



Office for Human Research Protections  
The Tower Building  
1101 Wootton Parkway, Suite 200  
Rockville, Maryland 20852  
Telephone: 240-453-8120  
FAX: 240-453-6909  
E-mail: [Lisa.Rooney@hhs.gov](mailto:Lisa.Rooney@hhs.gov)

August 15, 2012

Mary Simmerling, Ph.D.  
Director, Responsible Conduct of Research  
Weill Cornell Medical College  
445 E. 69<sup>th</sup> Street  
Olin 210  
New York, NY 10021

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

**Research Projects:**                      **Early Lung Cancer Detection Using Computed Tomography (also known as ELCAP)**

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

**HHS Protocol Numbers:**                **R01 CA063393  
R01 CA78905**

Dear Dr. Simmerling:

Thank you for your July 13, 2012 report in response to our April 5, 2012 letter that requested Weill Cornell Medical College (WCMC) to provide us with responses to the questions and concerns noted in the April 5, 2012 letter. Based on review of your response, we have made the following determinations regarding the above-referenced research:

1. A complainant alleged that the Early Lung Cancer Detection Using Computed Tomography (ELCAP) investigator continued to receive and analyze individually identifiable private information after WCMC IRB approval for this study expired on October 12, 2009 and until the investigator left WCMC in January 2010 in violation of Department of Health and Human Services regulations (HHS regulations) at 45 CFR 46.103(b) and 46.109(a), which require that an IRB review and approve all non-exempt human subject research covered by an assurance before the research can be conducted.

As part of WCMC's investigation, WCMC addressed this question to the ELCAP investigator and the ELCAP investigator responded that ELCAP investigators did not receive or analyze individually identifiable private information for research purposes after WCMC

IRB approval for the study expired on October 12, 2009 and until the ELCAP investigator left WCMC in January 2010. The ELCAP investigator also stated that no data or images from that time period (10/12/09 – 1/10) are stored in the ELCAP data system.

We also acknowledge that WCMC, as part of its investigation, conducted a

“review of its electronic medical records, specifically the Radiology Information System (RIS) and Picture Archival and Communication System (PACS), and found that 58 patients had CT [computed tomography] lung screening examinations performed at WCMC between October 12, 2009 and January 2010. For each of these 58 screening examinations, we reviewed the prescriptions from the referring physicians as well as the dictated clinical report of the scan. Although our records do not enable us to match these patients with subjects in ELCAP, it appears from notations in the orders from the treating physicians and clinical reports that at least some of these patients were enrolled in a research study, likely ELCAP. The notations do not indicate whether or not these particular scans were included in the ELCAP study. We also conducted a query of the audit trail for access to the electronic medical record and did not find any evidence that the clinical images and/or reports were transferred outside of the institution from the RIS or PACS.”

Moreover, WCMC explained that it did not find any evidence indicating that these 58 images/reports were transferred to ELCAP databases during this timeframe. In summary, WCMC’s investigation of this matter did not find any evidence that the ELCAP investigators continued to receive and analyze individually identifiable private information after WCMC IRB approved for the study expired on October 12, 2009 and until the investigator left WCMC in January 2010.

Based on the above, we have determined that this allegation of noncompliance could not be proven. No evidence was provided to us indicating that ELCAP investigators continued to receive and analyze individually identifiable private information after WCMC IRB approval for this study expired on October 12, 2009 and until the investigator left WCMC in January 2010.

2. We determine that (a) the two consent forms that were approved by the WCMC IRB in 1999 (IRB approved March 15, 1999 and July 19, 1999) did not include an alternatives section; and (b) the IRB-approved consent forms (IRB approved October 8, 2007) did not include a complete list of alternatives for lung cancer screening, as required by HHS regulations at 45 CFR 46.116(a)(4).

WCMC agreed that the WCMC IRB-approved 1999 consent forms for this study did not include a clear and complete alternatives section. According to the protocol and the consent documents, the subjects who enrolled in ELCAP could be generally categorized into three groups, based on what type of screening and diagnostic evaluations, if any, they would have

undergone had they not participated in the study. Given that various subjects were differently situated, describing alternatives for the study was complex. As a result, WCMC acknowledges that the consent forms failed to adequately explain the alternatives to participation in more detail for all of the variously situated subjects.

**Corrective Action:** WCMC informed us that the requirement to include alternatives to participation, including the option not to participate in a study and disclosing standard diagnostic procedures, is part of the current WCMC IRB Template Consent Form that WCMC investigators must use. According to WCMC, use of this form prompts researchers to consider all types of alternatives that should be included in the consent form. We determine that this corrective action adequately addresses our determination and is appropriate under the WCMC FWA.

3. As you are aware, HHS regulations at 45 CFR 46.103(b)(4)(iii) require that the IRB review and approve all proposed changes in a research activity, during the period for which IRB approval has already been given, prior to initiation of such changes, except when necessary to eliminate apparent immediate hazards to the subjects. We determine that the ELCAP investigator initiated a protocol change prior to obtaining IRB approval when the investigator enrolled at least one ineligible subject into the study, using a not yet approved informed consent form, before the WCMC IRB approved a change in eligibility. By way of background, the ELCAP investigator proposed to change the age entry criteria for the protocol from 60 years and older to 40 years and older. The ELCAP investigator requested this change on July 27, 1999. The ELCAP investigator enrolled one subject, who was under 60 years of age, into the ELCAP study on July 31, 1999. The WCMC IRB did not approve this change until August 5, 1999.

**Corrective Action:** We acknowledge WCMC's response that WCMC takes seriously its responsibility to ensure that the conduct of human subjects research is consistent with regulatory requirements. As such, WCMC educates researchers on the need to receive IRB approval prior to acting on any changes to an IRB-approved protocol and WCMC investigates protocol violations related to the conduct of research that is not consistent with the IRB-approved protocol and consent form. In addition, we note that WCMC IRB approval letters now include a clear statement that any changes to the IRB-approved protocol must be reviewed and approved by the IRB before changes can be implemented. Lastly, we understand that training for the WCMC research community includes specific training on this issue. We determine that these corrective actions adequately address our determination and are appropriate under the WCMC FWA.

We acknowledge that the remaining questions and concerns from our April 5, 2012 letter have been adequately addressed.

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In summary, we determine that the corrective actions adequately address the determinations noted above. As a result, 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. Claudia I. Henschke, Mount Sinai School of Medicine  
Dr. David Yankelevitz, Mount Sinai School of Medicine  
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