



DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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September 13, 2011

Ara Tahmassian, Ph.D.
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Boston University / Boston Medical Center
Boston U Medical Campus
715 Albany Street, Evans Bldg. 7
Boston, MA 02118-2526

Barry M. Fisch, O.D.
Vice President and Dean of Academic Affairs
The New England College of Optometry
424 Beacon Street
Boston, MA 02115

RE: Human Research Protections under Federalwide Assurances FWA-301 and FWA-2361

Research Project: Effects of Visual Signal Strength on Alzheimer Cognition
Principal Investigator: Alice Cronin-Golomb, Ph.D.
HHS Protocol Number: 5R01NS052914

Research Project: Visuospatial Function in Parkinson's Disease
Principal Investigator: Alice Cronin-Golomb, Ph.D.
HHS Protocol Number: 5R01NS050446

Dear Drs. Tahmassian and Fisch:

Thank you for your January 31, 2011 response to our November 9, 2010 request that your institution evaluate allegations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR part 46).

I. Determinations regarding the above-referenced research

- (1) A complainant alleges that the Boston University (BU) Institutional Review Board

(IRB) failed to ensure that risks to subjects are minimized in the above-referenced research projects, as required by Department of Health and Human Services (HHS) regulations at 45 CFR 46.111. In specific, the complainant alleges that unqualified personnel are conducting research interventions such as Optical Coherence Tomography (OCT) and Frequency Doubling Technology (FDT).

We note that Boston University's investigation revealed that all of the OCT and FDT exams associated with the above-referenced studies were performed by either Dr. Valenti (BU) or Dr. O'Donoghue (New England College of Optometry (NECO)), both of whom are licensed optometrists, or under their supervision. We acknowledge that Boston University verified through the Massachusetts Board of Registration in Optometry what types of practitioners were qualified to perform these tests and discovered that any doctor of optometry or trained technician can perform OCT and FDT procedures. Moreover, we note that the NECO investigation revealed that Dr. O'Donoghue, the supervising doctor for all care delivered at NECO, did all of the NECO OCT work associated with the above-referenced research and there was no delegation of work related to OCT. In addition, the NECO investigation revealed that while Dr. O'Donoghue did at times delegate some tests related to FDT, Dr. O'Donoghue only delegated such tests to students with proper credentialing; all other relevant tests were repeated by Dr. O'Donoghue to ensure high quality care. Given this, we have determined that this allegation of noncompliance is unproven. No evidence was presented to us indicating that the Boston IRB failed to ensure that risks to subjects were minimized in the above-referenced research projects.

- (2) A complainant alleges that the informed consent for the above-referenced research projects failed to include an adequate description of any reasonably foreseeable risks and discomforts, as required by HHS regulations at 45 CFR 46.116(a)(2). In specific, the complainant alleges that risks and side effects of a dilated eye examination were not explained to either the subject or the subject's legally authorized representative.

We note that the "Visuospatial Function in Parkinson's Disease" study consent documents include a description of the risks associated with dilation of the eyes, while the consents for "Effects of Visual Signal Strength on Alzheimer Cognition" indicated that the eye exams would be performed but did not include risks associated with the dilation of the eyes. As such, we determine that the consent documents for "Effects of Visual Signal Strength on Alzheimer Cognition" failed to describe the risks and discomforts associated with the dilation of the eyes, which constitutes a violation HHS regulations at 45 CFR 46.116(a)(2).

Corrective action: We note, per your response, that the investigator of the above referenced studies and the IRB received additional training regarding the requirements for informed consent as outline in HHS regulations at 45 CFR 46. 116. Further, we

acknowledge that the study entitled, "Effects of Visual Signal Strength on Alzheimer Cognition" has been transitioned to a new study, and the new study does include both a description of papillary dilation and its risks and discomforts.

- (3) A complainant alleges that the above-referenced research projects were conducted without IRB review and/or approval, in violation of HHS regulations at 45 CFR 46.103(b) and 46.109(a). In specific, the complainant alleges that the New England Eye Institute (NEEI) is engaged in the research and an IRB designated on their assurance has not reviewed and approved the research projects.

We have reviewed the materials, which included the service agreement between NEEI and BU and we note that the BU IRB determined, and we concur, that NEEI was not engaged in human subjects research per category B(1) of OHRP's 2008 Engagement Guidance (<http://www.hhs.gov/ohrp/policy/engage08.html>) which states:

Institutions whose employees or agents perform commercial or other services for investigators provided that all of the following conditions also are met:

- a. the services performed do not merit professional recognition or publication privileges;
- b. the services performed are typically performed by those institutions for non-research purposes; and
- c. the institution's employees or agents do not administer any study intervention being tested or evaluated under the protocol.

Given this information, we determine that this allegation of noncompliance is unproven.

II. Recommendation

- (1) HHS regulations at 45 CFR 46.103(b)(4)(iii) require that the 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. Based on the materials we reviewed, we note that although the IRB reviewed and approved changes in research activities, often those changes were only captured in the amendment requests and corresponding documents were not updated. For example, when the IRB received a request to add NEEI to perform eye exams for the studies referenced above, they were not informed that a key investigator who previously conducted those exams would no longer be on the study. Further, at least one subsequent grant application continued to include the name of this former investigator. We recommend that the IRB be notified when key study personnel have changed and that study documents be updated to reflect those changes.

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We determine that the above corrective actions adequately address our determinations and are appropriate under the Boston University FWA. At this time, there should be no need for further involvement by our office in this matter.

We appreciate 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,

Lisa Buchanan, MAOM
Compliance Oversight Coordinator
Division of Compliance Oversight

cc:

Ms. Mary A. Banks, IRB Director, Boston University / Boston Medical Center
Dr. Jonathan Woodson, IRB Chairperson, Boston University Medical Center IRB-
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Dr. James Feldman, IRB Chairperson, Boston University Medical Center IRB- Blue
Dr. Michael Lyons, IRB Chairperson, Boston University Medical Center IRB #1
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Dr. Paul F. White, Consultant/Professor, The New England College of Optometry
Dr. Sherry Mills, National Institutes of Health (NIH)
Mr. Joseph Ellis, Extramural Research, NIH
Dr. Story Landis, Director, National Institute of Neurological Disorders and Stroke