



DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of the Assistant Secretary for Health

Office for Human Research Protections
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852
Telephone: 240-453-8120
FAX: 240-453-6909
E-mail: Lisa.Rooney@hhs.gov

August 10, 2011

Daniel M. Dorsa, Ph.D.
Vice President for Research
Oregon Health & Science University
2170 Mackenzie Hall
3181 SW Sam Jackson Park Rd. L101
Portland, OR 97239-3098

RE: Human Research Protections Under Federalwide Assurance (FWA) - 161

Research Project: Teaching Vascular Surgery Skill: Reinforcing the Practice, A Randomized, Controlled Trial

Principal Investigator: Erica Mitchell, M.D.

Protocol Number: 4756

Research Project: Perioperative Venous Thromboembolism (VTE) in Patients with a Prior History of Deep Vein Thrombosis (DVT)

Principal Investigator: Timothy Liem, M.D.

Protocol Number: 5046

Dear Dr. Dorsa:

Thank you for your June 9, 2011 letter in response to our May 23, 2011 letter regarding research conducted under the above-referenced research projects. We acknowledge the responses provided and the steps taken to address our prior determinations.

A. In our letter dated May 23, 2011, we made the following determinations:

- (1) We determined that an investigator initiated human subject research without obtaining legally effective informed consent of subjects (who were enrolled between July 2008 and October 31, 2008) and without the Oregon Health & Science University Institutional Review Board (OHSU IRB) appropriately waiving these requirements in violation of Department of Health and Human Services (HHS) regulations at 45 CFR 46.116(c) or (d) or in accordance with the provisions for waiver of informed consent for research in emergency settings published in the Federal Register, Vol. 61, pp. 51531-

51533. Given this finding, you were asked to provide us with a corrective action plan that would ensure that no investigators involve human beings as subjects in research covered by the regulations unless (a) the investigators have obtained the legally effective informed consent of the subjects or the subject's legally authorized representative, or (b) the IRB has waived the requirements to obtain informed consent in accordance with 45 CFR 46.116(c) or (d), or in accordance with the provisions for waiver of informed consent for research in emergency settings published in the Federal Register, Vol. 61, pp. 51531-51533.

Corrective Action: We acknowledge receipt of the OHSU Human Research Protection Program (HRPP) Policies & Procedures regarding informed consent, waiver of informed consent and research in emergency settings. (We have provided you with recommendations for improving the informed consent policy and procedures in the Recommendations Section below.) Moreover, we note that while all OHSU human subjects investigators must complete an educational module and regular educational booster sessions addressing informed consent and waiver of informed consent requirements, OHSU will be re-educating the entire OHSU human subjects research community about these requirements. These corrective actions appear to be adequate under the terms of the OHSU FWA.

- (2) We determined that OHSU failed to report noncompliance involving study 4756 to our office as required by HHS regulations at 45 CFR 46.103(a) and 46.103(b)(5). As a result, you were asked to provide our office with a corrective action plan that would ensure prompt reporting to OHRP of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with 45 CFR part 46 or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval.

Corrective Action: We acknowledge receipt of OHSU HRPP Policies and Procedures regarding the reporting of unanticipated problems, serious or continuing noncompliance, protocol deviations, and suspension or termination of IRB approval. (We have provided you with recommendations for improving these policies and procedures in the Recommendations Section below.) We also acknowledge that OHSU will be implementing a process/protocol within your electronic IRB system that brings all reportable events to the attention of at least two OHSU administrators, e.g., the IRB Chair or Co-Chair, and at least one IRB analyst. These corrective actions appear to be adequate under the terms of the OHSU FWA.

B. In addition to the determinations noted above, we have made the following determinations:

- (1) A complainant alleged that the OHSU Department of Surgery, Division of Vascular Surgery has developed and maintains a deep vein thrombosis (DVT) database for research purposes without obtaining IRB review and approval for the establishment of the database, and that the DVT database is "expanded" as new research questions are

developed. The complainant alleges that the DVT database includes patient names, medical record numbers, dates of birth, procedure dates and results of procedures. The complainant believes that the OHSU Department of Surgery, Division of Vascular Surgery developed and maintains the database in contravention with HHS regulations at 45 CFR 46.103(b) and 46.109(a).

We note that OHSU conducted an investigation into this matter and discovered that while no such research database/repository exists, the OHSU Department of Surgery, Division of Vascular Surgery does maintain a clinical database of DVT procedures that are performed. Per OHSU, the Division maintains this clinical database for credentialing, re-licensure, Joint Commission requirements, and other regulatory reasons. Based on this information, we have determined that this allegation of noncompliance is unproven. No evidence was presented to us indicating that the OHSU Department of Surgery, Division of Vascular Surgery developed and maintains the database of DVT procedures for research purposes in contravention with HHS regulations at 45 CFR 46.103(b) and 46.109(a).

- (2) A complainant alleges that OHSU staff (a) routinely analyzes data maintained in the above-mentioned DVT database; (b) sometimes discovers interesting findings, trends, etc., after conducting such analysis; and (c) submits IRB protocols to cover such data analysis only after OHSU staff have completed the analysis. According to the complainant, the IRB submissions are worded prospectively when, in fact, the investigators have already completed the analysis in violation of HHS regulations at 45 CFR 46.103(b) and 46.109(a) which require that an IRB review and approve all non-exempt human subject research covered by an assurance before the research can be conducted.

Based on the information noted above under item B(1), we have determined that this allegation of noncompliance is unproven. No evidence was presented to us indicating that the OHSU Department of Surgery, Division of Vascular Surgery has violated HHS regulations at 45 CFR 46.103(b) and 46.109(a).

C. Recommendations

We make the following recommendations regarding certain OHSU HRPP Policies and Procedures. Please note that you are not required to adopt these recommendations.

- (1) Consent Forms: Assurance of the Required Elements of Informed Consent. We note that your current policy regarding the required elements of informed consent states that the additional elements of informed consent outlined in HHS regulations at 45 CFR 46.116(b) are not required for minimal risk studies. Please note that 45 CFR 46.116(b) provides that “When appropriate, one or more of the following elements of information shall also be provided to subjects. . . .” Thus, there may be instances when it would be appropriate to provide one or more of the additional elements of informed consent to

subjects that will be enrolling in a minimal risk study. As a result, we recommend that you revise this document accordingly.

- (2) Serious and Continuing Noncompliance. It appears that this document is exclusively focused on noncompliance associated with research and OHSU IRB requirements or determinations regarding such research; this document does not appear to address noncompliance with 45 CFR part 46 as it relates to IRB roles, authorities, and responsibilities. While we note that the authority section of this document states that federal regulations require that any serious or continuing non-compliance with ***DHHS human subjects regulations*** (emphasis added) or the determinations of the IRB must be promptly reported to certain entities, the document fails to include the procedures for addressing noncompliance as it relates to IRB roles, authorities, and responsibilities. For example, there is no information regarding where an individual can report noncompliance concerns regarding the OHSU IRB. Given this apparent omission, we recommend that you revise this document to include procedures for addressing noncompliance relating to IRB roles, authorities, and responsibilities or draft an additional policy and procedures document specific to such noncompliance.

At this time, there should be no need for further involvement by our office 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 A. Rooney, J.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Kara M. Drolet, Associate Director, Oregon Health & Science University