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Conflicts of interest in the spotlight

In late 2003 the Los Angeles Times triggered a major scandal by publishing information on the conflicts of interest of several staff members of the National Institutes of Health (NIH). Together, these NIH staff members had received several million dollars of external funding since 1995 (1,2).

Following these revelations, the Center for Science in the Public Interest (CSPI), a US consumer organisation (a), examined the frequency with which conflicts of interest failed to be disclosed in biomedical research publications.

Undeclared conflicts of interest. CSPI surveyed four biomedical and scientific research journals with strict policies on conflicts of interest (b)(3). They focused on primary publications, and tried to identify possible conflicts of interest among the first and last authors, both in ad hoc databases and in various freely accessible information sources.

Among a total of 176 articles published between December 2003 and February 2004, no conflicts of interest were declared by the first or last author in 163 articles. Yet the CSPI researchers found a clear conflict of interest for authors of 13 of these articles (8%). If a less restricted definition of conflict of interest had been adopted, the authors of another 11 articles (7%) would have had to declare conflicts of interest.

Most cases involved financial links, ranging from payments made by companies directly concerned by the study's outcome, to patents held by an author for a technology that was evaluated in the study, or whose sales might be boosted by the study. CSPI published the names of the authors who did not disclose their conflicts of interest and described the nature of the links they uncovered (3).

CSPI did not examine editorials, comments or review articles, and research into financial links was based on publicly accessible data. It is therefore likely that the true frequency of undeclared conflicts of interest was far higher.

A freely accessible database. Since 2001, CSPI has maintained a database, available through its website, describing the financial relationships of many American scientists, learned societies, universities, etc., with industries in the health and food sectors (4). When available, the financial transactions are quantified every year, backed up by a list of information sources.

Thus, in September 2005, CSPI revealed that, in a meeting of the Endocrinologic and Metabolic Drugs Advisory Committee of the Food and Drug Administration (FDA), three of the nine committee members who were asked to judge the risk-benefit balance of an inhaled insulin product had financial links to Pfizer, the manufacturer (c)(5).

In January 2006, the Korean scientist Hwang Woo-Suk published falsified cloning data in *Science* and *Nature*, even though he held several patents relating to these results. This led CSPI to ask the two journals to adopt stricter rules and to refuse, for a 3-year period, manuscripts submitted by authors who have not declared their financial conflicts of interest (6).



La revue Prescrire Contribution to Consultation on Pharmacovigilance in the EU

The new legislation must be fully applied, and provisions for patient safety and public transparency must be improved

Despite the obvious difficulties inherent in detecting financial ties, the Center for Science in the Public Interest is focusing public attention on the issue of conflicts of interest in the United States.

A general search and information source for conflicts of interest would be welcome elsewhere.

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a- This association is mainly funded by subscriptions to its bulletin *Nutrition Action Healthletter*, and receives 5% to 10% of its income from various foundations (ref 7). Its objectives are to provide the public and decision-makers with useful and objective information; to conduct specific research on technological and scientific aspects of food, alcohol, health, the environment, etc.; and to represent citizens before the regulatory, judicial and legislative authorities (ref 8). Its website address is <http://www.cspinet.org>
 b- The journals concerned were the *New England Journal of Medicine*, *JAMA*, *Environmental Health Perspectives*, and *Toxicology and Applied Pharmacology* (ref 3).
 c- One of the members of this committee, who usually chaired it, participated (without voting) despite receiving yearly payments of \$5000 to \$10 000 from Pfizer (ref 5).

Selected references from Prescrire's literature search.

- 1- Hopkins Tanne J "National Institutes of Health criticised for not preventing conflicts of interest" *BMJ* 2004; **329**: 10.
- 2- Labrador D "Damage control. A crackdown to prevent conflicts of interest at the NIH" *Scientific American* 2004. Website <http://www.sciam.com> accessed 12 October 2005.
- 3- Goozner M "Unrevealed: non-disclosure of conflicts of interest in four leading medical and scientific journals" Center for Science in the Public Interest - Integrity in Science, Washington 2004: 16 pages.
- 4- Center for Science in the Public Interest "The Integrity in Science Database". Website <http://www.cspinet.org> accessed 12 October 2005.
- 5- Center for Science in the Public Interest "FDA lets scientists with drug company ties evaluate new insulin product". Website <http://www.cspinet.org> accessed 12 October 2005.
- 6- Center for Science in the Public Interest "CSPI Calls on Journals to Strengthen Disclosure of Conflicts" Website <http://www.cspinet.org> accessed 12 February 2006.
- 7- Center for Science in the Public Interest "Our funding. CSPI's funding sources", Website <http://www.cspinet.org> accessed 12 October 2005.
- 8- Center for Science in the Public Interest "Mission statement". Website <http://www.cspinet.org> accessed 12 October 2005.

- The new European legislation offers an opportunity to improve pharmacovigilance in the EU. But it must be rigorously applied, without delay, and improved where necessary.
- This position statement is part of Prescrire's contribution to the public consultation on pharmacovigilance in the European Union.
- If it is to serve patients' best interests, pharmacovigilance must receive adequate public funding; public access to drug safety data must be facilitated; and the current confusion between the roles of drug companies and regulatory agencies must be eliminated.
- To help healthcare professionals and patients to identify the most important and most recent warnings, the relevant sections of the SPCs should be highlighted.
- Real transparency means easier access to data and clear justification for decisions based on pharmacovigilance data. "Commercial secrecy" must no longer serve as a pretext to hinder public access to data on drug utilisation.
- The health authorities, including regulatory agencies, must act mainly as advocates for patients and public health, and stop putting drug companies' interests first.
- Additional restrictions are needed on drug companies' influence over pharmacovigilance guidelines and drug safety decisions, given their clear conflicts of interest.
- Pharmacovigilance must be publicly funded, and no longer paid for solely through the licensing fees that regulatory agencies charge drug companies for their services. Sufficient funds must be made available to gather and analyse adverse drug reactions reported by members of the public; to exert effective public control over drug safety information; to require companies to conduct postmarketing studies when they are granted conditional product approval on the understanding that such studies will be conducted; to conduct independent pharmacovigilance studies; and to evaluate the impact of drug safety decisions.
- For safety-related marketing decisions to be made independently, a European Pharmacovigilance Committee needs to be established and endowed with the same authority as the Committee for Human Medicinal Products.

On 15 March 2006, the European Commission launched a public consultation on the current functioning of pharmacovigilance in the European Union, as governed by the European Directive and Regulation on medicines for human use published in the Official Journal of the European Union on 30 April 2004 (1-3). As a preamble to this very welcome consultation, the European Commission issued a report on the current strengths and weaknesses of pharmacovigilance in Europe (4). Patients, healthcare professionals and pharmaceutical firms were invited to express their opinions and suggest improvements (3).

For its part, *Prescrire* noted that the new European regulatory framework has still not been adequately applied, and that, as it stands, the new framework cannot be expected to create a system that fulfils public health requirements, as defined by the Berlin Declaration on Pharmacovigilance issued by the International Society of Drug Bulletins (ISDB) in 2005 (5). This article presents ►►