



DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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May 23, 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 December 3, 2010 letter in response to our November 4, 2010 letter informing you that the Office for Human Research Protections (OHRP) had received 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 on the information submitted, we have made the following determinations:

A. Determinations Regarding Study 4756:

- (1) A complainant alleged that study 4756 was conducted without Oregon Health & Science University Institutional Review Board (OHSU IRB) review and approval. In specific, the complainant alleged that study 4756 was started in July 2008, but did not receive Institutional Review Board (IRB) review and approval until October 2008.

As you are aware, HHS regulations at 45 CFR 46.103(b) and 46.109(a) require that an IRB review and approve all non-exempt human subject research covered by an assurance before the research can be conducted. We have determined that study 4756, a non-exempt human subjects research protocol, was conducted between July 2008 and October 31, 2008 without IRB review and approval in violation of HHS regulations at 45 CFR 46.103(b) and 46.109(a). We note that your investigation substantiated this allegation.

Corrective Action: We acknowledge that OHSU has provided IRB compliance and regulatory education to both of the investigators referenced above. We also note that a research nurse coordinator has been hired to assist OHSU Department of Surgery, Division of Vascular Surgery faculty, residents, fellows and interns who may be interested in conducting human subjects research. Lastly, we note that this newly hired research nurse coordinator is conducting bi-weekly meetings with division staff to inquire about research interests and planned activities. We determine that these corrective actions adequately address our determination and are appropriate under the OHSU FWA.

- (2) A complainant alleged that informed consent was not obtained from many subjects prior to their involvement in non-exempt human subjects research activities related to study 4756. We acknowledge your response that, due to “administrative errors,” vascular surgery interns who participated in study 4756 did not sign the IRB-approved ICF prior to participation in the study.

HHS regulations at 45 CFR 46.116 state that no investigator may involve a human being as a subject in research covered by the regulations unless (a) the investigator has 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 emergent settings published in the Federal Register, Vol. 61, pp. 51531-51533. We determine that the 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 IRB appropriately waiving these requirements. We note that when the OHSU IRB approved this study on October 31, 2008 (four months after the non-exempt human subjects research began) the IRB required the use of an IRB approved informed consent document -- a document that was not available to the investigator/subjects prior to this time.

Required Action: Please provide us with a corrective action plan that will 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 emergent settings published in the Federal Register, Vol. 61, pp. 51531-51533.

(3) As you are aware, HHS regulations at 45 CFR 46.103(a) and 46.103(b)(5) provide that institutions have written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, OHRP, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others, or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval. We note that at some time prior to our office opening an investigation into the above-referenced allegations, OHSU initiated an investigation into study 4756 and discovered that the investigator conducted nonexempt human subjects research between July 2008 through October 31, 2008 without first obtaining IRB review and approval. We note further that this investigation revealed that according to OHSU policy the period of unapproved research from July 2008 through October 2008 was considered to be reportable to our office. Notwithstanding this conclusion, we note that OHSU failed to report the period of unapproved research to our office. As a result, we have determined that the noncompliance involving study 4756 was not reported to OHRP as required by HHS regulations at 45 CFR 46.103(a) and 46.103(b)(5). Please note that OHRP considers the following scenarios, among others, to constitute serious noncompliance:

- Conducting non-exempt human subjects research without IRB review and approval;
- Failing to obtain the legally effective informed consent of subjects, when required by the IRB, prior to the involvement of such subjects in non-exempt human subjects research activities.

Required Action: Please provide our office with a corrective action plan that will ensure prompt reporting to OHRP of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval.

B. Determinations Regarding Study 5046:

(1) A complainant alleged that study 5046 was conducted without IRB review and approval in violation of HHS regulations at 45 CFR 46.103(b) and 46.109(a). We note that your investigation revealed that this study was reviewed and approved by the OHSU IRB on May 29, 2009, before the research began. Given this, we have determined that the allegations of noncompliance are unproven. No evidence was presented to us indicating that study 5046 was conducted without IRB review and approval.

C. Questions and Concerns Regarding OHSU's Human Subjects Protection Program:

(1) [Redacted]

[Redacted]

2. [Redacted]

[Redacted]

Please provide us with responses to the above required actions and questions and concern by June 13, 2011.

We appreciate your institution's continued commitment to the protection of human research subjects. Please do not hesitate to contact me should you have any questions.

Sincerely,

Lisa A. Rooney, J.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc:

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