DEPARTMENT OF HEALTH & HUMAN SERVICES

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Office of Public Health and Science

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February 11, 2009

Michael A. McRobbie, Ph.D.
President
Indiana University
Office of the President
107 S. Indiana Avenue, Bryan Hall 200
Bloomington, IN 47405

RE: Human Research Protections under Federalwide Assurance FWA-3544

Research Project: Partial Justice or Model for the Future
Principal Investigator: Jennifer Colanese
IU Protocol Number: 07-12451

Research Project: Accommodation and Defocus in the Infant Visual System
Principal Investigator: T. Rowan Candy
IU Protocol Number: 00-3851
HHS Protocol Number: R01EY014460-01A1

Research Project: Polarized Light Imaging and Related Normative Studies, Infants/Children 0-9 yr
Principal Investigator: Ann E. Elsner, Ph.D.
IU Protocol Number: 07-12085
HHS Protocol Number: R01EY007624

Research Project: Patterns of Participation in Programs that the Bloomington Boys and Girls Club
Principal Investigator: Geneva Travis
IU Protocol Number: 08-13012

Research Project: Evaluating the Quality and Impact of First Steps
Principal Investigator: Michael Conn-Powers
IU Protocol Number: 07-12647

Dear Dr. McRobbie:

Thank you for your July 24, 2008 report in response to our June 12, 2008 request that the Indiana University (IU) investigate allegations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR part 46). We appreciate your investigation into the matters outlined in our request.

We acknowledge that IU's FWA includes 15 institutional review boards and the allegations pertain only to research reviewed by the Indiana University, Bloomington (IUB) institutional review board (IRB), and that IU had launched a "Compliance Allegation audit" in response to reports made on the University's "reporting hotline" prior to receiving our inquiry letter. The audit revealed additional findings that are summarized in the report provided, titled "Other Findings During IU's Investigation." Corrective actions included a temporary transfer of studies from the IUB IRB to the accredited Indiana University Perdue University Indianapolis (IUPUI)/Clarian Human Research Protection Program until additional corrective actions could be implemented.

A. Determinations Regarding the Above-Referenced Research

(1) The complainant alleged that research was conducted without IRB review and approval, in contravention of HHS regulations at 45 CFR 46.103(b) and 46.109(a). In specific, the complainant alleged that study #07-12451 was conducted without IRB approval. The IRB reviewed the study at its November 15, 2007 meeting, and imposed several requirements that must be met before approval could occur. Those requirements appear to never have been met, and the research did not return to the convened IRB for approval, but a letter was sent to the investigator stating that the research had been approved. We have reviewed the documentation provided for study #07-12451 and found that the IRB provided contingent approval. A letter listing the contingencies should have been sent to the principal investigator (PI), but instead an approval letter was sent erroneously. Subsequently, the PI was notified of the error. The study did not commence, and study subjects were never enrolled. Given the facts at our disposal, we determine that this allegation is unproven.

(2) The complainant alleged that expedited review procedures were used inappropriately for initial or continuing IRB review, in contravention of HHS regulations at 45 CFR 46.110(b)(1). In specific, the complainant alleged that the IRB inappropriately applied expedited review to research that involves greater than minimal risk or that did not appear in the categories of research published in the *Federal Register*. The following studies are alleged to have been inappropriately reviewed and approved under an expedited review procedure: #00-3851 (continuing review in May 2008); and #07-12085 (continuing review in May 2008). Based on the available information, we determine that IUB IRB inappropriately used expedited review and approval in the continuing review of the studies referenced above.

Corrective Action: We acknowledge that the studies referenced above were subsequently re-reviewed by the IUPUI IRB; both were closed to enrollment and remained open for data analysis only. We also acknowledge that the IUB IRB has adopted IUPUI IRB written procedures which provide detailed procedure for appropriate expedited review procedures and that IUB IRB members and support staff have been trained on the appropriate use of expedited review procedures.

If IU has not already done so, it should identify all active research studies for which expedited review was performed by the Director of the HRPP on behalf of the IUB IRB and ensure that those research studies have or will receive appropriate IRB review.

(3) The complainant alleged that inappropriate use of expedited review procedures were used for review of protocol changes, in contravention of HHS regulations at 45 CFR 46.110(b)(2). In specific, the complainant alleged that an amendment to study #07-12451 was approved in an expedited manner, even though it was a greater than minor change. After reviewing the information provided, it appears that this amendment was in fact reviewed by the IUB IRB at a convened meeting, and changes were required. However, the amendment was subsequently withdrawn by the PI. Given the facts at our disposal, we determine that this allegation is unproven.

(4) The complainant alleged that expedited review procedures failed to be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB, as required by HHS regulations at 45 CFR 46.110(b). In specific, the complainant alleged that the Director of the Office of Human Research Protection Programs (HRPP) conducted expedited reviews, but has never been designated by the chairperson to do so. We determine that the expedited review and approvals conducted by the Director of the HRPP were in violation of the HHS regulations at 45 CFR 46.110(b) which specify that expedited review "…may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB."

Corrective Action: We acknowledge that the IUB IRB has adopted IUPUI IRB written procedures which provide detailed procedure for appropriate expedited review procedures and specify the process by which the IRB chairperson designates an expedited reviewer--in compliance with HHS regulations at 45 CFR 46.110(b).

(5) The complainant alleged that the IRB failed to require legally effective informed consent or parental permission, or find and document waiver of informed consent, as required by HHS regulations at 45 CFR 46.116. In specific, the complainant alleged that the Director of the HRPP allowed "passive" parental permission for study #07-12451 without finding and documenting the four specific criteria for waiver of informed consent/parental permission at HHS regulations at 45 CFR 46.116(d) and in accordance with HHS

regulations at 45 CFR 46.408(b). While initially requested, the IRB did not allow "passive" consent for the above research and subsequently reviewed and approved a consent process that required fully documented permission from the subjects' parents. Given the facts at our disposal, we determine that this allegation is unproven.

(6) The complainant alleged that the informed consent documents reviewed and approved for study #08-13012 by the IUB IRB failed to include and/or adequately address the following elements required by HHS regulations at 45 CFR 46.116(a):

(a) Section 46.116(a)(1)(ii): an explanation of the purposes of the research (i.e., the purpose was to provide information about how parental satisfaction with the Boys and Girls Club correlates with income of families);

(b) Section 46.116(a)(2): A description of any reasonably foreseeable risks and discomforts (i.e., the risks and discomforts were not described).

We have reviewed the documentation for this study, and while an information sheet that did not include the information above was submitted with the protocol--in lieu of an informed consent document--the IRB required an informed consent document containing each of the elements required by HHS regulations at 45 CFR 46.116(a). This consent document was reviewed and approved by the IRB. Given the facts at our disposal, we determine that this allegation is unproven.

(7) The complainant alleged that the IRB lacked sufficient information to make determinations required for approval of research, in contravention of HHS regulations at 45 CFR 46.111. In specific, the complainant alleged that study #07-12647 was approved even though the IRB never reviewed a description of the demographic and electronic data that was to be provided to and analyzed by the researchers; there were questions about confidentiality of data and how subjects were to be linked to data, which was not described in the informed consent document; there was concern about asking supervisors to encourage their employees to participate in the research; and follow-up emails to subjects were not reviewed by the IRB, nor were the number of follow-up interviews described.

Based on the available information, this study was reviewed by the IUB IRB chairperson and determined to be exempt from IRB review under category 45 CFR 46.101(b)(2). HHS regulations at 45 CFR 46.101(b) delineate six specific categories of exempt activities. We find that the institution has applied an exemption to research activities that exceeded these categories.

Corrective Action: We acknowledge that the IUPUI IRB subsequently reviewed this study, and no further data collection was permitted; it was approved for data analysis only. Additionally, we acknowledge that IUB IRB members, IRB staff, and investigators

were provided with training and education on current human subject regulations and have adopted exemption forms that clearly describe research as defined by HHS regulations.

B. Recommendation:

(1) The written IUB IRB standard operating procedures (SOP) on the IUB IRB website (http://research.iu.edu.rschcomp/hmpg.html) reference the IUPUI IRB. We recommend that the IUB IRB SOPs refer to the IUB IRB.

The corrective actions noted above for (2), (4) and (7) adequately address our determinations and are appropriate under the IU FWA. As a result, there should be no need for further OHRP involvement in this matter. Please notify us if you identify new information which might alter this determination.

We appreciate your institution's continued commitment to the protection of human research subjects.

Sincerely,

Lisa R. Buchanan, MAOM, CIP
Compliance Oversight Coordinator
Division of Compliance Oversight

cc:
Ms. Shelly Bizilia, Director, Research Compliance Administration, Indiana University
Dr. Peter R. Finn, Chair, Bloomington IRB, Indiana University
Ms. Jennifer Colanese, Indiana University
Mr. T. Rowan Candy, Indiana University
Dr. Ann E. Elsner, Indiana University
Ms. Geneva Travis, Indiana University
Mr. Michael Conn-Powers, Indiana University
Dr. Sherry Mills, NIH
Mr. Joseph Ellis, NIH
Dr. Paul A. Sieving, Director, National Eye Institute, NIH