DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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October 3, 2008

Stephen Joel Trachtenberg, J.D., M.P.A.
President
George Washington University
2121 Eye Street, N.W.
Washington, D.C. 20052

Anne N. Hirshfield, Ph.D.
Associate Vice President, Health Research, Compliance & Tech Transfer
George Washington University
2300 Eye Street, NW
Suite 712
Washington, DC 20037

RE: Human Research Protections Under Federalwide Assurance FWA-5945

Dear Mr. Trachtenberg and Dr. Hirshfield:

Thank you for your June 16, 2008 report in response to our May 6, 2008 letter regarding allegations of noncompliance by George Washington University (GWU) with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR part 46).

Based upon our review, we make the following determinations:

(1) The complainant alleged that protocol # 030729 entitled "A Phase I, Single-Center, Double-Blinded, Placebo-Controlled, Randomized, Dose-Escalation Study to Compare the Safety, Tolerability, and Immunogenicity of Three Intramuscular Administration of Na-ASP-2 Hookworm Vaccine in Healthy Adults without Evidence of Hookworm Infection" was initially reviewed by an independent IRB due to potential GWU institutional conflicts of interest. The complainant alleged that GWU IRB, at the behest of the Institutional Official (IO), inappropriately granted approval for a modification to this study via the

expedited review process in 2005 or 2006, in violation of HHS regulations at 45 CFR 46.110(b)(1), which limit the use of expedited procedures for review of minor changes in previously approved research during the period for which approval is authorized. We note your assertion that the "modification" was not actually a change to protocol # 030729, but instead a new study, protocol # 080525, "Changes in mRNA Expression Following Immunization with the Na-Asp-2 Hookworm Antigen." Given the facts at our disposal, we determine that this allegation is unproven.

(2) The complaint alleged the following with regard to study #120223 entitled "Medialization vs. Reinnervation for Vocal Cord Paralysis":

> In an email dated July 19, 2005, the GWU IO notified the investigator that the study was closed due to administrative reasons. In that memorandum, the investigator was asked to provide certain information to the GWU IO. The investigator responded to the July 19, 2005 memorandum with an August 1, 2005 memorandum. In that memorandum, the investigator requested that the GWU IO grant her a study extension for one patient even though the study had been terminated by the GWU IO. In a memorandum dated August 17, 2005, the GWU IO, not the IRB, granted permission to the investigator to collect research data on one subject even though the study was previously terminated.

We expressed concern as to whether or not these facts were consistent with the regulatory requirements at 45 CFR 46.112, which state that institutional officials may not approve research that has not been approved by the IRB.

We acknowledge your statement that the study was terminated by the IO, not the IRB, for administrative reasons, and "absent the administrative closure [by the IO], the final data collection by the PI would have taken place during the current IRB approval period for the study." Given the facts at our disposal, we determine that this allegation is unproven.

(3) With regard to GWU protocol #080214, study entitled "Viscocanalostomy: A Prospective, Randomized, Controlled Study," we note that you stated in your June 18, 2007 response to us:

> [T]he Institutional Official (IO) acted in accordance with her authority under 45 CFR 46.112 to protect human subjects…Before the PI responded with information to address the stipulations [of the GWU IRB], concerns arose regarding this study. The IO discussed these concerns with the IRB Chair, who agreed that these concerns should be raised. In an effort to ensure appropriate protections for human subjects, the IO, acting within her authority, overruled the IRB's conditional

approval of the study.

We note the information cited in our May 6, 2008 letter that the IO suspended GWU protocol #080214.

Further, we note that on December 9, 2005, the GWU IO sent a report to us stating the following regarding this protocol:

> …the **GWU IRB has suspended the study**, [emphasis added] as a precaution, following routine continuing review. **When the study was considered for continuing review, a number of questions arose** [emphasis added], including the following:
>
> 1. Does the informed consent document adequately describe the purpose of the study and the risks associated with each of the 3 study arms?
> 2. Has the investigator adequately justified inclusion of <sic> for one of the three study arms; and
> 3. Does the documentation provided to the IRB adequately describe the study design and the state of current knowledge in the field?

We acknowledge your clarification that when the study was considered for continuing review the then director of the Office of Human Research (OHR) had concerns about the design of the study but these concerns were not discussed during the review of this study by the convened IRB. Immediately after the meeting, the director of OHR discussed her concerns with the IO who discussed them with the IRB chairperson and agreed that the study should be suspended until the issue was addressed. Therefore the IO, not the IRB, suspended the study, when concerns were raised after continuing review by the convened IRB.

We applaud the actions of the director of OHR in raising concerns that were missed by the convened IRB and the actions of the IO in suspending the study until those concerns were addressed. However, we note that every attempt should be made to ensure that any reports submitted to our office to fulfill the requirements of reporting to OHRP described in HHS regulations at 45 CFR 46.103(a) and 46.103(b)(5) are accurate. We note that you have submitted a revised report on this issue that accurately reflects the events.

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.

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