DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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March 14, 2005

Charles F. Zukoski
Vice Chancellor for Research
University of Illinois at Urbana-Champaign
Fourth Floor Swanlund Building
601 East John Street
Champaign, IL 61820-5711

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1004

Research Project:	**Study of HIV/AIDS Perception, Attitudes, and Knowledge Among University of Illinois Students**
Principal Investigator:	**Jerry Ogbudimpka, Ph.D.**
Research Project:	**Study of 4% Lidocaine Intranasally to Treat Migraine**
Principal Investigator:	**Santiago Ulloa, M.D.**
Research Project:	**Name the Bug: Organism Identification for College Health Clinicians**
Principal Investigator:	**Robert Palinkas, M.D.**
Research Project:	**Diabetes on Campus: Working Toward Evidence-Based Practice in a College Environment**
Principal Investigator:	**David Lawrence, M.D.**
Research Project:	**Assessment, Implementation and Evaluation of Men's Health Clinic**
Principal Investigator:	**Connie Maske**
Research Project:	**Teaching Students to Manage Their Non-Traumatic Back and Neck Pain**
Principal Investigator:	**Melinda Flegel**

Research Project: **Ankle Sprains: A Simple Standardized Approach to Effective Care**
Principal Investigator: **Melinda Flegel**

Dear Mr. Zukoski:

The Office for Human Research Protections (OHRP) has reviewed the University of Illinois at Urbana-Champaign's (UIUC) May 27, 2004 and June 3, 2004 reports, which were submitted in response to OHRP's letters of April 7, 2004 and April 16, 2004.

After reviewing the UIUC reports, OHRP makes the following determination:

(1) Department of Health and Human Services (HHS) **regulations at 45 CFR 46.103(b) and 46.109(a) require that the IRB must review and approve all nonexempt human subjects research covered by an assurance. OHRP finds that** the human subjects research activities identified below **were conducted without institutional review board (IRB) review.** In specific, OHRP notes the following:

(a) Regarding the study entitled "Study of 4% Lidocaine Intranasally to Treat Migraine" UIUC 's May 27, 2004 report states:

(i) "The Study of 4% Lidocaine Intranasally to Treat Migraine (Lidocaine Study) was a retrospective evaluation (i.e., chart review) of 258 patients treated at MHC [McKinley Health Center] for acute migraine attack."

(ii) "The evaluation was initiated in 2000 by MHC as a quality assurance measure of one component of the clinical services provided by MHC."

(iii) "Dr. Guenther conducted an investigation and determined that the Lidocaine Study was research as it contributed to generalizable knowledge."

(iv) "The MHC believed they were conducting a quality assurance activity when they were conducting the retrospective chart review related to determining the effectiveness of a treatment protocol. Therefore, informed consent was not requested."

(b) Regarding the protocol entitled "Assessment, Implementation and Evaluation of Men's Health Clinic" the UIUC's June 3, 2004 report stated:

(i) "This project was presented to the MACHA [Mid-America College Health Association] conference on 11/4/02. However, since IRB approval was not obtained prior to this presentation, all elements of human subjects research were removed from the content."

(ii) "Determination - IRB application filed, awaiting RPI response to comments/questions; no IRB compliance issues."

(iii) "As mentioned above, Connie Maske submitted an IRB application due to a request following the investigation. The presentation at the MACHA conference in 2002 was a presentation of the assessment needs for a Men's Health Clinic at MHC. The assessment began in December 1998 and was completed in December 1999."

(iv) "The IRB request for modifications to the IRB application were not completed since the assessment had been completed, the men's health Clinic was established, and further assessment was not needed."

(c) Regarding the protocol entitled "Name the Bug: Organism Identification for College Health Clinicians," the UIUC's June 3, 2004 report states:

(i) "The project was presented to [Mid-America College Health Association 2002 Meeting] conference on 11/5/02. [Howard Guenther] met with Palinkas on 11/6/02 to review the project and presentation content."

(ii) "Determination - Project has IRB approval; no IRB compliance issues."

(iii) "Dr. Palinkas registered this work with the IRB at the request of Dr. Guenther following Dr. Guenther's investigation in 2002."

OHRP notes that this protocol was approved through a expedited review mechanism on November 4, 2002, as reported to the UIUC IRB in a list of approved expedited cases at its December 10, 2002 meeting.

(d) A memorandum dated June 3, 2004 from Robert D. Palkinas, M.D. to Van Anderson, Interim Associate Director, Beckman Institute and Associate Vice Chancellor for Research regarding the protocol entitled "Name the Bug: Organism Identification for College Health Clinicians" states:

(i) "Composite 'created' cases were used due to the late arrival of approval from the IRB for utilization of information about cases at the University of Illinois McKinley Health Center. In fact, the notification of approval from the IRB arrived November 4, 2002, and given the fact that the presentation was scheduled for November 5, there was inadequate time to prepare material from real cases at the University of Illinois McKinley Health Center in the short interval."

(ii) "In summer of 2003 I presented 'Name That Bug' cases at the ACHA meeting, and these involved three individuals listed below:

Subject 001, enrolled October 24, 2002, also known as a case of mumps
Subject 002, enrolled October 24, 2002, also known as a case of pertussis
Subject 003, enrolled October 25, 2002, also known as a case of hydatid cyst"

(e) Regarding the protocol entitled "Diabetes on Campus: Working Toward Evidence-Based Practice in a College Environment," the UIUC's June 3, 2004 report states:

(i) "an IRB application for this project was filed, an expedited review was completed, and stipulations were issued. This project was presented at the Mid-America College Health Association (MACHA) conference on 11/5/02. However, since IRB approval was not obtained prior to this presentation, all elements constituting human subjects research were removed from the content."

(ii) "Lawrence subsequently withdrew the IRB application on 11/15/02."

Corrective Action: OHRP acknowledges that the UIUC has (i) appointed an IRB member to the MHC Research and Grant Committee; (ii) provided additional human subject protections training to MHC personnel; and (iii) increased its oversight of research activities at the MHC.

Required Action: UIUC, in conjunction with its investigators and clinical practitioners, as well as relevant administrators, must audit and identify all ongoing research projects involving human subjects at the MHC that are not exempt under HHS regulations at 45 CFR 46.101(b) and must confirm that all such research has been reviewed and approved by the UIUC IRB. UIUC must suspend immediately any nonexempt research involving human subjects that has not been reviewed and approved by the UIUC IRB. By April 29, 2005, please provide OHRP with a report on the process and results of this audit, and a list of any research activities that have been suspended as a result of this audit.

(2) HHS regulations at 45 CFR 46.103(a) and 46.103(b)(5) require prompt reporting to the IRB, appropriate institutional officials, the Department or Agency head, and OHRP of any serious or continuing noncompliance. OHRP notes that regarding the Lidocaine Study, an investigative report dated December 23, 2002 from Howard R. Guenther, Associate Vice Chancellor for Research, to Patricia E. Askew, Vice Chancellor for Student Affairs, states the following:

(a) "It has been determined that (1) this project constituted human subjects

research; (2) IRB approval should have been obtained; (3) improved patient/subject consent and disclosure processes were needed at MHC; and (4) human subjects education/training should be provided to MHC by the IRB office."

(b) "It has been determined that this constitutes a minor non-compliance issue, not requiring subsequent report to the full IRB or federal agencies."

OHRP finds that conducting the Lidocaine Study without IRB review represented serious noncompliance, and that this noncompliance was not promptly reported to the UIUC IRB or OHRP.

<u>Required Action</u>: By April 29, 2005, UIUC must provide a satisfactory corrective action plan to address the above finding.

At this time OHRP has the following additional questions and concerns:

(3) [Redacted]

(4) [Redacted]

Please provide responses to the above questions and required actions no later than April 29, 2005.

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,

Patrick J. McNeilly, Ph.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Van Anderson, Associate Vice Chancellor for Research, UIUC
Ms. Susan Keehn, IRB Director, UIUC
Dr. Dale Brashers, IRB Chair, UIUC
Dr. Jerry Ogbudimpka, UIUC
Dr. Robert Palinkas, UIUC
Dr. David Lawrence, UIUC
Ms. Connie Maske, UIUC
Ms. Melinda Flegel, UIUC
Commissioner, FDA
Dr. David Lepay, FDA
Dr. Bernard Schwetz, OHRP
Dr. Melody H. Lin, OHRP
Dr. Michael Carome, OHRP
Dr. Kristina Borror, OHRP
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