DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852

Telephone: 301-435-8072
FAX: 301-402-2071
email: borrork@od.nih.gov

August 5, 2002

Steven G. Ullmann, Ph.D.
Vice Provost for Faculty Affairs,
University Admin
University of Miami
P.O. Box 248033
Coral Gables, FL 33124-4628

Norman Altman, VMD
Vice Provost for Research
University of Miami
1600 N.W. 10th Avenue (R-64)
Miami, FL 33101

RE: Human Research Protections Under Multiple Project Assurance (MPA) M-1196 and Federalwide Assurance FWA-2247

Research Project: Selenium Therapy to Slow HIV Progression in IDU's
Principal Investigator: Marianna Baum, Ph.D.
HHS Project Number: R01 DA113278
MU Protocol Number: 97/084

Research Project: Neuroprotection with Selenium Therapy in HIV-positive IDU's (Selenium Therapy Trial Cognition Study)
Principal Investigator: Gail Shor-Posner, Ph.D.
HHS Project Number: R01 DA12797
MU Protocol Number: 98/700

Dear Drs. Ullmann and Altman:

The Office for Human Research Protections (OHRP), formerly the Office for Protection from Research Risks (OPRR), has reviewed your July 31, 2000 report regarding the above-referenced research conducted at the University of Miami (UM) that was submitted in response to OPRR's May 17, 2000 letter. OHRP apologizes for the delay in its response.

Based on its review, OHRP makes the following determinations:

(1) Department of Health and Human Services (HHS) regulations at 45 CFR 46.103(b)(4)(iii) require that the Institutional Review Board (IRB) review and approve all proposed changes in a research activity, during the period for which IRB approval has already been given, prior to initiation of such changes, except when necessary to eliminate apparent immediate hazards to the subjects. OHRP finds that the following protocol change was implemented without IRB approval:

The protocol for #97/084 called for meetings of a Data and Safety Monitoring Board (DSMB) at six-month intervals. The protocol was approved on February 26, 1997, enrollment began on March 16, 1999, but the DSMB had not met by March of 2000. The DSMB met in April of 2000, after the IRB expressed concern about this. The UM IRB acknowledged that they could have noticed this delay sooner. UM's July 31, 2000 letter to OHRP noted "[i]f the decision were made to modify the DSMB meeting specifics approved by the [IRB], an amendment to the protocol should have been submitted to and approved by the [IRB]."

Corrective Action: OHRP acknowledges the UM IRB's statement that their reporting requirements should be broader and should require reporting of DSMB reports. The protocol application is being revised to solicit information about DSMBs, and the continuing review report form is being revised to include specific information about DSMB activities. OHRP finds that this corrective action adequately addresses OHRP's finding and is appropriate under the UM FWA.

(2) In your July 31, 2000 report to OPRR, UM expressed concern that deaths in these studies were not reported in a timely manner. UM noted that "there was an appreciable interval between the dates of the deaths and the dates that they were reported to the IRB." For example, a lapse of 4-7 months occurred between the dates of six deaths and the dates they were reported to the IRB. Three of those deaths were among subjects who had been randomized and were supposedly being visited monthly. Dr. Baum stated that she had learned about the deaths approximately one week prior to notification of the IRB. OHRP acknowledges that these deaths all appear to have been unrelated to the study (and were more or less anticipated given the health status of the participants). Therefore, OHRP finds that this allegation was not substantiated.

OHRP has the following additional concerns and questions:

(3) [redacted]

[redacted]

(4) [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

(5) [redacted]

[redacted].

(6) [redacted].

(7) [redacted].

Please submit to OHRP your response to the above questions and concerns no later than September 9, 2002. If upon further review of the concerns and questions, UM identifies instances of non-compliance with the HHS regulations for protection of human subjects, please include detailed corrective action plans to address the noncompliance. **Please note OHRP's new address.**

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,

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

cc: Ms. Maria J. Arnold, UM
Dr. Stephen P. Richman, UM IRB A Chair
Dr. Linda Belgrave, UM IRB #2 Chair
Dr. Rick Bollinger, UM IRB #4 Chair
Dr. Marianna Baum, UM
Dr. Gail Shor-Posner, UM

Dr. Laura Rosenthal, NIDA
Commissioner, FDA
Dr. David Lepay, FDA
Dr. Greg Koski, OHRP
Dr. Melody Lin, OHRP
Dr. Michael Carome, OHRP
Dr. Jeff Cohen, OHRP
Mr. George Gasparis, OHRP
Ms. Jan Walden, OHRP
Mr. Barry Bowman, OHRP