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Mary Simmerling, Ph.D.
Director, Responsible Conduct of Research
Weill Cornell Medical College
445 E. 69th Street
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New York, NY 10021

RE: Human Research Protections Under Federalwide Assurance (FWA) - 5656

Research Projects: **International Early Lung Cancer Action Program
Early Lung Cancer Detection Using Computed
Tomography (also known as I-ELCAP)**

Principal Investigators: **Drs. Claudia I. Henschke and David Yankelevitz**

Dear Dr. Simmerling:

Thank you for your July 5, 2011 letter in response to our May 6, 2011 electronic mailing in which we asked you to investigate indications of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR Part 46) involving the International Early Lung Cancer Action Program (I-ELCAP) study.

By way of background, OHRP had noted possible indications of noncompliance with HHS regulations for the protection of human research subjects involving the I-ELCAP study after becoming aware of two articles. One was from *The Cancer Letter*, Vol 37, No. 17, 2011, written by Paul Goldberg and entitled "Reviewers Find a Trial That Never Ends With 90% of Consent Forms Unobtainable." That entire issue of the journal was devoted to issues related to the I-ELCAP study. In addition, the *New York Times* published an article by Gardiner Harris entitled "Review Casts More Doubt on a Lung Cancer Study" (April 29, 2011). Based upon information contained in those articles, several issues relating to possible noncompliance with such regulations appeared to be raised:

1. The inability of Weill Cornell Medical College (Cornell) to provide documentation of written informed consent (for 90% of the subjects) as might be required by HHS regulations at 45 CFR 46.117(a).

2. The concern that informed consent may not have been obtained for subjects as required by HHS regulations at 45 CFR 46.116.
3. The failure of Cornell to report to our office unanticipated problems, noncompliance, suspensions and terminations associated with the I-ELCAP study in accordance with HHS regulations at 45 CFR 46.101(b)(5).

OHRP acknowledges Cornell's statement that

“Based on our review of federal awards, we do not believe I-ELCAP was federally supported human subjects research covered by 45 CFR Part 46, and we note that under the terms of WCMC's Federal-wide Assurance, non-federal research at WCMC was not subject to the 45 CFR Part 46 reporting requirements at relevant times during the I-ELCAP protocol.”

Following receipt of this information, we contacted the National Cancer Institute (NCI) to determine whether the I-ELCAP study was federally funded. A NCI representative confirmed that, while NCI did fund the Early Lung Cancer Action Program (ELCAP) study via two R01 grants (R01 CA063393 and R01 CA78905), NCI did not fund the I-ELCAP study.

Notwithstanding Cornell's conclusion that the I-ELCAP was not federally supported and was not covered by Cornell's FWA, we note that Cornell nevertheless investigated the above-referenced possible indications of noncompliance and provided information to our office about the study.

According to Cornell, the I-ELCAP study was approved by the Cornell IRB on August 31, 2001, as a study that involved the pooling of data from multiple institutions conducting their own IRB-approved lung cancer screening protocols. The Cornell IRB approved the I-ELCAP data-pooling protocol on the understanding that each institution that contributed data to the I-ELCAP study was required to obtain IRB approval of the lung cancer screening protocols and accompanying consent forms. Under the I-ELCAP protocol, the lung cancer screening protocol consent forms were to explicitly state that the subjects' data would be pooled as part of a larger I-ELCAP study. Consistent with the organization of the project, Cornell acknowledged that it did not maintain and was not required to maintain copies of the signed consent forms for each research participant who enrolled at each of the external institutions participating in the lung cancer screening project. According to Cornell, the signed consent documents from external institutions were to be maintained at the external institutions in accordance with the Cornell IRB-approved I-ELCAP data-pooling protocol, the external institutions' IRB-approved lung cancer screening protocols and HHS regulations at 45 CFR 46.115, 46.116 and 46.117.

Moreover, Cornell concluded, and we concur, that there were no unanticipated problems, noncompliance, suspensions or terminations associated with the I-ELCAP study and as a result there were no incidents to report to OHRP.

Given the facts as outlined above, we have determined that we do not have jurisdiction over the I-ELCAP study. We note that the I-ELCAP study was not a federally supported research project. We also note that during the time in question Cornell did not voluntarily extend its FWA to all research regardless of funding source. Lastly, even if we did have jurisdiction over the I-ELCAP study, we would have determined that the indications of noncompliance were unproven. For the reasons stated above, no evidence was presented to us indicating that Cornell was required to maintain documentation of written informed consent for subjects who enrolled into the I-ELCAP study as required by HHS regulations at 45 CFR 46.117(a). In addition, no evidence was provided to us suggesting that informed consent may not have been obtained for subjects as required by HHS regulations at 45 CFR 46.116. In fact, we were provided with a report which stated that the I-ELCAP principal investigator collected attestations from each I-ELCAP site investigator documenting that IRB approvals and documented informed consents were obtained in accordance with HHS regulations. Lastly, we found no evidence that unanticipated problems, noncompliance, IRB suspensions or terminations associated with the I-ELCAP study occurred.

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 institution's continued commitment to the protection of human research subjects.

Sincerely,

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

cc: Dr. Rosemary Kraemer, Director, Human Research Protections Program, Weill Cornell Medical College
Dr. David A. Behrman, IRB Chair, Weill Cornell Medical College
Dr. Margaret Hamburg, Commissioner, Food and Drug Administration (FDA)
Dr. Joanne Less, FDA
Dr. Sherry Mills, National Institutes of Health (NIH)
Mr. Joseph Ellis, NIH