DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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November 6, 2007

Brian Peters
Executive Director
Health Foundation
Michigan Health & Hospital Association
6215 W. St. Joseph Highway
Lansing, MI 48917

RE: Human Subjects Research Protections

Research Project: Keystone: ICU, Accelerating Patient Safety in Michigan
Principal Investigator: Christine A. Goeschel

Dear Mr. Peters:

The Office for Human Research Protections (OHRP) has reviewed the Michigan Health & Hospital Association's (MHA) August 28, 2007 letter responding to OHRP's July 19, 2007 letter containing allegations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR Part 46) involving the above-referenced research.

Based upon its review, OHRP makes the following determinations regarding the research described in the above-referenced publication:

(1) In accordance with HHS regulations at 45 CFR 46.103(a), each institution engaged in non-exempt research conducted or supported by HHS must provide written assurance satisfactory to the Secretary of HHS that it will comply with the requirements of HHS regulations at 45 CFR part 46. Furthermore, in accordance with HHS regulations at 45 CFR 46.103(b) and 46.109(a), an institutional review board (IRB) designated under an OHRP-approved assurance must review and approve all non-exempt human subject research covered by the assurance.

OHRP finds that the implementation of the Comprehensive Unit-based Safety Program that included the ICU Safety Reporting System at Michigan and Rhode Island hospitals, the subsequent collection and analysis of data from ICU patients

exposed to those interventions, and the surveys of hospital personnel, represented non-exempt human subjects research that was conducted without appropriate IRB review and approval, in contravention of HHS regulations at 45 CFR 46.103(b) and 109(a). OHRP also finds that MHA, as the primary awardee, is engaged in the research and failed to obtain an appropriate OHRP-approved assurance of compliance as required by HHS regulations at HHS regulations at 45 CFR 46.103(b) and 46.109(a).

(2) HHS regulations at 45 CFR 45.116 state that, except as provided elsewhere in the regulations, no investigator may involve a human being as a subject in research covered by the regulations unless the investigator has obtained the legally effective informed consent of the subjects or the subjects' legally authorized representative. The above-referenced publication stated, "Informed consent was waived because the study was considered exempt from review."

OHRP finds that, given that the project involved non-exempt human subjects research, MHA failed to ensure that the requirements for obtaining and documenting the legally effective informed consent of the subjects or the subjects' legally authorized representative under HHS regulations at 45 CFR 46.116 and 46.117 were satisfied. OHRP notes that the subjects of the research were both the healthcare providers at the participating ICUs and their patients.

Corrective Action: OHRP acknowledges that MHA has advised the participating hospitals that the above-referenced activity ("the Initiative") should have been characterized as human subjects research and that participating hospitals have been advised to immediately suspend all activities related to the Initiative until such a time as IRB approval has been obtained. MHA has also advised participating hospitals with a Federalwide Assurance (FWA) of the need to submit the Initiative for IRB review and approval and shall advise those without an FWA that an FWA may be required in order to allow continued participation in the Initiative. MHA has requested that Johns Hopkins University instruct the principal investigator to suspend all activities related to the Initiative, submit the Initiative to all applicable IRBs for review an approval, and obtain legally effective informed consent from all hospital personnel and patients participating in the Initiative unless such consent is waived by the applicable IRB. MHA requested assistance and guidance from OHRP regarding when such activities are human subjects research. Please note that OHRP is in the process of developing guidance on the definition of "research."

By December 18, 2007 please provide OHRP with a report on the status of the above-mentioned corrective actions. Please also provide the FWA number of MHA when it is approved by OHRP.

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.
Director
Division of Compliance Oversight

cc:

Dr. Daniel E. Ford, MD, John Hopkins University School of Medicine
Dr. Janet A. DiPietro, Johns Hopkins Bloomberg School of Public Health
Dr. Eaton E. Lattman, Ph.D., Johns Hopkins University
Ms. Christine A. Goeschel, Michigan Health & Hospital Association
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