DEPARTMENT OF HEALTH & HUMAN SERVICES

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Office of Public Health and Science

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May 6, 2008

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RE: Human Research Protections Under Federalwide Assurance FWA-5945

Dear Mr. Trachtenberg and Dr. Hirshfield:

Thank you for your June 18, 2007 and October 25, 2007 reports in response to our April 30, 2007 request that George Washington University (GWU) evaluate allegations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR part 46).

A. Determinations regarding your institution's system for protecting human subjects

(1) The complainant alleged that the GWU institutional review board (IRB) failed to conduct continuing review of some research studies at least once per year, as required by HHS regulations at 45 CFR 46.109(e). We note that in April 2006 GWU implemented a policy under which GWU IRB approval would no longer be required for studies where the GWU Biostatistics Center was the direct awardee under a federal grant and employees or agents of GWU were not interacting or intervening with human subjects.

We note that GWU sought consultation with OHRP on the policy referenced above in October 2006. You stated in your June 18, 2007 report that as a result of the meeting with OHRP, GWU re-reviewed and re-approved all Biostatistics

Center studies in which GWU was the direct awardee that had lapsed as result of the former policy that was "based upon an inaccurate interpretation of guidance received from OHRP." We want to clarify that during our February 22, 2007 meeting with GWU and representatives from the National Institutes of Health (NIH), we agreed that, given the specific circumstances in this case, GWU was not engaged in human subjects research in these situations.

Since OHRP agrees that, in this circumstance, GWU is not engaged in human subjects research for studies where the GWU Biostatistics Center is the direct awardee under an HHS grant in which no employees or agents of GWU are interacting or intervening with human subjects, from the information before us, we determine that the allegation is unproven.

(2) The complainant alleged that the minutes of GWU IRB meetings failed to be in sufficient detail to show actions taken by the IRB and a written summary of the discussion of controverted issues and their resolution, as required by HHS regulations at 45 CFR 46.115(a)(2). With regard to GWU protocol #12404, we determine that this allegation is unproven. We are aware of no information that demonstrates the GWU IRB minutes failed to meet the above-referenced regulatory requirements.

With regard to GWU protocol #080214, study entitled "Viscocanalostomy: A Prospective, Randomized, Controlled Study," the complainant alleged that the IRB minutes for the April 11, 2006 meeting failed to be in sufficient detail to show all of the actions taken by the IRB. The April 11, 2006 minutes state in the "Old Business" section the following:

> This study was placed on hold following routine continuing review in order to obtain answers to questions that arose concerning the risk/benefit ratio in the study. The IRB discussed the study and determined that there were issues and concerns that needed further clarification. The principal investigator (PI) will be asked to respond to the following:…" The minutes then list 23 stipulations.

The complainant alleged that the April 11, 2006 minutes contained errors and did not correctly reflect the history of the study, such as reflecting that the study was placed on hold following continuing review even though the IRB conditionally approved the study at continuing review and the Institutional Official (IO) who executed the GWU FWA subsequently suspended the study based on her own concerns. We note that the IRB minutes are ambiguous as to who placed the study on hold and who raised the questions concerning the risk/benefit ratio in the study that led to the hold. We also note that the action to place the study on hold was made by the IO, and, as such, does not need to be documented in the minutes of the IRB meeting. As a result, with regard to

GWU protocol #12404, we determine that this allegation is unproven.

We acknowledge that GWU identified a need for a quality assurance process to ensure high quality minutes of IRB meetings and provided a list of corrective actions in its June 18, 2006 response designed to improve both the IRB minutes and the process for creating IRB minutes for the GWU IRB.

(3) The complainant alleged that GWU failed to prepare and maintain written IRB procedures that adequately describe the following activities, as required by HHS regulations at 45 CFR 46.103(a) and 46.103(b)(4) and (5). We acknowledge your statement that during the time period in question, GWU maintained written IRB procedures in one of several forms, but that while new procedures were being developed the IO requested that the written procedures be removed from the GWU Office of Human Research (OHR) website and instead the website directed readers to the OHR to obtain written procedures. As a result, we determine that this allegation is unproven.

(4) The complainant alleged that GWU failed to adequately maintain IRB records required under HHS regulations at 45 CFR 46.115(a)(1), (3), (4), and (7). In specific, the complainant alleged that a letter that was to be sent from an OHR Administrator to NIH was not maintained in the IRB records for that study, and that IRB files were destroyed in an archiving project. We acknowledge your statement that the letter was drafted and was never sent and therefore was not required to be maintained in the IRB records for that study. As a result, we determine that this allegation is unproven. We note, however, your statement that eight IRB files may have been destroyed prematurely during the archiving project. We acknowledge that GWU has drafted and implemented policies and procedures for management of IRB documents that minimize the likelihood of recurrence.

(5) The complainant alleged that GWU failed to report the suspension or termination of IRB approval to OHRP, as required by HHS regulations at 45 CFR 46.103(a) and 46.103(b)(5). In specific, the complainant alleged that a suspension of IRB approval of study #110539 was not reported to OHRP. We acknowledge your statement that the IO suspended this study, not the IRB, and therefore this action did not need to be reported to OHRP as a suspension of IRB approval. As a result, we determine that this allegation is unproven.

B. Questions and Concerns

(1) [Redacted]

(2) [Redacted]

(3) [Redacted]

(4) [Redacted]

(5) [Redacted]

C. Recommendation

We make the following recommendation regarding GWU's human subject protection program:

> We note that GWU policy #03g, entitled "Continuing Review (Renewal Requests)" states the following in item #4.b., "Expiration of protocol":
>
> > "Investigators may not enroll new subjects after the approval expires. The

> IRB Chair may permit exceptions to this rule in the rare instances where failure to enroll new subjects could jeopardize the safety or well-being of an individual prospective subject. If <sic> such instances, the PI should notify the IRB Chair in writing, detailing the circumstances."

OHRP notes that the January 15, 2007 OHRP "Guidance on Continuing Review" contains the following statement:

> The IRB and investigators must plan ahead to meet required continuing review dates. If an investigator has failed to provide continuing review information to the IRB or the IRB has not reviewed and approved a research study by the continuing review date specified by the IRB, the research must stop, unless the IRB finds that it is in the best interests of individual subjects **to continue participating** in the research interventions or interactions. Enrollment of new subjects cannot occur after the expiration of IRB approval.

It is acceptable under some circumstances to allow subjects to continue participating after the expiration of a study if a best interests determination can be made by the IRB, as stated in the above-referenced OHRP guidance document. However, it is <u>not</u> acceptable to allow enrollment of new subjects after expiration. We recommend that the GWU policy be revised to conform with 45 CFR 46.109(e).

Please forward your response to the concerns and questions raised in section B above so that OHRP receives it no later than June 20, 2008.

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:

Ms. Leody A. Bojanowski, Director, Office of Human Research, GWU
Dr. David M. Parenti, Chair, GWU IRB #1
Dr. Katherine H. Goodrich, GWU IRB #3
Commissioner, FDA
Dr. Joanne Less, FDA