



Unrevealed:  
Non-Disclosure of Conflicts of Interest In Four Leading  
Medical and Scientific Journals

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## EXECUTIVE SUMMARY

The exponential growth of financial conflicts of interest in medical and other academic research represents a serious challenge to guardians of scientific integrity. Conflicts of interest can bias research in numerous ways – from the questions asked to the samples selected to the interpretation of data. Many leading journals have adopted policies requiring disclosure of conflicts of interest as their preferred method for managing such conflicts. Some journals, like the *Lancet*, bar conflicted authors from writing reviews or editorials. As the editors of the *Journal of the American Medical Association* said in 2001, “Full disclosure . . . serves to highlight the potential for bias, but cannot and does not eliminate the conflicts.”

However, a conflict-of-interest disclosure policy is only as good as its enforcement. Journals that publish research from authors with undisclosed conflicts of interest undermine the credibility of the journal and the broader scientific enterprise. Yet past studies have shown that academic journals’ compliance with conflict-of-interest disclosure policies is poor.

In light of recent revelations about failure by industry-funded scientists to disclose clinical-trial results and the undisclosed conflicts of interest among top scientists at the National Institutes of Health, the Center for Science in the Public Interest investigated the quality of conflict-of-interest disclosures at four leading academic journals: the *New England Journal of Medicine (NEJM)*, the *Journal of the American Medical Association (JAMA)*, *Environmental Health Perspectives (EHP)*, and *Toxicology and Applied Pharmacology (TAP)*. All four journals have detailed but narrowly defined conflict-of-interest disclosure policies.

CSPI investigated the lead and last authors who declared that they had no conflicts to disclose in 163 original articles that appeared in those four journals from December 2003 to February 2004. Using publicly available databases and the definitions of conflicts of interest contained in the journals’ policies, CSPI found 13 articles (8.0 percent) where relevant conflicts of interest were not reported to readers. In most cases, the authors failed to provide the relevant information to the journals.

The cases included:

- A University of Arkansas College of Medicine professor, Dr. John Shaughnessy, who filed for a patent on a monoclonal antibody to fight the effects of multiple myeloma less than three weeks after an article appeared in the *NEJM* outlining its potential efficacy. He is also a paid consultant for drug companies developing vaccines for the condition.

- A Procter and Gamble scientist, William Owens, who was only identified as an official of the Organization for Economic Co-operation and Development in an article in *EHP* that validated a toxicity test that would likely be used on P&G products.
- Two scientists at the U.S. Armed Forces Institute of Pathology, Frank D. Kolodgie and Renu Virmani, whose article in *NEJM* about the formation of plaque in coronary arteries did not disclose their consulting relationships with over 20 companies in the heart disease treatment field, including Medtronic, Guidant, Boston Scientific and Novartis.
- NIH senior scientist Daniel Levy, whose article in the Journal of the American Medical Association on “Predictors of New-Onset Kidney Disease in a Community-Based Population” did not disclose his consulting relationships during 2003 with Merck & Co., Bristol-Myers Squibb, GlaxoSmithKline, and Pfizer Inc., all of which sell products whose marketing could benefit from the insights gleaned from that study.

Given this surprisingly frequent failure to report conflicts of interest in leading academic journals (which have the most rigorous policies), journal editors must take steps to ensure that their policies are strong and are followed by contributing authors. To improve compliance:

- Authors of original articles, reviews and editorials that appear in academic journals should be required to disclose to journal editors all financial arrangements with private firms within the past three years, whether or not those arrangements are directly related to the subject of the article. Any patents that are still active should also be disclosed as well as patent applications and intentions to apply for patents.
- Journal editors should amend their disclosure policies to include all conflicts of interest that are in any way related to the articles submitted for publication. Standards that require “relevance” or “direct relevance” for a conflict to be disclosed provide a loophole for many researchers who do not wish their relationships with companies revealed.
- Journal editors should adopt strong sanctions for failure to disclose conflicts of interest, such as a three-year ban on publication within the pages of that journal when an undisclosed conflict of interest is brought to light. The threat of sanctions will improve compliance in this self-regulated field.

## BACKGROUND

The problem of conflicts of interest in scientific research has taken on new urgency in the past year. Major pharmaceutical firms came under attack from New York Attorney General Eliot Spitzer after failing to publish the results of industry-funded clinical trials that could affect the health and safety of American youths. The National Institutes of Health, the nation's flagship medical research enterprise, has become embroiled in a conflict-of-interest scandal after *The Los Angeles Times* revealed that many of its senior scientists had received hundreds of thousands of dollars from outside firms. Regulators with a political agenda have increasingly turned to the work of scientists with close ties to either the religious right or regulated industries to justify decisions that contradict the preponderance of scientific evidence in fields ranging from reproductive health to global warming.

For more than 20 years, the editors of peer-reviewed academic journals – the gatekeepers of new scientific information – have wrestled with the problem of how to manage conflicts of interest that can lead to bias in the conduct and publication of scientific research. The reasons for adopting strong policies for managing conflicts of interest are well documented. Numerous studies of medical research have shown that published studies sponsored by private companies with a stake in the studies' outcome tend to yield pro-industry conclusions. (A Center for Science in the Public Interest study in February 2004, "SSRI Use in Children: An Industry-Biased Record," documented this effect in the field of pediatric use of anti-depression medications.<sup>2</sup>) Other studies have shown that industry sponsorship often results in publication delays, data confidentiality and reduced cooperation between academic researchers.<sup>3</sup>

One way to manage conflicts of interest in published research has been to require disclosure of researchers' financial ties with private firms when their articles appear in journals. The idea behind disclosure is to provide readers – whether they are other scientists, members of the public, or regulators – with additional information that will help them evaluate the quality and validity of that research. "(Disclosure) serves to highlight the potential for bias, but cannot and does not eliminate the conflicts."<sup>4</sup>

In order for regulators to receive truly independent scientific information about the health effects and safety of products, procedures, and industrial inputs, the government needs to adopt new rules requiring that science submitted for regulatory purposes be conducted by independent agencies and scientists free from all relevant conflicts of interest.

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<sup>2</sup> See [http://cspinet.org/new/pdf/ssri\\_paper.pdf](http://cspinet.org/new/pdf/ssri_paper.pdf).

<sup>3</sup> Bekelman AB, Le Yan, Gross C, "Scope and Impact of Financial Conflicts of Interest in Biomedical Research, A Systematic Review," *Journal of the American Medical Association* 2003; 289:454-465.

<sup>4</sup> DeAngelis et al., "Reporting Financial Conflicts of Interest and Relationships Between Investigators and Research Sponsors," *Journal of the American Medical Association*, 2001; 286:89-91.

Still, disclosure of conflicts of interest when research appears in the scientific literature is a minimal first step and has emerged as a policy of choice for managing those conflicts. It dates from 1984, when Dr. Arnold Relman, editor of the *New England Journal of Medicine*, wrote an editorial suggesting that all medical journals require that authors submitting scientific manuscripts identify any relevant financial connections with industry.<sup>5</sup> It soon became *NEJM* policy and was copied by many other leading academic journals in various fields.

Within a few years, enforcement of the disclosure policy became a major issue. In 1990, the *NEJM* policy was strengthened to forbid authors of reviews or editorials from having financial ties with companies whose products figured prominently in the article. However, a newspaper investigation in late 1999 revealed widespread violations of the policy. Many review and editorial writers had undisclosed relationships with companies that made the products under discussion. A subsequent internal probe by the editors at *NEJM* revealed that nearly half of the drug reviews published over a three-year period had been written by researchers with undisclosed conflicts of interest. In the wake of the scandal, the ban was reaffirmed and a tighter policy for disclosing conflicts to editors was implemented.<sup>6</sup>

In 2001, the editors of 13 leading medical journals published a joint editorial decrying the impact that the commercialization of medical research was having on researcher behavior, especially in the conduct of clinical trials. They called for the adoption of a strengthened “Uniform Requirements for Manuscripts Submitted to Biomedical Journals” written by the International Committee of Medical Journal Editors. Those guidelines point out that:

The potential for conflict of interest can exist whether or not an individual believes that the relationship affects his or her scientific judgment. Financial relationships (such as employment, consultancies, stock ownership, honoraria, paid expert testimony) are the most easily identifiable conflicts of interest and the most likely to undermine the credibility of the journal, the authors, and of science itself...Editors should publish this information if they believe it will be important to readers in judging the manuscript.<sup>7</sup>

However, that appears to have been a highpoint in the movement toward greater conflict-of-interest disclosure. In recent years there has been retrenchment in the rules at least one major journal. In 2002 *NEJM* editor Jeffrey Drazen, citing the ubiquity of industry relationships by the leading thinkers in many medical fields, implemented a new rule that allowed reviewers or editorial writers to have industry ties as long as they did not have “any significant financial interest in a company (or its competitor) that makes a product

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<sup>5</sup> Relman A, “Dealing with Conflicts of Interest,” *New England Journal of Medicine*, 1984; 310:1182-83.

<sup>6</sup> Monmaney T, “Top Medical Journal Admits 19 Lapses of Ethics Policy,” *Los Angeles Times*, Feb. 24, 2000, pg. A1.

<sup>7</sup> Davidoff et al., “Sponsorship, authorship, and accountability,” *The Lancet*, 2001; 358:854-856.

discussed in the article.” He also said, “It is our intent to focus on the financial relationships that, in our judgment, could produce bias, or the perception of bias.” Drazen defined “significant” as receipt of \$10,000 or more from any individual company or major research support in the prior two years. The standard for original research articles remained the same: “We report all relevant financial relationships . . . that, in our judgment, are pertinent to the article.”<sup>8</sup>

The weakened rules at *NEJM* drew a backlash from the editors at *The Lancet*. Last January, they reaffirmed the need for rigorous conflict-of-interest disclosure policies among academic journals. In 2003, *The Lancet* stopped commissioning articles from anyone with “substantial financial interests” (defined as industry employees or those with stock ownership in companies that make the product or a competitor) and began turning down all reviews written by scientists with broadly defined conflicts of interest. “Academics have a choice,” the editors wrote, “to develop their entrepreneurial skills or to maintain a commitment to public-interest science – and we do not accept that the two options are mutually compatible.”<sup>9</sup>

One other factor must be considered before turning to the results and implications of this study. Enforcement of conflict-of-interest disclosure guidelines at scientific journals is largely voluntary. The journals develop short but comprehensive disclosure forms that researchers fill out and submit along with their manuscripts. Editors review those disclosures. The editors then determine if any of the disclosed conflicts of interest are “relevant” (or whatever standard the journal has adopted) to the article that is about to be published. Those that meet what are often ambiguous standards get published in a “disclosure statement” at the end of the article.

Over the years, researchers have pointed out the inadequacies in those arrangements. Editors have no readily accessible databases to check the quality of the conflict-of-interest disclosures provided by authors. Authors often have their own definitions of what constitutes a conflict of interest which must be disclosed. The editors of *JAMA* in 2001 cautioned authors that if they “are uncertain about what might constitute a potential financial conflict of interest, they should err on the side of full disclosure.”<sup>10</sup> Despite such warnings, a 2003 overview of financial conflicts of interest in biomedical research published in *JAMA* found that “overall compliance of academic institutions and peer-reviewed journals with these guidelines appears poor.”<sup>11</sup>

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<sup>8</sup> Drazen J, Curfman G; “Financial Associations of Authors,” *New England Journal of Medicine*, 2002; 346:1901-1902.

<sup>9</sup> James A et al., “The Lancet’s policy on conflicts of interest – 2004,” *The Lancet*, 2004; 363:2-3.

<sup>10</sup> Op. Cit. DeAngelis C et al.

<sup>11</sup> Op. cit. Bekelman

## THE STUDY

The Integrity in Science project at the Center for Science in the Public Interest evaluated compliance with conflict-of-interest disclosure policies at four leading academic journals: the *New England Journal of Medicine*, the *Journal of the American Medical Association*, *Environmental Health Perspectives*, and *Toxicology and Applied Pharmacology*. We only evaluated disclosures attached to original research articles, not reviews, editorials or letters. The articles were published from Dec. 1, 2003 to Feb. 29, 2004.

To determine if article authors had undisclosed conflicts of interest, we used publicly available information and databases. Because of the labor-intensive nature of such research, we looked only at first and last authors since they usually play the leading roles in studies. Needless to say, many researchers had undisclosed conflicts of interest if one broadly defines that term; i.e., they were employed by or consulted for industry, owned stock or stock options, received research support or honoraria from industry, held or applied for patents or had similar financial arrangements with any private firm, no matter how distant its relationship from the subject of the article. However, in classifying someone as having an undisclosed conflict of interest, we tried to adhere to the policy of the journal under evaluation, which usually had some qualifying statement such as “relevant,” “directly relevant,” or “pertinent” when considering whether a conflict of interest needed to be disclosed.

## THE RESULTS

We evaluated a total of 176 original articles in the four journals. Private firms funded 38 or 21.6 percent of the studies, ranging from 40.8 percent in *NEJM* to 5.4 percent in *EHP*. Editors printed conflict-of-interest disclosure statements in 38 or 21.6 percent of the studies.

However, industry funding and conflict-of-interest disclosures did not always overlap. In many cases, the disclosure statements accompanied industry-funded studies. But in some cases, the statements accompanied government-funded studies. Some industry-funded studies did not contain additional conflict-of-interest disclosures, in which case we investigated those authors. As a result, we evaluated the first and last authors in every study where there was no disclosure statement for either author, a total of 163 studies. When we uncovered a conflict of interest that was potentially disclosable under the journal’s guidelines, we communicated with the authors to find out if they communicated those potential conflicts to the journal editors. We also asked if there were circumstances that warranted their inclusion or exclusion from our list of undisclosed conflicts of interest. Most authors responded to those requests and in many cases, their responses led to adjustments in our data.

We found 13 articles (8.0 percent or one out of every 13 of the 163 studied) where an author did not disclose a conflict of interest that should have been disclosed, according to the journal disclosure policy. We found another 11 articles where there were undisclosed conflicts of interest if one used a somewhat looser definition of conflict “relatedness” to the subject of the article.

Nondisclosure of conflicts of interest was a problem at all four journals. However, it ranged from a high of 11.3 percent (6 of 53 articles) at *JAMA* to a low of 4.8 percent (2 of 42 articles) at *NEJM*. The undisclosed conflicts ran the gamut of financial arrangements, from consulting fees from companies that were immediately involved in the study subject to patents on technologies that may one day prove valuable because of information contained in the study.

What follows is a detailed accounting of the specific problems found at each journal.

### ***The New England Journal of Medicine***

The *NEJM* is generally recognized as the leading medical journal in the United States. The editors of the *NEJM* currently interpret their policy to mean that a conflict of interest must be “directly relevant to the manuscript” they publish if it is to be disclosed in the journal.<sup>12</sup> That appears to be narrower than the interpretation offered in the June 13, 2002 article, “Financial Associations of Authors,” which states *NEJM* reports “all relevant financial relationships . . . that, in our judgment, are pertinent to the article.”

Based on current *NEJM* practices, however, it is difficult to understand where the editors draw the line. In issues that appeared in recent months, there were instances of disclosed conflicts totally unrelated to the article (an article on six interventions for post-operative vomiting, for instance, listed one physician’s grants from six firms for research totally unrelated to antiemetics -- Vol. 350, No. 24:2449). Another article disclosed conflicts marginally related to the subject of the article (Vol. 350, No. 23:2373).

During the study period of December 2003 to February 2004, conflict-of-interest disclosure statements accompanied 26 of 49 original articles or 46.9 percent. Consistent with *NEJM*’s published policy, the most common pattern in the printed disclosures involved studies of drugs, devices or tests, whether funded by industry or government, where the authors of the study had some other financial arrangement with a company with a stake in the outcome of the study, either directly or as a competitor. In all 26 cases, the conflicts of interest involved at least the first or last authors.

There were inconsistencies in what was considered a conflict for interest in those disclosures. In some cases the disclosures did not include relationships with competitors. For instance, the Dec. 18, 2003, article, “The Long-Term Effect of Doxazosin, Finasteride, and Combination Therapy on the Clinical Progression of Benign Prostatic

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<sup>12</sup> Letter from Jeffrey M. Drazen, M.D., editor of *NEJM*, to Merrill Goozner, CSPI, May 27, 2004.



Hyperplasia,” funded by NIH, Merck and Pfizer, *NEJM* did not report Dr. Douglas Milam’s consultancy with Abbott Laboratories, which makes a competitive product (Flomax) for the prostate condition. In other cases, *NEJM* disclosed conflicts with companies not directly involved in the study. See, for instance, the Feb. 5, 2004, article “Effect of Changing the Priority for HLA Matching on the Rates and Outcomes of Kidney Transplantation in Minority Groups,” where a grant from Amgen was included in two of the disclosures. Amgen is not involved in transplantation, although it obviously has a huge stake in the treatment of kidney disease.

Given those inconsistencies, we have not included in our examples of non-disclosure studies where there were only partial disclosures. We only identified studies where no conflicts of interest for the first or last authors were disclosed, but one or more does, in fact, exist.

At least two papers, for purposes of our study, did not disclose conflicts of interest:

1. The Dec. 11, 2003, article, “Intraplaque Hemorrhage and Progression of Coronary Atheroma,” written by Frank D. Kolodgie et al., did not disclose any conflicts of interest. However, Dr. Renu Virmani and Frank D. Kolodgie of the Armed Forces Institute of Pathology in Washington, DC, have consulting relationships with many companies in the heart disease field, including Medtronic, Guidant and Boston Scientific and have received grant support from Novartis. Dr. Kolodgie, in an email communication with CSPI, confirmed relationships with over 20 companies in the field. He also said he did not disclose these relationships to *NEJM*, stating, “None of them had anything to do with the *NEJM* paper. Why give them free advertising?” We believe an article on the relationship of plaque and coronary heart disease written by researchers who routinely consult with stent and heart-drug manufacturers meets whatever “relatedness” standard *NEJM* has.
2. The Dec. 25, 2003, article, “The Role of the Wnt-Signaling Antagonist DKK1 in the Development of Osteolytic Lesions in Multiple Myeloma,” was co-authored by Dr. John Shaughnessy of the University of Arkansas College of Medicine. According to the previous day’s HealthDayNews, an Internet news service widely available to the public, Dr. Shaughnessy is working on a monoclonal antibody that would “soak up DKK1 like a sponge.” He is quoted as saying it will be in clinical trials within “a year or two.” Dr. Shaughnessy filed for a patent on this monoclonal antibody technology on Jan. 14, 2004, less than three weeks after the article appeared. Dr. Shaughnessy is also conducting clinical trials for Celgene Corp. and Immunex Corp. for myeloma vaccinations, clearly a related field. None of those relationships or the pending patent application was disclosed.

These studies constitute two of 42 studies where either the first or last author did not make adequate disclosure, or a 4.7 percent failure rate.

## *Environmental Health Perspectives*

*EHP* is the journal of the National Institute of Environmental Health Sciences, a division of the National Institutes of Health. Each month, *EHP* publishes about a dozen studies documenting environmental impacts on human health. It is a leading journal for scientists in fields ranging from children's health to environmental toxicology.

*EHP* has a conflict-of-interest disclosure policy that outlines a comprehensive list of "competing financial interests" that an author must disclose along with a published article. They include "grant support, employment whether recent, present or anticipated, travel, consultancies, advisory board positions, patent and royalty arrangements, stock shares and the like."

However, the *EHP* policy has two major limitations. It restricts disclosure to situations where an author "may gain or lose financially through publication." Also, the journal editors eschew any effort at enforcement, relying instead on the veracity of authors. *EHP* encourages its readers to scrutinize disclosure statements and offers to publish letters that address inaccuracies or deficiencies.

During the study period of December 2003 through February 2004, *EHP* published 37 major scientific studies. Only two of those studies were directly funded by industry. Only these two articles included conflict-of-interest disclosure statements for any author.

CSPI investigated 65 first and last authors involved in the 35 studies that did not disclose conflicts of interest. This investigation revealed at least three articles (8.6 percent) where either the first or last authors should have disclosed conflicts outlined in the disclosure policy. They included:

- The December 2003 study, "OECD Validation of the Hershberger Assay in Japan: Phase 2 Dose Response of Methyltestosterone, Vinclozolin, and p,p'-DDE" where a Procter and Gamble scientist, William Owens, was identified only as a representative of the Organization for Economic Co-operation and Development (OECD). The article validated an assay that may be used on P&G products.<sup>13</sup> There was no disclosure of that corporate affiliation in this article despite Owens' having disclosed his P&G employment in a previous *EHP* article.
- A second December 2003 study, "In Vitro Activation of Cord Blood mononuclear Cells and Cytokine Production in a Remote Coastal Population Exposed to Organochlorines and Methyl Mercury," in which a Quebec, Canada group led by Pierre Ayotte of CHUQ-Laval University Medical Center studied the effects of organochlorines and methyl mercury on a remote coastal population. Though there was no disclosure of a conflict of interest, the study was funded in part by the

Canadian Network of Toxicology Centers, which is funded in part by the Canadian Chemical Producers Association, an industry trade group. Several of Prof. Ayotte's previous studies were funded by the Canadian Chemical Producers Association and the Canadian Chlorine Coordinating Committee.

- The January 2004 study, "Identification of Sources of Lead in Children in a Primary Zinc-Lead Smelter Environment," where an Australian group of scientists at Macquarie University investigated the sources of lead in children near a zinc-lead smelter. The lead author, Brian L. Gulson, a professor in Macquarie's graduate school of the environment, did not disclose that he is a member of the advisory board of a consulting group that advised Pasminco, Ltd., the company that ran the smelter. In an email communication, he divulged that while he was unpaid for his role with the consulting firm, a co-author was the wife of the owner of that firm.

In each of those cases, the authors stood to gain financially from publication of the article, thus meeting the test of the *EHP* policy. Dr. Owens was directly employed by a company that might be affected by his findings. Dr. Ayotte had previously received research funding or compensation from industry trade groups directly affected by the subject matter of their articles. And a co-author of Dr. Gulson's study was the financial beneficiary of a consulting company that works for the mining firm that was the subject of the study.

While the articles themselves may not have been funded by those companies or industry trade groups, it is clear that results could affect the authors' funding from those sources in the future.

### ***Journal of the American Medical Association***

*JAMA*'s disclosure policy, enunciated in the July 4, 2001, edition, states that "editors have an obligation to present pertinent information related to the financial aspects of the articles they publish so readers can interpret the findings in light of this information." It embraces the Association of American Medical Colleges' definition of conflict of interest as "situations in which financial or other personal considerations may compromise, or have the appearance of compromising, an investigator's professional judgment in conducting or reporting research." It concludes that such conflicts "may be potential or actual, perceived or real, and harmful or insignificant."

To determine if conflicts that need reporting exist, *JAMA* requires authors offer editors "complete disclosure of all relevant financial relationships and potential financial conflicts of interest, regardless of amount or value" and cautions authors to err on the side of full disclosure. The standard for printing disclosures is "relevant financial interests."

Judging the effectiveness of *JAMA*'s policy hinged on the definition of the word "relevant." Based on a close reading of conflict-of-interest disclosure statements that

appeared in *JAMA* during the study period, it is difficult to determine how the editors are interpreting that word.

For the most part, detailed conflict-of-interest statements involved relationships between authors and companies that either made the product under study or competitive products. But that was not universal. For instance, in the Jan. 28, 2004, article, “Association Between Cholesterol Level and Mortality in Dialysis Patients,” co-author Dr. Josef Coresh disclosed his receipt of research grants from Baxter and Amgen. While both companies have extensive stakes in the treatment of kidney dialysis and end stage renal disease and their future prospects might be affected by the study’s outcome, neither currently sells statins or other drugs or devices that might affect cholesterol levels and thus be *immediately* impacted by the study.

Several other studies and disclosures fell into the same category. So based on those disclosed conflicts of interest, we interpreted *JAMA*’s standard as being whether the study might one day affect the commercial prospects of a company or patent with which the author has ties.

We surveyed the 57 original articles published in *JAMA* from December 2003 to February 2004. Those articles contained 13 conflict-of-interest statements (22.8 percent), with 12 of those conflicts involving either the first or last authors. In 53 papers neither the first nor last author disclosed any conflicts of interest. We found six cases (11.3 percent) where either the first or last author failed to disclose a relevant financial conflict of interest.

These six cases are:

1. The Dec. 17, 2003, study, “Efalizumab for Patients With Moderate to Severe Plaque Psoriasis,” which did not disclose that Dr. Alan Menter received funding from numerous companies that manufacture psoriasis drugs, including Genentech, the maker of Efalizumab. In an email communication with CSPI, Dr. Menter said he informed *JAMA* of that fact, but *JAMA* chose not to publish it.
2. The Jan. 28, 2004, study, “Prognostic Value of Placental Growth Factor in Patients With Acute Chest Pain,” where lead author Christopher Heeschen did not report that he holds a patent issued in 2004 for “a method of treating and preventing diseases and ailments involving tissue damage, such as in myocardial and cerebral infarctions.” Another patent issued in 2002 to Dr. Heeschen involved “induction of angiogenesis to treat coronary or peripheral arterial disease.” A study that provides “an independent biomarker of adverse outcomes in patients with acute coronary syndrome” may one day impact the value of Dr. Heeschen’s patents, and the patents should have been deemed relevant.

3. The Jan. 28, 2004, study, “Effect of Breast Augmentation on the Accuracy of Mammography and Cancer Characteristics,” discloses that one author serves as a consultant to the manufacturer of breast implants. But it does not disclose last-author Dr. Karla Kerlikowske’s patent issued in 2003 for a “Device and method for determining proportions of body materials,” which “could be useful as a marker to predict cancer risk.” Again, while the patent is not directly related to the study, if the patented technology for automating the measurement of breast density in mammograms finds use in mammography, its market potential could be impacted by the results of this study.
4. In the Feb. 4, 2004, article, “Antiphospholipid Antibodies and Subsequent Thrombo-occlusive Events in Patients With Ischemic Stroke,” author Dr. Steven Levine does not disclose that he was a consultant for La Jolla Pharmaceuticals, which is developing a treatment for antibody-mediated thrombosis such as recurrent stroke. In an email communication, Dr. Levine says he has not had contact with the company in almost two years, and was only reimbursed for collecting patient samples. We have included this case of failure to disclose the conflict because most policies suggest the time standard for reporting conflicts of interest is two years at a minimum. Moreover, the NIH grant credited with funding this study began in August 2002, suggesting that the consulting relationship existed when this study was being designed.
5. The Feb. 28, 2004, article, “Predictors of New-Onset Kidney Disease in a Community-Based Population,” is part of the long-running Framingham Heart Study. Dr. Daniel Levy, an employee of NIH, did not disclose that during 2003 he was a consultant for Merck & Co., Bristol-Myers Squibb, GlaxoSmithKline, and Pfizer Inc. In an email communication, he said that none of these consulting contracts involved kidney disease and that these relationships ended in 2003. But clearly he was consulting with those companies when the study was being designed and conducted. Several of those companies manufacture products that are useful in combating aspects of kidney disease and they could glean valuable marketing information from this particular aspect of the Framingham study. Thus Dr. Levy’s relationships with those companies should have been disclosed.
6. The Feb. 11, 2004, article, “A Founder Mutation of the MSH2 Gene and hereditary Nonpolyposis Colorectal Cancer in the United States,” does not disclose that last author Dr. Albert de la Chapelle owns a patent issued in 1999 for “tumor classification as indication of hereditary non-polyposis colorectal carcinoma.” This patent is directly related to the subject of the article and could provide financial rewards if genetically-based colon cancer treatments, which could be facilitated by this scientific discovery, come into widespread use.

In most cases, according to email communications with CSPI, the authors said they did not disclose the relevant information to *JAMA*. In at least one case, the author (Dr. Alan Menter) informed the journal of his conflict of interest but it did not appear in the article.

## ***Toxicology and Applied Pharmacology***

This journal, published by privately-owned Reed Elsevier plc, is a leading toxicology journal. Its conflict-of-interest disclosure policy describes conflicts as any situation “when an author or the author’s institution has a financial or other relationship with other people or organizations that may inappropriately influence the author’s actions.” It also says that all such relationships within the past three years that could be viewed as “presenting a potential conflict of interest” must be disclosed.

CSPI surveyed 33 articles or about half of the original articles that appeared in *TAP* from December 2003 to February 2004. Articles by authors from non-English speaking countries were eliminated from our research. Five of the 33 articles surveyed contained conflict-of-interest disclosure statements. However, at least one lead or last author in every article did not disclose any conflicts of interest, so we tested all 33 articles.

At least two articles (6.1 percent) met any interpretation of relationships that “may inappropriately influence the author’s actions.”

1. The Dec. 1, 2003, article, "Transcriptional and posttranscriptional role for p38 mitogen-activated protein kinase in upregulation of TNF-expression by deoxynivalenol (vomitoxin)," reported the authors had no conflicts of interest to disclose. On March 25, 2003, Dr. James J. Pestka, the last author, was awarded patent No. 6,537,762 (assigned to Michigan State University) for the “peptide mimotope to mycotoxin deoxynivalenol and uses thereof.”
2. The Dec. 15, 2003, article, "Lovastatin-induced cardiac toxicity involves both oncotic and apoptotic cell death with the apoptotic component blunted by both caspase-2 and caspase-3 inhibitors," reported no conflict-of-interest disclosures by the authors. However, author Simon W. Rabkin is listed as the inventor for U.S. Patent No. 6,348,567, issued Feb. 19, 2002, for a peptide to ameliorate apoptosis in, among other things, cardiovascular disease, which is directly related to the subject of the article (the effect of lovastatin on cardiovascular apoptosis and the identification of inhibitors for reducing cardiac apoptosis). That patent has been assigned to a private firm, CV Molecular Therapeutics, Inc.

Even with a narrow definition of conflict of interest, there was a significant level of non-compliance (6.1 percent) with *TAP*’s conflict-of-interest policy. We could not determine if the authors disclosed the relevant information to *TAP* or if they provided the information but the editors chose not to publish it.

## **CONCLUSION**

Disclosure of relevant conflicts of interest in academic journals is considered an important tool for managing such conflicts. However, we have discovered that several leading journals that have conflict-of-interest disclosure policies define a conflict of interest so narrowly that many conflicts are not disclosed to readers. A researcher can earn large sums from consulting deals, honoraria, patents and the like from private firms, but none of it is considered relevant unless it directly relates to the article being published—and even then many conflicts are not disclosed. For that and other reasons, many observers consider disclosure of conflicts to be a totally inadequate response to the growing problem of commercialization of scientific research.

Moreover, the value of disclosure as a tool for managing conflicts of interest is completely undermined if researchers fail to provide or journals fail to publish conflicts that meet their narrow definitions. This study suggests that even when using their narrow definitions of conflicts of interest, leading journals have a failure rate that would be unacceptable in any other scientific endeavor.

Based on responses or non-responses to email communications, we have identified three possible reasons for this high failure rate:

1. By narrowing the definition of conflicts of interest to direct relevance, journal editors have created a climate where researchers exclude from their financial disclosure forms filed with journal editors many arrangements that a disinterested observer would consider a conflict of interest. Obviously, journal editors cannot publish what they do not know about.
2. Some researchers simply do not wish to disclose their financial conflicts of interest, or, perhaps, have arranged the timing of events (such as a patent application) so that they can claim that there was not a conflict at the time of publication.
3. Editors have been made aware of potential conflicts of interest, but either by liberal interpretation of an ambiguous standard or gross oversight, those conflicts are not published.

To improve conflict-of-interest disclosure, journal editors should adopt the following policies:

- Authors of original articles, reviews and editorials that appear in academic journals should be required to disclose to journal editors all financial arrangements with private firms within the past three years, whether or not those arrangements are directly related to the subject of the article. Any patents that are still active should also be disclosed as well as patent applications and intentions to apply for patents.
- Journal editors should amend their disclosure policies to include all conflicts of interest that are in any way related to the articles submitted for publication. Standards

that call for “relevance” or “direct relevance” provide a giant loophole for many researchers who do not wish their relationships with a particular industry or set of companies revealed. The sad fact of academic life is that a researcher’s desire to maintain the additional income provided by industry ties is a powerful incentive that can skew research priorities, interpretation of data, and other science-related questions, even in studies that at first glance may not seem relevant to the companies that provide that outside income.

- Journal editors should adopt strong sanctions for failure to disclose conflicts of interest, such as a three-year ban on publication within the pages of that journal should an undisclosed conflict of interest be brought to light. The threat of sanctions could improve compliance in this unregulated field.