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ONE HUNDRED ELEVENTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE

2125 RAYBURN HOUSE OFFICE BUILDING

WASHINGTON, DC 20515-6115

MAJORITY (202) 225-2927
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MINORITY (202) 225-3641

energycommerce.house.gov

March 19, 2009

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Mr. Raynard R. Kington, M.D., Ph.D.
Acting Director
National Institutes of Health
1 Center Drive, Room 126
Bethesda, MD 20892

Dear Dr. Kington:

Under the stimulus bill, the American Recovery and Reinvestment Act of 2009, the National Institutes of Health (NIH) will be the recipient of over \$10 billion in new funding, of which \$7.4 billion is designated "to be used to support additional scientific research," including extramural grants. We question whether some of this new funding will be available for distribution to researchers before the issues concerning disclosure of financial interests and conflict of interest are addressed by the NIH.

Last summer, we Republican Committee leaders sent then-NIH Director Elias Zerhouni a letter requesting more information about a National Cancer Institute (NCI) trial called the National Lung Screening Trial (NLST). In particular, we were interested in how the NCI handled conflict-of-interest issues with respect to researchers in the trial. In addition, we wanted to know how the conflict-of-interest rules apply to researchers who receive funding from the NIH, either individually or through a research institution, and who also have a financial, patent or royalty interest in the technology that is the subject of NIH-funded research. Copies of our letter and your response are attached.

The response provided by the NCI is troubling. The NCI's letter confirms that oversight of extramural conflicts of interest is self-policed by the grantees, and the grantees have control and discretion over what is reported about financial interests to the NIH. The NCI's letter and recent events also raise doubts about the accuracy of relevant information to conflicts of interest. For example, NCI reported that one of the researchers in the NLST, Dr. Henschke, last received NIH/NCI funding in 2000. However, NIH's CRISP database shows Dr. Henschke received

funding in 2003. In addition, the Wall Street Journal last week reported that the Office of Inspector General of the Department of Health and Human Services is investigating whether a grantee university misled the NIH about an investigator's outside consulting work with a drug company.

It also seems that the NIH recognizes that oversight of extramural conflicts of interest needs to be strengthened. Recently, NIH began to review its regulations pertaining to researchers' financial conflicts of interest. In December 2008, you made public comments suggesting that it would be six months to one year before NIH would be prepared to act on new conflict-of-interest rules.

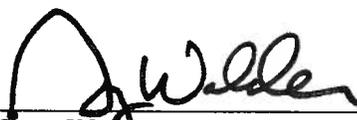
While the new funding may support research that will benefit the public health, we need to ensure that the integrity of that NIH-funded research is not compromised by potential conflicts of interest on the part of the researchers. For this reason, we respectfully request that you explain how NIH will address this situation. For example, will NIH accelerate the adoption of new conflict-of-interest rules so that the new rules will be in place when the stimulus grants are distributed? Will NIH delay the distribution of the stimulus funding to extramural researchers until it can finalize the new conflict-of-interest rules? We request that you provide this explanation in writing no later than two weeks from the date of this letter.

Thank you for your consideration of this request. Please do not hesitate to contact Alan Slobodin or Karen Christian of the Minority Committee Staff at (202) 225-3641 if you have any questions about this request.

Sincerely,



Joe Barton
Ranking Member
Committee on Energy and Commerce



Greg Walden
Ranking Member
Subcommittee on Oversight and Investigations

Attachments

HENRY A. WAXMAN, CALIFORNIA
EDWARD J. MARKEY, MASSACHUSETTS
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ONE HUNDRED TENTH CONGRESS

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

JOHN D. DINGELL, MICHIGAN
CHAIRMAN

June 6, 2008

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JOHN SHIMKUS, ILLINOIS
HEATHER WILSON, NEW MEXICO
JOHN B. SHADEGG, ARIZONA
CHARLES W. "CHIP" PICKERING, MISSISSIPPI
VITO FOSSELLA, NEW YORK
ROY BLUNT, MISSOURI
STEVE BUYER, INDIANA
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JOHN SULLIVAN, OKLAHOMA
TIM MURPHY, PENNSYLVANIA
MICHAEL C. BURGESS, TEXAS
MARSHA BLACKBURN, TENNESSEE

DENNIS B. FITZGIBBONS, CHIEF OF STAFF
GREGG A. ROTHSCILD, CHIEF COUNSEL

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

Dear Dr. Zerhouni:

The National Institutes of Health (NIH) has played a vital role in improving the public health of the United States for more than a century. Given the enactment of the National Institutes of Health Reform Act of 2006, we expect that NIH research efforts will provide the foundation for future scientific and medical advancement.

We note with concern that the National Cancer Institute (NCI) has been recently caught in the middle of a dispute between clinical researchers over whether former smokers and others at high risk for lung cancer should be screened using computed tomography (CT) scans. The NCI is attempting to help resolve this dispute by investing \$200 million in a huge clinical trial called the National Lung Screening Trial (NLST), the largest cancer screening test ever conducted, hopefully generating data in 2010 to evaluate such CT scans. Last fall the leader of an advocacy group that favors such CT imaging for lung-cancer screening, unhappy that the NIH has not yet endorsed CT imaging, accused two researchers involved with NLST of bias and conflicts of interest because these researchers agreed to testify for tobacco companies about how screening might do more harm than good. The Majority side of this Committee has decided to pursue these accusations.

Several months later, the Cancer Letter and the New York Times published articles exposing potential conflicts of interest on the other side of the debate. These articles reported that the two leading researchers (part of a project known as the International Early Lung Cancer Action Project (I-ELCAP)) who claim unprecedented success with CT screening for lung cancer have a financial stake in CT scanning technology used in their studies. Although these I-ELCAP researchers applied for 27 patents and have accepted royalty income from one license, they did not properly disclose these financial interests in medical journal articles, according to the Cancer Letter and the New York Times. In addition, these publications reported that most of the funds supporting the I-ELCAP researcher project came from a tobacco company gift of \$3.6 million made to a foundation headed by one of the researchers.

It is not our purpose to weigh in on one side or the other in this dispute. Rather, our interest is in protecting America's interest in getting the best scientific evaluation on early lung cancer screening. To that end, we believe that there is a public interest in safeguarding the American taxpayer's \$200 million investment in the NCI's National Lung Screening Trial, and in ensuring the integrity of NIH research. In light of those concerns, we respectfully request that the NIH provide the following information by June 16, 2008:

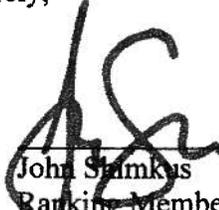
1. A status report on the NCI National Lung Screening Trial. Please include an explanation of NCI's expectation about the kind of data generated in 2010, and what kind of key results the NCI would be examining to reach any conclusions about the value of early lung cancer screening. Please identify any factors that could cause a delay in data being generated in 2010. Please also explain how the NCI has handled conflict-of-interest issues with respect to the researchers involved in the NLST.
2. Has the NCI audited the I-ELCAP data? If not, would the NCI be able to audit the data or be interested in auditing the data?
3. With respect to the I-ELCAP researchers, please explain whether the researchers individually or through their institution were receiving partial NIH support, and if so, whether they were required to disclose their financial stake in the CT scanning technology (including information on patents and royalties). If they were not receiving any NIH funds or they were not required to disclose, please explain under what circumstances a researcher receiving NIH funds would be required to disclose patent and/or royalty information. In addition, please explain whether and how NIH policy and/or regulations cover NIH-funded researchers who set up private foundations to receive donations that also support NIH-funded research projects. Finally, do NIH policy and/or regulations require disclosure to the human subjects of the researcher's financial interests in patents and/or royalties, or about private donations supporting the study? If so, please explain and detail what the nature of the disclosure involved. If not, why not?

Thank you for your consideration of this request. If you have any questions, please do not hesitate to contact Alan Slobodin and Karen Christian of the Minority Committee Staff at (202) 225-3641.

Sincerely,



Joe Barton
Ranking Member



John Shimkus
Ranking Member
Subcommittee on Oversight and Investigations

cc: The Honorable John D. Dingell, Chairman
The Honorable Bart Stupak, Chairman
Subcommittee on Oversight and Investigations



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20892

JUL 17 2008

The Honorable John Shimkus
House of Representatives
Washington, D.C. 20515

Dear Mr. Shimkus:

Thank you for your June 6, letter, addressed to Elias Zerhouni, M.D., Director of the National Institutes of Health (NIH), regarding protecting America's interest in getting the best scientific evaluation on early lung cancer screening and ensuring the integrity of research conducted at NIH. As the Director of the National Cancer Institute (NCI), I am responding on behalf of Dr. Zerhouni.

In your letter, you requested information on three major areas of concerns. The information that you requested included a status report on the NCI National Lung Screening Trial (NLST), auditing information regarding the International Early Lung Cancer Action Project (I-ELCAP) data, and information relating to I-ELCAP researchers and NIH funding. Our responses to your three concerns are provided in the enclosure.

Thank you for your support of cancer research and the NIH. I hope the information provided is helpful to you. Please feel free to contact me should you have any questions or require additional information. A similar response has also been sent to Representative Joe Barton.

Sincerely,

John E. Niederhuber, M.D.
Director
National Cancer Institute

Enclosure

1. Provide a brief status report on the NLST trial, including an explanation of NCI's expectation about the kind of data generated in 2010, and what kind of key results the NCI would be examining to reach any conclusions about the value of early lung cancer screening. Please identify any factors that could cause a delay in data being generated in 2010. Please also explain how the NCI has handled conflict-of-interest issues with respect to the researchers involved in the NLST.

The National Lung Screening Trial (NLST) is an NCI-sponsored prospective, randomized clinical trial designed to answer the question of whether deaths from lung cancer can be reduced through the use of helical CT screening. The study opened to accrual in September 2002 and had enrolled 53,464 participants by April of 2004. The study is designed to have a 90 percent statistical power to detect a 20 percent mortality difference between the CT and Chest x-ray (CXR) arms. This means that the NLST should be able to tell us with a 90 percent level of certainty that helical CT screening results in a 20 percent improvement in lung cancer mortality when compared to standard CXR. NLST participants receive three annual screens and mortality data will be collected through December 31, 2008. Screening is complete and all participating sites are in the process of data collection for follow-up and outcomes reporting.

It is anticipated that the first two papers resulting from the conduct of this trial will be an omnibus paper on the methodology of the trial and a report on the socio-demographics of the population under study. It is expected that these papers will be published prior to the completion of the follow-up for this trial. The primary paper, reporting on lung cancer incidence and lung cancer specific mortality in the two arms, is expected to be released once the data analyses for the trial is complete. Currently this is anticipated to be late in 2010 at the earliest. The specific timing of this paper will depend on reaching statistical significance. Because the trial was designed to achieve 90 percent power to see a 20 percent difference, it is unlikely that the Data Safety Monitoring Board will release the trial data until the 90 percent power has been achieved. It is difficult to know precisely how long this will take as it is dependent on the occurrence of lung cancer cases and deaths in the study population. Once the data has been released, NCI will look at key data from this trial to evaluate the value of early lung cancer screening.

NCI and NIH take concerns about potential conflicts of interest on the part of researchers participating in the NCI NLST very seriously. In December 2007, in response to concerns raised by the Committee Chairman, NCI sent written requests to all of the institutions that are participating in the NLST and asked for copies of the institution's conflict of interest policy and information relating to the disclosures of Significant Financial Interests held by NLST Investigators. All of the NLST sites responded to this request and NIH conducted an in-depth review and analysis of the financial conflict of interest policies submitted. NIH is in the process of following up with the institutions to clarify portions of their policies and will work with institutions to ensure that any identified policy deficiencies are corrected.

Respondents indicated that none of the Investigators involved with NLST had reported any Significant Financial Interests relevant to the NLST. In April 2008, NCI sent out a second, broader request to NLST institutions asking them for written confirmation that NLST investigators did not have (or ever have) funds or financial interests related to NLST. In response

to this broader request, the institutions reported that no Investigator had financial interests related to the NLST.

Q#2

Has NCI audited the I-ELCAP data? If not, would NCI be able to audit the data or be interested in auditing the data?

NCI is committed to ensuring that all clinical research is above reproach and would be supportive of efforts to reinforce the trust and credibility of these pursuits in the minds of the American public. NCI is not providing any funding for the I-ELCAP study. Due to the possible perceived conflict of interest on the part of NCI as a result of its current investment in the National Lung Screening Trial, the Institute believes that it would not be the best entity to participate in an audit of the I-ELCAP data. The Institute would be willing to assist in identifying experts in the field who may be able to conduct an audit and provide an objective report.

Q#3a (Please note: For clarity, we have separated your question into 3 separate questions.)

With respect to the I-ELCAP researchers, please explain whether the researcher individually or through their institution were receiving partial NIH support, and if so, whether they were required to disclose their financial stake in the CT scanning technology (including information on patents and royalties). If they were not receiving any NIH funds or they were not required to disclose, please explain under what circumstances a researcher receiving NIH funds would be required to disclose patent and/or royalty information.

Dr. Yankelevitz, one of the I-ELCAP researchers identified in the March 26, 2008, New York Times article, has received NIH support since 2000 to conduct research on the growth of pulmonary nodules as evidenced on CT scans.

When Dr. Yankelevitz applied for continuation funding in 2005, his application did contain a disclosure of invention. The patent title was: Computer Screening of Lung Cancer. Under the applicable conflict of interest regulations (42 CFR Part 50, Subpart F), income resulting from patents and royalty payments is a Significant Financial Interest when it is expected to exceed \$10,000 over the next twelve months, when aggregated for the Investigator and the Investigator's spouse and dependent children. Investigators must disclose to their Institution those Significant Financial Interests (1) that would reasonably appear to be affected by the research for which PHS funding is sought; and (2) in entities whose financial interests would reasonably appear to be affected by the research. However, the regulation specifically excludes royalties or other remuneration from the applicant Institution from the definition of Significant Financial Interest. Therefore, Investigators receiving such payments from their Institution are not required to disclose them. Under the regulations at 42 CFR Part 50, Subpart F, Dr. Yankelevitz would be expected to disclose to his institution the income resulting from any patents and/or royalties received from a source other than the applicant Institution, if it constituted a significant financial interest. NCI did not, at any point, receive reports from Dr. Yankelevitz's home

institution that a conflict of interest had been identified. The NIH is reviewing the issues raised in your letter and will follow-up with Dr. Yankelevitz's home institution, as necessary.

Dr. Claudia Henschke, the other investigator identified by the March 26th New York Times article, has not receive research support from NIH since before 2000.

Q. 3(b) In addition, please explain whether and how NIH policy and/or regulations cover NIH-funded researchers who set up private foundation to receive donations that also support NIH-funded research projects.

Whether and how the regulation at 42 CFR Part 50, Subpart F, and 45 CFR Part 94 would cover NIH-funded researchers who establish private foundations to receive donations would depend on the facts of the particular situation. As noted above, under the regulations, Investigators must disclose to their Institution those Significant Financial Interests (1) that would reasonably appear to be affected by the research for which PHS funding is sought; and (2) in entities whose financial interests would reasonably appear to be affected by the research. 42 CFR 50.604(c) and 45 CFR 94.4(c). If an Investigator receives a donation that constitutes a Significant Financial Interest under the applicable regulations, the Investigator would be expected to disclose the donation to his or her Institution, consistent with the requirements set forth in 42 CFR 50.604(c) and 45 CFR 94.4(c).

Q. 3(c) Finally, do NIH policy and/or regulations require disclosure to the human subjects of the researcher's financial interests in patents and/or royalties, or about private donations supporting the study? If so, please explain and detail what the nature of the disclosure involved. If not, why not?

Investigators engaged in NIH-funded research involving human subject participants are bound by Department of Health and Human Services (DHHS) regulations on the protection of human subjects found at 45 CFR Part 46. Although these regulations do not address investigator conflict of interest, DHHS issued guidance on "Financial Relationships and Interests in Research Involving Human Subjects"¹ on May 5, 2004. This guidance provides that investigators conducting research involving human subjects should consider whether information should be included in informed consent documents regarding a) the source of funding and funding arrangements for the conduct and review of the research, or b) information about a financial arrangement of an institution or an investigator and how it is being managed. In addition, if a potential or actual conflict does exist, investigators should consider using special measures to modify the informed consent process. Such measures could include involving an independent individual in the consent process, and/or independent monitoring of the research.

¹ <http://www.hhs.gov/ohrp/humansubjects/finreltn/fguid.pdf>



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20892

JUL 17 2008

The Honorable Joe Barton
House of Representatives
Washington, D.C. 20515

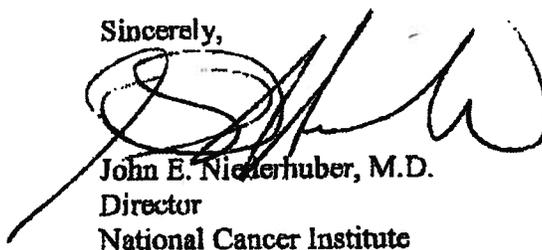
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Thank you for your support of cancer research and the NIH. I hope the information provided is helpful to you. Please feel free to contact me should you have any questions or require additional information. A similar response has also been sent to Representative John Shimkus.

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Director
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Whether and how the regulation at 42 CFR Part 50, Subpart F, and 45 CFR Part 94 would cover NIH-funded researchers who establish private foundations to receive donations would depend on the facts of the particular situation. As noted above, under the regulations, Investigators must disclose to their Institution those Significant Financial Interests (1) that would reasonably appear to be affected by the research for which PHS funding is sought; and (2) in entities whose financial interests would reasonably appear to be affected by the research. 42 CFR 50.604(c) and 45 CFR 94.4(c). If an Investigator receives a donation that constitutes a Significant Financial Interest under the applicable regulations, the Investigator would be expected to disclose the donation to his or her Institution, consistent with the requirements set forth in 42 CFR 50.604(c) and 45 CFR 94.4(c).

Q. 3(c) Finally, do NIH policy and/or regulations require disclosure to the human subjects of the researcher's financial interests in patents and/or royalties, or about private donations supporting the study? If so, please explain and detail what the nature of the disclosure involved. If not, why not?

Investigators engaged in NIH-funded research involving human subject participants are bound by Department of Health and Human Services (DHHS) regulations on the protection of human subjects found at 45 CFR Part 46. Although these regulations do not address investigator conflict of interest, DHHS issued guidance on "Financial Relationships and Interests in Research Involving Human Subjects"¹ on May 5, 2004. This guidance provides that investigators conducting research involving human subjects should consider whether information should be included in informed consent documents regarding a) the source of funding and funding arrangements for the conduct and review of the research, or b) information about a financial arrangement of an institution or an investigator and how it is being managed. In addition, if a potential or actual conflict does exist, investigators should consider using special measures to modify the informed consent process. Such measures could include involving an independent individual in the consent process, and/or independent monitoring of the research.

¹ <http://www.hhs.gov/ohrp/humansubjects/finreltn/fguid.pdf>