ONE HUNDRED TENTH CONGRESS

U.S. House of Representatives
Committee on Energy and Commerce
Washington, DC 20515–6115

JOHN D. DINGELL, MICHIGAN
CHAIRMAN

October 19, 2007

The Honorable Elias Zerhouni, M.D.
Director
National Institutes of Health
1 Center Drive, Room 126
Bethesda, MD 20892

The Honorable John E. Niederhuber, M.D.
Director
National Cancer Institute
National Institutes of Health
31 Center Drive, Room 11A48
Bethesda, MD 20892

Dear Drs. Zerhouni and Niederhuber:

We are writing to raise concerns about the potential for conflicts of interest that could damage the credibility of the National Cancer Institute's (NCI) National Lung Screening Trial (NLST). The NLST is established to determine whether lung cancer deaths can be reduced by detecting cancers early through use of low-dose helical computerized tomography (CT) scans as compared to conventional lung X-ray screening. We are concerned that neither the National Institutes of Health (NIH) nor the National Cancer Institute (NCI) has evaluated conflicts of interest involving the principal investigators or co-investigators of the NLST. This letter requests that you evaluate these potential conflicts and report to us on your findings.

The NLST is the largest randomized clinical study in the agency's history, with a projected budget of $225 million. The outcome of this 10-year, randomized case-control study could determine whether low-dose CT screening for lung cancer for at-risk individuals should become the standard of care in the United States. This study was spurred by observational trials that have shown lung cancer survival rates increased when cancers were detected at the earliest and most curable stages. Lung cancer is the single largest cause of cancer deaths in the United States, and lung cancer kills more people than the next four most prevalent causes of cancer death combined.

The Committee became aware of the potential for conflicts of interest in the NLST when it learned that the tobacco industry hired at least two of the principal NLST investigators as expert witnesses for their defense in certain liability cases. In one lawsuit, the tobacco industry was opposing a remedy to include early lung cancer detection using CT scans for an at-risk population of smokers and former smokers in Louisiana. The other lawsuit also sought early lung cancer screening for heavy smokers in New York. In both cases, the tobacco industry had clear economic interest in opposing early lung cancer screening.

The lead NLST investigator, who oversees 23 medical centers that are carrying out Federally-financed clinical trials, was compensated for her services as an expert witness in the matter of *Gloria Scott and Deania Jackson v. the American Tobacco Company, et al.* (District Court, Parish of Orleans, State of Louisiana, No. 96-8461). Among the credentials outlined by this witness in qualifying her as an expert was her role as "the national principal investigator" for the NLST, and her work at the University of California at Los Angeles (UCLA), the site of early lung cancer trials.

During a trial in New Orleans in June 2003, this investigator testified, "I was asked to review the medical monitoring plan for low-dose screening CT and to render an opinion, and I did so."

At the trial, she was asked:

Q. Doctor, do you believe that doctors who recommend the use of low-dose CT for the early detection of lung cancer are reckless?

A. At this time, yes.

She was also asked whether it would make sense to start screening smokers or former smokers in Louisiana because delaying this screening may fail to save lives that could otherwise be saved. She replied:

"And if you're wrong, you may kill a whole lot more than lung cancer will."

Inasmuch as there are no published scientific studies that low-dose spiral CT screening will lead to more deaths than lung cancer itself, the basis for her conclusion is also unclear.

According to an October 8, 2007, article in the Wall Street Journal, this investigator received $30,750 in expert witness fees from legal counsel for the tobacco industry, and she apparently used the money for "academic enrichment," such as business-related travel and entertainment expenses or subscriptions to journals, according to sources at UCLA. UCLA found no conflict of interest. The investigator contends she does not have a potential conflict of interest and disclosed this consulting to individuals within NCI; however, the NCI ethics office never undertook a formal review of her potential conflict of interest.

Another investigator who is employed at the Dartmouth-Hitchcock Medical Center, an NLST participating clinic, submitted a September 26, 2006, "Declaration and Expert Report" on behalf of Phillip Morris in *Caronia et al. v. Philip Morris USA Inc., CA-06-224*. In this Declaration, the investigator states that his qualifications include serving as a principal investigator and a member of the Executive Committee for the NLST. He concluded that implementation of an early lung cancer-screening program proposed by the plaintiffs in this lawsuit "may do more harm than good." We understand this investigator returned the $700

consulting fee to the counsel for Philip Morris and withdrew from the matter after a critical letter was sent by the Lung Cancer Alliance. Although this information was disclosed by the investigator, no conflict of interest was found by the Dartmouth Conflict of Interest Committee. Although the amount at issue is insignificant, his testimony goes to the heart of the research questions at issue in the NLST.

The tobacco industry has clear financial interest in the outcome of the NLST. If the NLST produces a negative or inconclusive result, the tobacco industry could use these findings to defend itself from litigation seeking low-dose CT screening of lung cancer as a remedy.

On February 3, 2005, the Department of Health and Human Services issued supplemental ethical standards for employees of the NIH and the Food and Drug Administration, which restrict financial holdings, outside activities and awards, and increased disclosure requirements. These ethical standards, however, apply only to Federal personnel and do not apply to extramural researchers. With respect to extramural investigators, NIH requires that institutions they fund have conflict of interest polices in place, and that those policies meet the requirements of NIH, pursuant to 42 CFR Part 50, Subpart F. Given this delegation of responsibility to the research institution, extramural investigators are not subject to an NIH conflict-of-interest review. Absent this knowledge, NCI is trusting non-Federal institutions, which by necessity depend in significant part on the overheads from these Federal grants, to police themselves.

The ethical standards required of NIH employees and its extramural researchers are strikingly different. With respect to extramural researchers, NIH relies upon each academic or medical institution to determine "whether a significant financial interest could directly and significantly affect the design, conduct, or reporting" of NIH-funded research. This contrasts with the intramural researchers for which the goal "is to assure...that public health decisions would be made without even the appearance of influence from extraneous financial interests."

Based on an NCI briefing to Committee staff, we understand that NCI has not assessed whether any NLST investigators have potential conflicts of interest, and are relying exclusively on the reviews performed by institutions that employ the investigators. Given the study's magnitude and the commitment of Federal resources, however, it seems prudent for NIH to ensure that the integrity of this study is not compromised. For that reason, the Committee respectfully requests that NCI secure and evaluate financial disclosures from each of the NLST site principal investigators and co-investigators using disclosure standards required for NIH Federal investigators. To the extent that the Data and Safety Monitoring Board members have not been subject to a careful review, we would urge that as well.

Such disclosure should include income received directly or indirectly (e.g., through university departments, such as Departmental Practice Accounts) during the course of their involvement in the NLST, from the following sources:

1. Employment or consulting, including the name of the employing entity, the purposes of the employment or consultancy, and the amounts received each year;

2. Research sponsors, including the name of the research sponsor, the funding source, the purpose of the research, and the amounts received each year;

3. Expert witness services, including a list of the name of the cases where the individual served as an expert witness (whether testifying or not), the entity which retained the individual (e.g., a law firm or a party to the litigation), the amount received, and a copy of expert reports, declarations, and verbatim testimony; and

4. Other activities that are in any way related to those who may have an interest in the outcome of the NLST (e.g., screening equipment manufacturers, insurance companies, pharmaceuticals, medical devices, advocacy groups, etc.).

After receiving this information, the Committee requests that NCI analyze these disclosures, and prepare a summary for the Committee on Energy and Commerce, identifies each individual who was queried, whether they responded to NCI's request, and identify the specific activities that would present the potential for conflict of interest or bias under NIH's current ethical standards governing Federal investigators. Such summary should also identify any actions taken by NIH and NCI to mitigate or eliminate potential conflicts or bias. The Committee requests a response to this inquiry within 45 days of receipt of this letter.

In addition, the Committee requests that you provide answers to the following questions:

1. Under its current regulations at 5 CFR 5501, would NIH require a Federal employee who is an investigator in an intramural clinical study or a member of a Data and Safety Monitoring Board to receive prior approval before earning income as an expert witness in private litigation related to the NIH study?

2. Does NIH believe the tobacco industry has a financial interest in the NLST? If so, should the tobacco industry be designated as a "substantially affected organization" with respect to the agency's standard of ethical conduct involving this lung cancer trial?

3. Under 5 CFR 2635 and 5 CFR 5501, would NIH specifically prohibit a Federal employee who is an investigator in the NLST or a member of the NLST Data and Safety Monitoring Board from testifying for compensation as an expert witness for the tobacco industry on research issues related to the NLST?

4. Notwithstanding the disparity in legal requirements applied to intramural and extramural research, why, as a matter of policy, should NIH apply a lesser ethical standard and a narrower financial disclosure requirement with respect to Federally-

funded extramural investigators than it applies to Federal employees who are investigators in clinical trials?

5. Did Dr. Sylvan Green resign as the chair of the Data Safety and Monitoring Board for the NLST on or about December 8, 2004? Did Dr. Green decline to sign the required financial disclosure form? Did he have a disqualifying conflict, and if so, what was this conflict?

6. Please provide a copy of the current NIH conflict of interest disclosure forms used by NIH pursuant to 5 CFR 5502.

The Committee requests a response to the 6 questions outlined above within 30 days of receipt of this letter.

If you have questions, please contact us or have your staff contact Richard Miller or Joanne Royce with the Committee on Energy and Commerce staff at (202) 226-2424.

Sincerely,

John D. Dingell
Chairman

Bart Stupak
Chairman
Subcommittee on Oversight and Investigations

cc: The Honorable Joe Barton, Ranking Member
Committee on Energy and Commerce

The Honorable Ed Whitfield, Ranking Member
Subcommittee on Oversight and Investigations