DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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May 15, 2007

Kathleen Matt, Ph.D.
Assistant Vice President for Research
Arizona State University
Foundation Building, Ste 245, PO Box 877105
Tempe, AZ 85287-7105

RE: Human Research Subject Protections Under Federalwide Assurance (FWA) 9102

Research Project: Mechanisms of Protections in HIV – Exposed Seronegative Partners of HIV Seropositive Patients
Principal Investigator: Charles Arntzen
Project Number: HS # 0407001903 and HS # 0509000193

Research Project: Early Language and Literacy Interventions
Principal Investigator: Jeanne Wilcox
Project Number: HS # 0309001372 and HS # 0512000492

Research Project: Molecular Regulation of Muscle Glucose Metabolism in Man
Principal Investigator: Lawrence Mandarino
Project Number: HS #0501002211

Research Project: Gila River Diabetes Reduction Initiative
Principal Investigator: Pamela Kulinna
Project Number: HS # 0509000171

Research Project: Salt River Pima-Maricopa Indian Community Physical Activity and Health Education Initiative
Principal Investigator: Pamela Kulinna
Project Number: HS # 0408001947

Research Project: Coordination of Control of Muscle Activity for Grasping Movements
Principal Investigator: Marco Santello
Project Number: HS #0601000564

Research Project: Analysis of Blood Samples
Principal Investigator: Bert Jacobs
Project Number: HS # 0506000016

Research Project: Olivenol Study in Individuals with Arthritis
Principal Investigator: Kathleen Matt
Project Number: HS # 0308001356

Research Project: Use of Composite Images in Eyewitness Identification
Principal Investigator: Dawn McQuiston-Surrett
Project Number: HS # 0309001408 and # 0507000070

Dear Dr. Matt:

The Office for Human Research Protections (OHRP) has reviewed the Arizona State University's (ASU) letter dated May 18, 2006 and electronic correspondence dated April 17, 2007, as well as the accompanying materials that were submitted in response to OHRP's April 5, 2006 letter to ASU, regarding allegations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human subjects (45 CFR part 46) involving the above-referenced research.

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

1) OHRP finds that the following unanticipated problems involving risks to subjects or others and serious or continuing noncompliance were not reported to OHRP as required by HHS regulations at 45 CFR 46.103(a) and 46.103(b)(5):

   a) In a May 20, 2005 memo from the Research Compliance Manager to the institutional review board (IRB) Chair, it was stated that there was an "adverse event" reported by the principal investigator Irwin Sandler for the study entitled "Six-Year Follow-up of the Family Bereavement Program", HS # 07494-04, consisting of "loss of data due to theft of materials including a family packet containing consent documents, payment receipts, and authorization forms from a study personnel's car which was broken into in the driveway of her home." This unanticipated problem involving risks to subjects or others was not reported to OHRP. OHRP notes that during the period in which this unanticipated problem occurred, the ASU FWA in effect at that time was applicable to all research involving human subjects, regardless of sponsorship.

   b) As noted in the ASU response, there was a 12-month lapse in IRB approval from September 25, 2004 through September 15, 2005 for the study entitled "Community Connections: Promoting Language and Literacy Skills in Young Children," HS #0309001372. This continuing noncompliance was not reported to OHRP.

Corrective Action: OHRP notes that ASU has developed two policies to address reporting of unanticipated problems: 1) SOP 07-001, "Noncompliance with IRB Policies and Procedures," with a corresponding "Noncompliance Reporting Form", and 2) SOP 07-002, "Reporting requirement for Unanticipated Events, Serious and Continuing Non-compliance and/or Suspension or Termination of IRB Approval." OHRP finds that these corrective actions adequately address the above finding and are appropriate under the

ASU FWA.

OHRP notes that the term "unanticipated events" is used in the ASU procedures, rather than the phrase found in 45 CFR 46. 103(b)(5), "unanticipated problems involving risks to subjects or others."

The January 15, 2007 OHRP guidance document entitled "Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events" states the following:

> The phrase "unanticipated problems involving risks to subjects or others" is found but not defined in the HHS regulations at 45 CFR part 46. OHRP considers *unanticipated problems*, in general, to include any incident, experience, or outcome that meets **all** of the following criteria:
>
> - unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
>
> - related or possibly related to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
>
> - suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

OHRP suggests that the ASU policy be revised to more closely reflect the criteria outlined in the OHRP guidance document. OHRP also notes that SOP 07-002 does not include the applicable sections of 45 CFR part 46 in the list of Applicable Regulations and Guideline section. OHRP suggests that these references be added to the procedure.

2) HHS regulations at 45 CFR 46.109(e) require that continuing review of research be conducted by the IRB at intervals appropriate to the degree of risk and not less than once per year. OHRP finds that the ASU IRB failed to conduct timely continuing review for the study entitled "Community Connections: Promoting Language and Literacy Skills in Young Children," HS #0309001372, which resulted in a 12-month lapse in IRB approval from September 25, 2004 through September 15, 2005.

3) HHS regulations at 45 CFR 46.115(a)(4) require that an institution, or when appropriate an IRB, prepare and maintain adequate documentation of IRB activities, including copies of all correspondence between the IRB and the investigators. OHRP finds that ASU IRB protocol records for the following studies did not include this information stipulated at

45 CFR 46.115(a)(4):

a) Gila River Diabetes Reduction Initiative, HS #0509000171

b) Salt River Pima-Maricopa Indian Community Physical Activity and Health Education Initiative, HS #0408001947

4) HHS regulations at 45 CFR 46.110(c) require that each IRB which uses an expedited review procedure shall adopt a method for keeping all members advised of research proposals which have been approved under the procedure.

OHRP finds that ASU IRB members were not advised that the study entitled "Gila River Diabetes Reduction Initiative," HS #0509000171, had been approved at initial and continuing review using expedited review procedures.

OHRP notes that it was alleged that the study entitled "Coordination of Control of Muscle Activity for Grasping Movements," protocol number 0601000564, was greater than minimal risk and therefore was not eligible to be reviewed under an expedited review procedure. OHRP makes no finding on this issue but notes that in January 2006 the ASU IRB reevaluated the risk assessment of this study and decided to review the study at a convened meeting, rather than using expedited review.

Required Actions: By June 26, 2007, please provide OHRP with corrective action plans to address findings (2) – (4) above.

OHRP has the following additional questions and concerns:

5) [Redacted]

[Redacted]

[Redacted]

6) [Redacted]

7) [Redacted]

[Redacted]

8) [Redacted]

[Redacted]

Please submit your responses to the above questions and concerns so that OHRP receives them no later than June 26, 2007

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,

Karena Cooper, JD, MSW
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Susan Metosky, IRB Administrator, ASU
Debra Murphy, Research Compliance Office, ASU
Dr. Mike Roose, ASU IRB #1 Chairperson
Dr. Anna Schwartz, ASU IRB #2 Chairperson
Dr. Bernard Schwetz, OHRP
Dr. Melody H. Lin, OHRP
Dr. Michael Carome, OHRP
Dr. Kristina Borror, OHRP
Ms. Shirley Hicks, OHRP
Dr. Irene Stith-Coleman, OHRP
Ms. Patricia El-Hinnawy, OHRP
Ms. Carla Brown, OHRP