

# COMMENTARY

## **The Lancet's policy on conflicts of interest—2004**

Conflicts of interest (or competing interests as they are also called) are ubiquitous. Editors, authors, and reviewers of manuscripts in *The Lancet* all have conflicting interests that can lead to bias in what we publish. What we can do, though, is reduce the potential for bias by having systems for managing conflicts of interest in the journal. In January, 2003,<sup>1</sup> we described our systems for managing potential or actual conflicts of interest for editors, authors, and reviewers. There has been no change in our policy for managing the conflicts of editors or reviewers since January, 2003, so we do not discuss those here.

As a signatory journal to the Uniform requirements for manuscripts submitted to biomedical journals,<sup>2</sup> and following publication of a joint statement by members of the International Committee of Medical Journal Editors (ICMJE),<sup>3</sup> the principles for our management of conflicts of interest for original research largely follow ICMJE guidelines. For commissioned material, though, we have developed our own policy which extends the ICMJE recommendations.

For original research, from the beginning of 2002, we have included details of the role of the funding source and detailed conflict of interest statements for individual authors in print. From the beginning of 2003, also following ICMJE recommendations for original research, we have asked the corresponding author to confirm that he or she had full access to all the data in the study and had final responsibility for the decision to submit for publication. We have rejected one protocol submitted for online publication because it was stated that the sponsor maintained full control over the data. We have also rejected one submitted manuscript because the protocol (we ask for protocols to be submitted with all randomised controlled trials) stated that "publication of such data [generated in the trial] can only be by mutual agreement". This statement does not equate to the corresponding author having final responsibility for the decision to submit for publication. The extent of conflicts described by authors has contributed to our decision to reject original research in several instances—eg, in a phase I study in which safety was prematurely claimed, all authors were employees or consultants to the study sponsor, and one of the recommended reviewers was on the sponsor's advisory board. Two articles documenting a high prevalence of a disease have been rejected partly because the authors worked for or had consultancy agreements with companies that marketed treatments for the disease.

Commissioning for *The Lancet* and its specialty review journals throws up different challenges. We can choose whom we approach to review an area or comment on a study, and that choice allows us to develop guidelines that some will see as too exclusive. ICMJE guidelines on commissioning are vague in that they are limited to disclosure of conflicts of interest and editors using what is

disclosed to make decisions. Disclosure sets a minimum standard that is slowly spreading beyond medical journals. In October, 2003, the Nature Publishing Group announced that its journals would require authors of review papers to disclose financial ties to relevant products.<sup>4</sup> This change in policy came about after it became clear after publication that an author of a review of experimental treatments for depression in *Nature Neuroscience* held a patent, stock options, and received consultancy fees related to products or companies that were discussed in the review.

In our experience, disclosure of conflicts by authors either before the commission is agreed, or, worse, on submission of the commissioned paper, is not enough. Commissioned material, by its very nature, depends on selection of relevant references to build an argument. The whole point of commissioning a commentary, for example, is to elicit an opinion from a credible expert whose views will be valued and useful. Even with a detailed description of the methods used to select references cited in reviews, it is extremely difficult to judge whether the selection is sound or is subject to commercially driven bias. Evidence is accumulating that conflicts do change the conclusions. Reviews of passive smoking are less likely to conclude that environmental tobacco smoke is harmful if the authors have financial ties to tobacco manufacturers.<sup>5</sup> Studies funded by the pharmaceutical industry are less likely to find that third-generation oral contraceptive pills cause thrombosis than are studies funded by public money.<sup>6</sup> In a study that examined five reports of original research, 32 reviews, and 33 letters to the editor, authors who supported the use of calcium-channel blockers were more likely to have financial relations with the manufacturers than neutral or critical authors.<sup>7</sup> And a systematic review of studies looking at financial arrangements between authors and industry concluded that industry-sponsored research tends to draw pro-industry conclusions.<sup>8</sup>

Editors or reviewers may be uneasy or uncertain about actual or perceived bias. For example, we rejected a spontaneously submitted review in 2001 despite excellent reviewers' comments because one of the two authors was an employee of a relevant manufacturer. A clinical adviser who regularly attends our manuscript discussion meeting was concerned about how the review would be perceived by readers, and so were some editors, leading to the decision to reject. We do not expect readers to have to work out whether a review is biased, and would rather risk rejecting the occasional objectively balanced paper than ask readers to invest their time deciding for themselves.

How far should we go if disclosure is not enough? As *The New York Times* commented on Sept 30, 2003, "Full disclosure of financial ties is a powerful disinfectant, but when the conflicts loom too large, the journals should

simply shop around for a less conflicted author".<sup>9</sup> But defining the level of "acceptable" conflict is not easy. For a decade, *The New England Journal of Medicine (NEJM)* had a policy of excluding those with any financial conflict from writing reviews or editorials.<sup>10</sup> The policy proved impossible to adhere to in practice, leading to public explanations of why, for example, an editorial on drugs for obesity was commissioned from two paid consultants for companies that stood to gain from the sale of dexfenfluramine, an appetite suppressant,<sup>11</sup> and why 19 drug therapy reviews were published between 1997 and 1999 despite the authors receiving grants or consultancy fees from relevant companies.<sup>12</sup> In 2002, the *NEJM* revised its policy to exclude only authors with "significant" financial interests from writing reviews or editorials, stating that it was impossible to find experts without some conflicts.<sup>13</sup> By "significant", the *NEJM* means receipt of US\$10 000 annually per company to an author; holding of company stock, stock options, or patent positions; or major research support from relevant companies, all within 2 years before the publication date of a paper. Critics have pointed out that this policy would allow an author who received money from many companies to write for the *NEJM*, so long as each sum was less than US\$10 000.

Since the beginning of January, 2003, we have elected to avoid commissioning from those with substantial financial interests (defined as industry employees or those with stock ownership) in a company that makes a product or competitor to be discussed in the paper. At least the same standards (and there is a case for more rigorous criteria since the motivation for writing may be different) apply to spontaneously submitted reviews. We have rejected two spontaneously submitted reviews where authors stood to gain, albeit in the future, from commercialisation of their intellectual property. We have taken this stance because academics have a choice—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.

Now, in 2004, *The Lancet* and its specialty review journals—*The Lancet Oncology*, *The Lancet Infectious Diseases*, and *The Lancet Neurology*—take an even tougher stance. We avoid commissioning commentaries, rapid reviews, seminars, reviews, or series (or considering spontaneously submitted papers to these journal sections or their equivalents in the specialty review journals) from anyone who, within the past 3 years, and with a relevant company or competitor, has any stocks or shares, equity, a contract of employment, or a named position on a company board; holds (or is applying for) a relevant patent; or has received (or will do) a fee from any organisation other than *The Lancet* or its review journals to write, be named on, or to submit the paper. Financial conflicts of interest that are not exclusions to commissioning or considering spontaneously submitted items, but must be declared in the published paper, are: consultancies, honoraria, speakers' fees; research funding or funding for equipment or drugs; travel or accommodation payments; or expert testimony fees. We have not introduced a financial cut-off such as US\$10 000 because we do not accept that there is a universally agreed sum of money that if exceeded will result in bias.

We recognise, of course, that many authors will believe that they remain objective despite potential financial gain. We also recognise that there are many excellent review papers that do inform practice or research no matter what the authors' affiliations are. However, we have a responsibility to draw some lines to separate "acceptable"

from "unacceptable" financial conflicts of interest. We will judge how this policy works in practice, update it as necessary, and report any changes.

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- 1 James A, Horton R. *The Lancet's* policy on conflicts of interest. *Lancet* 2003; **361**: 8–9.
- 2 International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. November, 2001: <http://www.icmje.org> (accessed Dec 10, 2003).
- 3 Davidoff F, DeAngelis CD, Drazen JM, et al. Sponsorship, authorship, and accountability. *Lancet* 2001; **358**: 854–56.
- 4 Editorial. Financial disclosure for review authors. *Nat Neurosci* 2003; **6**: 997.
- 5 Barnes DE, Bero LA. Why review articles on the health effects of passive smoking reach different conclusions. *JAMA* 1998; **279**: 1566–70.
- 6 Vandenbroucke JP. Medical journals and the shaping of medical knowledge. *Lancet* 1998; **352**: 2001–06.
- 7 Stelfox HT, Chua G, O'Rourke K, Detsky AS. Conflict of interest in the debate over calcium-channel antagonists. *N Engl J Med* 1998; **338**: 101–06.
- 8 Bekelman JE, Li Y, Gross CP. Scope and impact of financial conflicts of interest in biomedical research. *JAMA* 2003; **289**: 454–65.
- 9 Editorial. *New York Times* Sept 30, 2003: 28.
- 10 Relman AS. New "information for authors"—and readers. *N Engl J Med* 1990; **323**: 56.
- 11 Angell M, Kassirer JP. Editorials and conflicts of interest. *N Engl J Med* 1996; **335**: 1055–56.
- 12 Angell M, Utiger RD, Wood AJJ. Disclosure of authors' conflicts of interest: a follow-up. *N Engl J Med* 2000; **342**: 586–87.
- 13 Drazen JM, Curfman GD. Financial associations of authors. *N Engl J Med* 2002; **346**: 1901–02.

## Drug combinations for malaria: time to ACT?

See pages 9 and 18

The scientist and popular writer Robert Desowitz calls malaria "the oldest emerging disease". Malaria is certainly old: the written records of the earliest human civilisations describe the distinct periodic fevers. From the vantage point of populations suffering under the burden of malaria, the thought that malaria might also be emerging or re-emerging is frightening but accurate. Despite its already enormous toll of human suffering, deaths due to malaria are increasing. A major factor contributing to the resurgence of malaria is drug resistance. For 50 years after its discovery, chloroquine was a cheap, safe, and effective oral drug for malaria in Africa. In many parts of Africa, chloroquine is no longer effective because of chloroquine-resistant parasites that are spreading rapidly throughout the remainder of the continent. Sulfadoxine-pyrimethamine is the most feasible and economical alternative, but its effectiveness declined precipitously after it was introduced as first-line therapy in several African countries over the past decade.

Ironically, the best new medicine for malaria is one of the oldest. Artemisinin (qinghaosu) is the antimalarial extract of *Artemisia annua* (sweet wormwood) that has been used for centuries in traditional Chinese medicine to cure fevers. First isolated in 1971 by Chinese chemists, artemisinin is a sesquiterpene lactone with a peroxide group, and is chemically unrelated to quinine or other existing antimalarial agents. Artemisinin and its derivatives, artemether and artesunate, can clear parasitaemia and reverse coma more rapidly than other drugs,<sup>1</sup> but parasite recrudescence is common after monotherapy unless treatment is extended to 7 days.<sup>2</sup>