



DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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February 16, 2012

Bruce E. Jarrell, M.D., FACS
Vice Dean for Research and Academic Affairs
University of Maryland Baltimore, School of Medicine
655 W. Baltimore Street
Room 14-031
Baltimore, MD 21201

**RE: Human Research Protections Under Federalwide Assurance FWA-00007145;
Research Projects Under Principal Investigator Dr. Stephen Davis**

Dear Dr. Jarrell:

As you know, earlier this year the Office for Human Research Protections (OHRP) initiated an off-site compliance oversight evaluation of the University of Maryland, Baltimore (UMB) concerning research projects being conducted by Dr. Stephen Davis. We thank you for your November 29, 2010 and May 11, 2011 reports in response to our October 25, 2010 and April 21, 2011 letters. Moreover, as you are aware, our office subsequently conducted an on-site evaluation of human subject protection procedures at UMB from October 18, 2011 to October 20, 2011. The evaluation, conducted by four OHRP staff with the assistance of a representative from the Department of Health and Human Services (HHS) Office of the General Counsel and three consultants, included meetings with you, institutional review board (IRB) Chairs, IRB members, the administrative staff of the IRB, a HHS-supported principal investigator who submits protocols to one or more of the UMB IRBs, and his research team. Lastly, the evaluation involved a review of IRB policies and procedures, IRB files for approximately 40 open protocols, and the minutes of approximately 30 IRB meetings held after February 2011.

In the course of the OHRP on-site evaluation, the IRB chairs, members, and administrative staff displayed an enthusiastic and sincere concern for the protection of human subjects.

Based on the documentation provided to us as part of your November 29, 2010 and May 11, 2011 reports, information gathered during interviews conducted during the on-site evaluation, information reviewed during the on-site evaluation, and your November 10, 2011 follow-up letter, we make the following determinations. Please note that all questions and concerns relative to Dr. Davis's studies (protocols 44672, 44868, 44874 and 44875) are based on the complete IRB files that UMB provided to OHRP on May 11, 2011.

A. Determinations Regarding Research Projects Under Dr. Stephen Davis

1. A complainant alleged that the UMB IRB failed to ensure that risks to subjects were minimized in the above-referenced research, as required by HHS regulations at 45 CFR 46.111. To be specific, the complainant alleged that unqualified personnel were conducting research interventions such as microneurography, hyperinsulinemic, hypoglycemic, euglycemic and hyperglycemic clamp procedures, and writing orders in Dr. Davis' research studies.

UMB responded that Dr. Davis's foreign-trained staff underwent University of Maryland Medical Center (UMMC) credentialing procedures before being permitted to perform specific procedures in the research setting. In specific, we understand that Dr. Davis's foreign-trained staff was credentialed under the UMMC Credentialing Category entitled Research Resident, an established category which is used occasionally to credential unlicensed physicians to perform specific procedures in a research setting. We further understand that you, as UMB Institutional Official, approved this process as a method of ensuring that foreign-trained staff was qualified by training and experience to engage in Dr. Davis's research protocols. Based on the documentation provided in your November 29, 2010 correspondence, coupled with information gathered during our site visit, we have determined that this allegation of noncompliance is unproven. No evidence was presented to us indicating that unqualified personnel were conducting research interventions in the above-referenced research studies.

2. A complainant alleged that Dr. Davis enrolled his research nurse and lab staff into one or more of his studies in contravention of HHS regulations at 45 CFR 46.116 which require that investigators seek consent only under circumstances that minimize the possibility of coercion or undue influence.

In a May 11, 2011 report, you responded that one or more fully convened UMB IRBs had agreed to allow Dr. Davis to enroll his employees, lab personnel and students into one or more of his research studies under conditions outlined by Dr. Davis in his UMB IRB applications. According to your report, employees, lab personnel and students of Dr. Davis must initiate any contact with the study staff about enrolling in the study. Subsequently, in a report dated October 6, 2011 we were notified that on September 16, 2011 you, as the UMB Institutional Official, determined that Dr. Davis could not enroll any further employees, students or lab personnel into any study for which he serves as the principal investigator. Based on the documentation provided in your May 11, 2011 correspondence, coupled with information gathered during our site visit, we have determined that this allegation of noncompliance is unproven. No evidence was presented to us indicating that Dr. Davis coerced or unduly influenced his research nurse and lab staff into one or more of his studies in contravention of HHS regulations at 45 CFR 46.116.

B. Determinations Regarding Research Projects Under Other Investigators

1. HHS regulations at 45 CFR 46.116(a) require that when seeking informed consent, specific information shall be provided to each subject unless the IRB approves a consent procedure which does not include, or which alters, some or all of the required basic elements of informed consent in accordance with HHS regulations at 45 CFR 46.116(c) or (d). We have determined that the informed consent document for HP-00046741, which was reviewed and approved by the IRB, failed to include a description of the appropriate alternative procedures or courses of treatment that might have been advantageous to the subjects as required by HHS regulations at 45 CFR 46.116(a)(4). In specific, we have found that the consent form does not provide subjects with sufficient information about the option of receiving the research interventions outside of the research protocol. Of note, this protocol involves comparing two different standards of care surgeries - mitral valve replacement vs. mitral valve repair – for severe mitral valve leakage.

Corrective Action: We note that UMB found that the IRB-approved consent form did not include an adequate description of the alternatives to participation in the study. In particular, UMB found that the investigator failed to modify the alternatives section as requested by the UMB IRB. As a result of this finding, the UMB IRB plans to re-review this protocol, including the consent form, at an upcoming IRB meeting in order for the IRB to consider the adequacy of the consent form.

Required Action: Please provide our office with a copy of the IRB meeting minutes at which this study is discussed as well as a copy of any consent form that is modified as a result of this re-review. Also, please provide our office with a plan to ensure that informed consent documents include adequate information on the appropriate alternative procedures or courses of treatment that may be advantageous to the subjects (as required by HHS regulations at 45 CFR 46.116(a)(4)), including the option of receiving research intervention(s) outside of the research, when appropriate.

2. We have determined that complete IRB records, as outlined under 45 CFR 46.115(a), were not accessible for inspection and copying by authorized representatives of HHS at reasonable times and in a reasonable manner as required by HHS regulations at 45 CFR 46.115(b). Of note, UMB was unable to provide us **at reasonable times and in a reasonable manner** with copies of or access to:
 - (a) Final meeting minutes;
 - (b) Approved sample consent forms; and
 - (c) Original research proposals, as submitted to the IRB.

Corrective Action: We recognize that as of October 31, 2011, UMB created a new activity within the UMB electronic IRB system to address our determination specific to final meeting minutes. This new activity attaches final approved IRB meeting minutes into individual meeting workspaces. As of October 31, 2011 all IRB meetings for which there are minutes in pdf format have been updated by attaching the pdf documents to the appropriate meeting space in the electronic system.

Required Action: Please provide our office with a plan to ensure that complete IRB records, as outlined under 45 CFR 46.115(a), will be accessible for inspection and copying by authorized representatives of HHS at reasonable times and in a reasonable manner as required by HHS regulations at 45 CFR 46.115(b).

C. Questions and Concerns Regarding Research Projects Under Dr. Davis

1. [Redacted]

2. [Redacted]

[Redacted]

3. [Redacted]

[Redacted]

[Redacted]

D. Questions and Concerns Regarding Research Projects Under Other Investigators

[Redacted]

[Redacted]

2. [Redacted]

[Redacted]

3. [Redacted]

Please provide us with responses to the above determinations, questions and concerns by March 29, 2012 including a corrective action plan for each of our determinations.

Bruce E. Jarrell, M.D – University of Maryland Baltimore, School of Medicine
February 16, 2012
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We appreciate the continued commitment of your institution to the protection of human research subjects. Please do not hesitate to contact me if you should have any questions.

Sincerely,

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

cc:

Dr. Jay A. Perman, President, UMB (220 North Arch Street, 14th Floor, Baltimore, MD 21201)

Ms. Susan C. Buskirk, Assistant Dean, Human Research integrity & Compliance, University of Maryland Baltimore, School of Medicine

Dr. Robert Edelman, Associate Director, Clinical Research/IRB Chair, University of Maryland, Baltimore, School of Medicine

Dr. Stephen Davis, University of Maryland, Baltimore, School of Medicine

Dr. Sherry Mills, National Institutes of Health (NIH)

Mr. Joseph Ellis, NIH