

New England Journal Sanctioned For Giving CME Credit For Controversial Paper On Lung Cancer Screening

By Paul Goldberg

The publisher of the New England Journal of Medicine has been sanctioned for dispensing continuing medical education credits stemming from a controversial paper by the International Early Lung Cancer Action Program, The Cancer Letter has learned.

The paper, published by NEJM on Oct. 26, 2006, claimed that the I-ELCAP regimen of computed tomography screening and follow-up in current and former smokers could make lung cancer into a curable disease.

However, the authors failed to disclose that they held patents covering the screening methodology embedded in the protocol, collected royalties from some of this technology, and received research funds from the parent company of Liggett Tobacco Group.

The Massachusetts Medical Society, which publishes NEJM, has been sanctioned for violating the guidelines of the Accreditation Council for Continuing Medical Education, which require disclosure and management of conflicts. ACCME's mission is to separate medical education from commercial interests.

MMS "failed to disclose accurate and complete information about certain relevant financial relationships causing conflict of interest in a continuing medical education activity presented as part of their ACCME accredited continuing medical education program," an ACCME official disclosed in a letter to The Cancer Letter.

"The MMS was found in non-compliance with the ACCME Standards for Commercial Support because the MMS procedures failed to identify, and therefore resolve and disclose, relevant financial conflicts of interest of the authors of an article on which a CME activity was based," wrote Steve Singer, ACCME director of education, monitoring and improvement.

"Per ACCME policy, MMS was required to submit Notice of Corrective Action through which the ACCME could determine that these issues had been brought into compliance," Singer wrote. "The MMS submitted, and the ACCME subsequently accepted, a Notice of Corrective Action in October 2008. In their Notice of Corrective Action, the MMS identified changes it made to its process for identifying and resolving conflicts of interest so as to ensure that the relevancy and completeness of disclosure information is adequately addressed in journal-based continuing medical education activities."

The ACCME letter to The Cancer Letter is posted at <http://www.cancerletter.com/publications/special-reports>.

The accreditation group initiated an investigation of MMS and NEJM after reviewing The Cancer Letter's detailed account of conflicts of interest on the part of the paper's lead authors, Claudia Henschke and David Yankelevitz, both of Weill Cornell Medical College (The Cancer Letter, March 14, 2008).

Since ACCME actions are confidential, errant CME providers are usually spared public embarrassment. However, in this case, ACCME decided to classify The Cancer Letter as a "complainant," and therefore was able to describe its findings in a letter to the publication. ACCME officials said they received permission from MMS "to release some information to The Cancer Letter as the complainant in the case." The Cancer Letter didn't seek to be classified as a complainant.

The sanctions against NEJM raise questions that may reach beyond the I-ELCAP controversy, since they may point to a systemic flaw in disclosure and management of conflicts of interest. Each journal has its own set of requirements for dealing with conflicts of interest, and often, editors are allowed to make judgments on relevance of conflicts.

However, another set of criteria has to come into play when a journal accredited by ACCME seeks to provide CME credit. This set of detailed, uniform criteria should have been applied to the I-ELCAP paper, ACCME states.

The I-ELCAP conflicts have affected the world's most prestigious medical journals.

The Journal of the American Medical Association, the Lancet, and NEJM published corrections, clarifications, and editorials as a result of the controversy. However, NEJM, the journal that gave I-ELCAP its highest-profile publication, systematically resisted correcting the record.

Meanwhile, CME credits dispense by the journal will stand. According to a corrective plan submitted by the journal to ACCME, physicians who earned them will not be given any notification beyond a brief correction that appeared in NEJM last April, following a barrage of international coverage of I-ELCAP's conflicts. The corrective plan, which was released to The Cancer Letter by ACCME, with permission from MMS, is posted at <http://www.cancerletter.com/publications/special-reports>.

NEJM's correction was surprisingly brief: "Drs. Henschke and Yankelevitz report receiving royalties from Cornell Research Foundation as inventors of methods to assess tumor growth and regression on imaging tests for which pending patents are held by Cornell Research Foundation and licensed to General Electric. No other potential conflict of interest relevant to this article was reported."

By way of comparison, the JAMA correction to a 2006 paper by Henschke and Yankelevitz, published in the April 16, 2008, issue of that journal, was 572 words long. It listed the authors' intellectual property, stock ownership, and consulting arrangements.

"It is not a trivial matter that one of the world's leading medical journals was sanctioned by the ACCME for the way it mishandled an egregious conflict of interest in one of its publications," said Sheldon Krinsky, professor of urban and environmental policy and planning at Tufts University and author of a book titled "Science in the Private Interest: Has the Lure of Profits Corrupted Biomedical Research?"

"It is sobering that after two years, the Massachusetts Medical Society changed some of its disclosure policies that most people familiar with 'Conflict of Interest for Dummies' would have picked up immediately," Krinsky said. "The physicians who received the CME credits were asked the wrong questions."

NEJM could use this embarrassing event as an opportunity to help doctors think deeply about corrosive impact of undisclosed conflicts, Krinsky suggested. "They should be notified about the failure of complete disclosure and asked two questions," he said.

Alternative questions would be:

—"Could the authors' attitudes reflected in the study about the scanning technology be affected by their financial interests in the technology?"

—"Can you think of any reason why the tobacco industry would be interested in supporting this technology for lung scanning?"

Physicians who may be recommending CT screening to their patients based on the NEJM paper require meaningful notification, said Merrill Goozner, director of the Integrity in Science Project at the Center for Science in the Public Interest.

"NEJM has never notified physicians who read that article for CME credit that its authors had significant conflicts of interest that were never disclosed," Goozner said. "If ACCME has accepted NEJM's corrective action without NEJM actually having corrected the situation, then both organizations are making a mockery of the rules. ACCME should order NEJM to print a full conflict of interest disclosure in the pages of the journal and notify every physician who read the article for credit by separate letter about that correction."

"Failing to do that should result in NEJM having its ACCME accreditation suspended into it comes into compliance," Goozner said.

Arthur Caplan, director of the University of Pennsylvania Center for Bioethics, said NEJM did a poor job of handling of the Henschke controversy. "The NEJM, as the premier medical publication in the world, must act as the ethical role model for biomedical publication," Caplan said. "The journal's preeminence comes with a duty to go the extra moral mile in terms of

handling disclosure issues including those linked to CME activities. While judgment is always involved in managing conflicts, the

CME requirements for disclosure concerning papers seem clear. What is not clear is why they have not been met.”

Never Apologize, Never Explain Attitude Backfired

A chronology of NEJM’s response to the I-ELCAP situation shows how the journal’s editors continued to stand by their original determination, disregarding questions and evidence repeatedly provided to its editors by The Cancer Letter and other publications:

—**Oct. 26, 2006:** NEJM published an I-ELCAP paper stating that I-ELCAP investigators had no conflict of interest relevant to the publication.

The disclosure line on the paper read: “No potential conflict of interest relevant to this article was reported.”

Doctors who answered three simple questions stemming from the paper were able to obtain CME credit through the Massachusetts Medical Society.

—**Oct. 8, 2007:** The Wall Street Journal quoted an acknowledgement by Henschke and Yankelevitz that they received royalties from General Electric, a manufacturer of CT scanners. Yankelevitz also acknowledged stock ownership and consulting agreements with PneumRx, a company that makes a biopsy needles used in lung cancer diagnosis.

Henschke told The Wall Street Journal that she informed the NEJM of the GE royalty agreement, “but that the journal decided not to disclose it.”

If this is correct, NEJM knew about the licensing agreement prior to the paper’s publication.

The article, which quoted a GE spokesman confirming that the companies is paying royalties to the Cornell researchers, is posted at <http://blogs.wsj.com/health/2007/10/08/tangled-web-of-conflicts-over-lung-cancer-screening/?mod=WSJBlog>.

—**Jan. 18, 2008:** The Cancer Letter reported that Henschke and Yankelevitz were listed as inventors on one issued U.S. patent and ten patent applications in the U.S. Altogether, I-ELCAP leaders were listed as inventors on 27 patents and applications worldwide.

All of these patent claims covered lung cancer screening technology and appeared to be embedded in the I-ELCAP screening protocol, which constituted the foundation of the NEJM paper.

The Cancer Letter’s questions to NEJM editors included a link to the Wall Street Journal story that cited Henschke’s and Yankelevitz’s admission that they were receiving royalties from GE.

NEJM and other journals launched investigations of Henschke’s and Yankelevitz’s conflicts.

—**Jan. 30, 2008:** NEJM editors completed their internal investigation and reported that they found no flaws in the disclosure.

In a statement sent to The Cancer Letter by an NEJM spokesman, the editors said that they were aware of the patents and deemed them irrelevant to the I-ELCAP paper. The journal’s statement e-mailed to The Cancer Letter read:

“The editors and authors followed standard editorial procedures on disclosure. The authors disclosed all potentially relevant information, including patents pending to the editors, and the editors reviewed this information in the light of the content of the article.

“Because it was not considered to be directly relevant to the point of the article, it was not published.”

Asked to elaborate on the journal’s criteria for determining relevance of conflicts, Karen Pedersen, a spokesman for NEJM, said that the editors “felt that the disclosures were not relevant to the outcomes of the paper, as the technology wasn’t being tested or required to be used.”

No correction would be warranted, the journal’s editors said.

—**March 14, 2008:** The Cancer Letter raised questions about NEJM’s compliance with the ACCME rules on disclosure and management of conflicts of interest.

The story demonstrated inconsistencies in disclosures Henschke made in her CME presentations.

The NEJM editors responded to several questions submitted by The Cancer Letter, but ignored the question on conflict of interest as it affected CME.

An NEJM spokesman said that the editors stood by the decision to provide CME credit for the paper “because the questions were about the paper, not the screening field.”

ACCME requires disclosure of any relationship with commercial interests that has produced a benefit “in any financial amount” over 12 months preceding the educational event.

“Intellectual property rights” are specifically included in the definition of financial relationships, and are construed to include patent applications.

ACCME started an investigation of the journal.

—**March 26, 2008:** The Cancer Letter and The New York Times jointly reported that Henschke had received \$3.6 million in research funding from the parent company of Liggett Tobacco Group, and placed the money into a non-profit foundation that funded her research. The NEJM paper acknowledged funding from the non-profit, but not the actual source of these funds.

—**April 2, 2008:** NEJM reversed its original position, publishing a correction, a clarification, and an editorial on the Henschke controversy.

However, these corrective actions failed to address the CME issues. Once again, an NEJM spokesman didn’t respond to The Cancer Letter’s questions about conflicts as defined by CME.

The correction published by the journal stated that the disclosure on the Oct. 26, 2006, paper should have read: “Drs. Henschke and Yankelevitz report receiving royalties from Cornell Research Foundation as inventors of methods to assess tumor growth and regression on imaging tests for which pending patents are held by Cornell Research Foundation and licensed to General Electric. No other potential conflict of interest relevant to this article was reported.”

The editors shouldn’t have been too surprised by the licensing agreement.

They should have learned about it from the WSJ blog story Oct. 8, 2007. (The article states that the medical journal didn’t respond to the reporter’s questions.)

Even if the editors missed that story, a link to it was placed before them several weeks later, as The Cancer Letter prepared its first story on conflicts of interest at I-ELCAP in January 2008.

Another reminder arrived in March, when The Cancer Letter asked NEJM to comment specifically on the CME issues. The questions presented to the journal included a table of business dealings that should have been disclosed and managed in the context of CME.

Elaborating on the correction at the time, NEJM spokesman Karen Pedersen said “the correction we issued today has nothing to do with disclosed or undisclosed patents.”

“We learned from the JAMA letter from Henschke on March 24 that there was a financial relationship that existed at the time of publication of our article, which was not disclosed to us,” Pedersen said in an e-mail. “The disclosure statement has now been corrected to include that information.”

Unlike NEJM, JAMA put together a lengthy correction, which was first published online, then expanded as knowledge of the researchers’ entanglements evolved. Also unlike NEJM, JAMA offered no CME credit in connection with its Henschke publication.

Along with the correction, NEJM published a clarification stemming from the revelation that Henschke and Yankelevitz had received Liggett money and placed it in a non-profit group that funded I-ELCAP’s work. An accompanying editorial established a policy on acceptance of support from tobacco companies. Since cigarette makers aren’t engaged in health care, tobacco ties aren’t relevant to CME.

—**Oct. 1, 2008:** MMS, the publisher of NEJM, submitted a Notice of Corrective Action to “bring our policies into full compliance with ACCME policies.”

Explaining their failure to identify conflicts, NEJM and MMS officials said that at the time of the paper's publication "it was not routine NEJM editorial policy to publish details about pending patents."

"Since that time, our thinking on this issue has evolved," the letter stated. Indeed, pending patents can be licensed, as was the case with the intellectual property that produced royalties from GE.

"As soon as information that clarified Dr. Henschke's relationship to the patent was provided to us, we sought clarification on the issue from the author," the letter read, apparently neglecting to note that the journal's initial investigation, as communicated to The Cancer Letter, revealed no impropriety.

At the time the allegations emerged, CME questions were no longer active, the document stated. "We also informed our learners about the updated conflict by publishing a correction that updated the disclosure," the letter reads.

Also, since the start of the controversy, NEJM updated its policy on conflicts of interest in CME. The proposed policy is under review by the MMS Committee on Medical Education.

The letter was signed by NEJM Editor Jeffrey Drazen, MMS Executive Vice President Corinne Broderick, and MMS Director for Continuing Education and Certification Caroline Carregal.

A copy of the document, which was released to The Cancer Letter by MMS in response to a reporter's questions.

"As you can see from this letter, we have demonstrated our willingness to improve and to remain transparent and compliant with ACCME requirements to the satisfaction of ACCME, which has accepted the MMS Notice of Corrective Action," MMS official Carreal said in an accompanying email. "Both parties now consider this issue to be resolved and the matter closed."

From Undisclosed Conflicts to Retracted Claims

The justification for disclosure and management of conflicts is founded in part on concern that the researchers' self-interest may color their conclusions.

Indeed, the I-ELCAP NEJM paper has been challenged both on failure to disclose conflicts and the soundness of science.

Less than two years after publishing the NEJM paper, Henschke had to withdraw some of her paper's central scientific claims.

In a letter published in the Aug. 21, 2008, issue of NEJM, Henschke described several protocol violations and retracted the crucial claim of the 2006 paper: that the patients who were found through CT to have early stage lung cancer had died.

"The correct number of patients who were untreated and had a diagnosis of stage I lung cancer is 3, not 8," Henschke acknowledged.

The original paper cited the deaths of the eight patients as proof that CT screening was diagnosing clinically relevant disease, and that patients who dismissed the diagnosis did so at their peril.

NEJM hasn't withdrawn the paper.

In a 2007 update of her study, published in *The Oncologist*, Henschke and Yankelevitz claimed that the number of patients who refused treatment had grown from eight to 13. Challenged by a critic, Peter Bach, a pulmonologist and health systems researcher at Memorial Sloan-Kettering Cancer Center, Henschke acknowledged that the five additional patients were similarly misclassified.

Unlike NEJM, *The Oncologist* withdrew CME credit on its Henschke-Yankelevitz paper immediately after learning about the conflicts, and the journal's editor, Bruce Chabner, clinical director of the Massachusetts General Hospital MGH Cancer Center, called for an audit of the I-ELCAP data.

The American Cancer Society, which funded some of Henschke's work, similarly called for an audit (The Cancer Letter, Sept. 18, 2008).

"I am very concerned about the I-ELCAP data and the I-ELCAP findings, and I can't justify using I-ELCAP at this time," ACS Medical Director Otis Brawley said at a meeting last fall. "I think we can only use the I-ELCAP data if there is an external audit to verify that data, and there is an independent reanalysis of that data."

ACS has asked NCI to co-sponsor the audit.

Eliminating vs. Managing Conflicts

Instead of seeking to manage conflicts of interest, CME should be seeking to eliminate them entirely, Goozner said.

This would mean that researchers who are tightly connected with industry or who are pushing their own inventions should be barred from offering CME activities.

"The physicians should never have been offered the ability to earn CME credit on the basis of patently commercially driven research. That paper was not continuing medical education. It was continuing medical advertising."

Caplan said that the journal editors are ill-equipped to manage conflicts.

"The controversy over the claims made in the Henschke *et al.* paper show just how far we are from having a functional, meaningful conflict of interest policy in biomedical publication," Caplan said. "Donors and funders at all major institutions have many pathways available for recycling funds as appears to have happened with Liggett and GE at Cornell.

"To presume that disclosure will suffice as the solution to conflict of interest is to ignore the complex realities of university and not-for-profit funding. Moreover, when journals and their owners have their own commercial interests that must be served then the management of conflict of interest becomes all the more difficult.

"Journal editors are increasingly finding themselves in an untenable ethical situation when it comes to the balancing act that trying to handle conflicts of interest in a highly competitive publishing environment among commercial sponsors of research, scientists and schools with extensive links to industry, government officials increasingly concerned to both stimulate economic return and demand accountability to the public interest for government support, publishers and owners of publications who are increasingly being pressured to perform with both eyes on the bottom line, and monetary flows derived from patents, royalties and equity that require a phalanx of lawyers to chart and administer," Caplan said.

"It is not at all obvious who can truly navigate this morass, but it is becoming increasingly clear that editors and their editorial boards cannot do so by themselves."

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