this project as exempt was appropriate.

As a result, 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 provides the following additional guidance:

(1) Please note that the exempt category of research stipulated by HHS regulations at 45 CFR 46.101(b)(2) (i.e., research involving the use of educational tests, survey procedures, interview procedures or observations of public behavior) does not apply to behavioral

research that involves manipulation of the subjects' environment in order to measure a behavioral response, even if that behavioral response is measured with a survey or interview procedure.

(2) Please note that the exempt category of research stipulated by HHS regulations at 45 CFR 46.101(b)(2) does not apply to research where (i) subjects' responses are audio or videotaped, even for a brief period of time; and (ii) any disclosure of the subjects' responses outside the research could place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

(3) The GMU's written IRB policies and procedures need to be expanded to provide a description of the operational details for each of the following activities, as required by HHS regulations at 45 CFR 46.103(b)(4) and (5):

(a) The procedures which the IRB follows for conducting its initial and continuing review of research (including reviews by the convened IRB and reviews conducted under an expedited review procedure).

(b) The procedures which the IRB follows for reporting its findings and actions regarding initial and continuing review to investigators and the institution.

(c) The procedures which the IRB follows for determining which projects require review more often than annually.

(d) The procedures which the IRB follows for determining which projects need verification from sources other than the investigators that no material changes have occurred since the previous IRB review.

(e) The procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, the head of any supporting Federal Department or Agency, and, if appropriate, OHRP of each of the following events:

(i) Any unanticipated problems involving risks to subjects or others.

(ii) Any serious or continuing noncompliance with the requirements of 45 CFR Part 46, or the requirements or determinations of the IRB.

(iii) Any suspension or termination of IRB approval of research.

To assist GMU in revising its IRB policies and procedures, please see the enclosed Guidance for Formulating Written IRB Policies and Procedures.

(4) Please note that in accordance with the requirements of HHS regulations at 45 CFR 46.115(a)(2), minutes of IRB meetings must be in sufficient detail to show the vote on actions taken by the IRB, including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution. These requirements apply to both the initial and continuing review of research protocols.

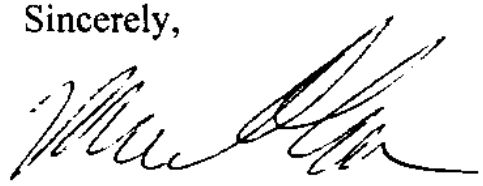
(5) Continuing IRB review of research must be substantive and meaningful. In conducting continuing review of research not eligible for expedited review, all IRB members should at least receive and review a protocol summary and a status report on the progress of the research, including (a) the number of subjects accrued; (b) a description of any adverse events or unanticipated problems involving risks to subjects or others and of any withdrawal of subjects from the research or complaints about the research; (c) a summary of any recent literature, findings obtained thus far, amendments or modifications to the research since the last review, reports on multi-center trials and any other relevant information, especially information about risks associated with the research; and (d) a copy of the current informed consent document. Primary reviewer systems may be employed, so long as the full IRB receives the above information. Primary reviewers should also receive a copy of the complete protocol including any modifications previously approved by the IRB. Furthermore, the minutes of IRB meetings should document separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB.

When conducting research under an expedited review procedure, the IRB Chair (or designated IRB member(s)) should receive and review all of the above referenced documentation.

(6) Where HHS regulations require specific findings on the part of the IRB, such as (a) approving a procedure which alters or waives the requirements for informed consent [see 45 CFR 46.116(d)]; (b) approving a procedure which waives the requirement for obtaining a signed consent form [see 45 CFR 46.117(c)]; (c) approving research involving prisoners (see 45 CFR 46.305-306); or (d) approving research involving children (see 45 CFR 46.404-407), the IRB should document such findings. OHRP strongly recommends that all required findings be fully documented in the IRB minutes, including protocol-specific information justifying each IRB finding.

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,



Michael A. Carome, M.D.
Director, Division of Compliance Oversight

Enclosure

cc: Commissioner, FDA
Dr. David Lepay, FDA
Dr. James F. McCormack, FDA
Dr. Greg Koski, OHRP
Dr. Melody H. Lin, OHRP
Dr. J. Thomas Puglisi, OHRP
Dr. Clifford C. Scharke, OHRP
Dr. Jeffrey M. Cohen, OHRP
Mr. George Gasparis, OHRP
Mr. Barry Bowman, OHRP