DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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February 11, 2008

Susan Kelly, Ph.D.
President
Charles R. Drew University of Medicine & Science
1731 East 120th Street
Los Angeles, CA 90059

Re: Human Research Subject Protections Under Federalwide Assurance FWA-2736

Dear Dr. Kelly:

Thank you for your March 3, 2007 report in response to our January 23, 2007 request that Charles R. Drew University of Medicine & Science (Drew) evaluate allegations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR part 46). The complainant alleged that institutional review board (IRB) members with conflicting interest participated in IRB review of research, in violation of HHS regulations at 45 CFR 46.107(e). Specifically, a complainant has alleged that the Drew IRB Chairperson takes part in the review and approval of studies in which he is an investigator and studies in which he mentors the investigators.

I. Determination

Based on the documentation provided in your March 3, 2007 correspondence, we have determined that the allegations of noncompliance are unproven. No evidence was presented to us indicating that the Drew IRB Chairperson participated in the review and approval of studies in which he was an investigator, or studies in which he mentors investigators. Specifically, we note the following.

(a) In its March 3, 2007 letter, you listed research proposals submitted to the IRB for review, in which the IRB Chairperson was an investigator or in which students that he mentored were investigators. The list included one study that was approved on February 1, 2006 by the convened IRB: "Does Systemic Corticosteroid Therapy Improve Voice-Related Outcomes Following Thyroid/Parathyroid Surgery"? (#05-09-896-01).

(b) The February 1, 2006 IRB meeting minutes reflected that the IRB Chairperson recused himself from the review of study #05-09-896-01 due to his status as a co-investigator on the study.

(c) In our January 23, 2007 letter, we requested that you provide copies of the minutes of IRB meetings where protocols in which the IRB chairperson was an investigator, or in which students that he mentored were investigators, were reviewed or approved. You provided meeting minutes from March, July, August, September and October of 2006, in your March 3, 2007 response to us. These minutes documented any conflicts of interest reported by any IRB member at the meetings. Except for the February 1, 2006 IRB meeting minutes referenced in subparagraph (b) above, none of these IRB meeting minutes documented conflicts of interest on the part of the IRB Chairperson.

(d) Your March 3, 2007 letter lists seven exemption applications that were submitted to the IRB by the IRB Chairperson or by students that the IRB Chairperson mentored. The letter indicated that these seven exemption applications were reviewed by IRB members other than the Chairperson for a determination of whether they involved research activities exempt from the HHS regulations for the protection of human subjects, as described at 45 CFR 46.101(b).

II. Recommendations

We make the following recommendations regarding Drew's human subject protection program:

(1) The July 26, 2006 Drew IRB meeting minutes state, with respect to IRB protocol #00-06-041-07 (page 4), that the IRB voted to "accept the continuing review pending receipt of the progress report." We note that the continuing review progress report may have contained important information bearing on the criteria required for approval of research under 45 CFR 46.111, and provide the following guidance to Drew.

Continuing review of research must be substantive and meaningful. HHS regulations at 45 CFR 46.111 set forth the criteria that must be satisfied in order for the IRB to approve research. These criteria include, among other things, determinations by the IRB regarding risks, potential benefits, informed consent, and safeguards for human subjects. The IRB must ensure that these criteria are satisfied at the time of both initial and continuing review. The procedures for continuing review by the convened IRB may include a primary reviewer system.

In conducting continuing review of research not eligible for expedited review, all IRB members should at least receive and review a protocol summary and a status report on the progress of the research, including: (i) the number of subjects accrued; (ii) a summary of adverse events and any unanticipated problems involving risks to subjects or others and

any withdrawal of subjects from the research or complaints about the research since the last IRB review; (iii) a summary of any relevant recent literature, interim findings, and amendments or modifications to the research since the last review; (iv) any relevant multi-center trial reports; (v) any other relevant information, especially information about risks associated with the research; and (vi) a copy of the current informed consent document and any newly proposed consent document.

At least one member of the IRB (i.e., a primary reviewer) also should receive a copy of the complete protocol including any protocol modifications previously approved by the IRB. Furthermore, upon request, any IRB member also should have access to the complete IRB protocol file and relevant IRB minutes prior to or during the convened IRB meeting. The minutes of IRB meetings should document separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB.

When conducting continuing review of research under an expedited review procedure, the IRB Chairperson (or designated IRB member(s)) should receive and review all of the above-referenced documentation, including the complete protocol.

(2) On September 21, 2006 the Drew IRB approved protocol #06-08-002-01 titled "Sociocultural Determinants of Menthol Smoking Among Blacks: Focus Group Protocol" through use of expedited review procedure category 1. There is no documentation in the October 18, 2006 IRB minutes that the IRB was notified of the expedited approval of protocol #06-08-002-01. We recommend that the Drew IRB, in accordance with HHS regulations at 45 CFR 46.110(c), adopt a method for advising all members of research proposals which have been approved under an expedited review procedure. This can be accomplished in many ways, such as listing all research approved under an expedited review procedure in the agenda or minutes of each IRB meeting and distributing such agenda or minutes documents to all IRB members.

(3) HHS regulations at 45 CFR 46.102(i) define *minimal risk* to mean that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

HHS regulations at 45 CFR 46.303(d) set forth a separate definition of *minimal risk* for research involving prisoners: *minimal risk* means the probability and magnitude of physical harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons. We note that discussions in the Drew IRB meeting minutes of the risk level of proposed research activities on at least two occasions reference the definition of minimal risk at 45 CFR 46.303(d) although there is no other indication that subjects are to include prisoners. (See February 1, 2006 minutes, section IV(a)(4), discussing risk associated with IRB #06-01-928-01; March 1,

2006 minutes, section V(B)(4), discussing risk associated with IRB #06-02-933-01). We recommend that the Drew IRB use the definition of minimal risk at 45 CFR 46.102(i) in its deliberations of research where prisoners will not be enrolled, and note that HHS regulations at 45 CFR 46.304 require modification of IRB membership for review of research involving prisoners, in that at least one member of an IRB that reviews such research shall be a prisoner or a prisoner representative with appropriate background and experience to serve in that capacity.

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 continued commitment to the protection of human research subjects.

Sincerely,

Carol J. Weil
Division of Compliance Oversight

cc: Mr. Junko Nichitani, Director of the IRB, Charles R. Drew University of Medicine & Science
Dr. Kenneth Wolf, IRB Chairperson, Charles R. Drew University of Medicine & Science
Commissioner, FDA
Dr. Joanne Less, FDA