

Translated from *Rev Prescrire* July-August 2005; 25 (263): 555-556

Do some French academic clinicians have interests in common with the pharmaceutical industry?

You recently published an article on the painful experience with Cox-2 inhibitors (*Prescrire International*, issue 74, page 236). I was surprised to see that, from the very first paragraph, you criticised certain French opinion leaders and directly quoted a sentence from a book written for patients by Professor Dougados.

You did not directly attack these opinion leaders or Professor Dougados, but this criticism is implied, as the sentence in question immediately follows another sentence criticising advertising campaigns for anti-inflammatory drugs.

The relevant paragraph begins as follows: "The French advertising campaigns for anti-inflammatory drugs [...] were among the biggest so far this decade. Many French opinion leaders had no hesitation whatsoever in declaring [...]. This implies that these opinion leaders, including Professor Dougados, supported the promotional campaigns.

This is unfair and unacceptable. You make insinuations instead of launching a head-on attack. Nevertheless, the underlying message is clear.

This followed a press campaign during which, in an article recently published in *Le Monde*, the Director of 'la Revue Prescrire' directly accused professors of medicine of having interests in common with the pharmaceutical industry. I am extremely shocked by these insinuations, and by the way in which you imply that some academic clinicians can be "bought" by the pharmaceutical industry. These accusations challenge our scientific and medical integrity.

This also suggests that we used our moral authority to influence not only physicians but also patients.

Upon our return from the conference of the American College of Rheumatology, we were informed of the real medical reasons for the withdrawal of rofecoxib, both by the co-ordinating scientists (APPROVe study) and by FDA representatives. Your readers would surely be more interested in knowing the real methodological reasons that led to this type of scientific error, rather than this "advertising campaign" of gutter-press gossip (not entirely separate from financial considerations). I am enclosing some recent papers, which are scientific and "non commercial", which show that your message does not necessarily take into account all available scientific information (one can also lie by omission...).

Bernard Duquesnoy
Rheumatologist
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Do French academic clinicians have interests in common with pharmaceutical companies? Do the references provided by Bernard Duquesnoy (1-4) indeed prove that *Prescrire* "lies by omission"?

Clear common interests. The conflicts of interest statements by members of various committees and task forces of the French regulatory agency take up an entire 141-page "annex" in the Agency's 2003 yearly report (5).

Does Professor Dougados have financial links to pharmaceutical firms? There is no doubt that he has. The book to which Bernard Duquesnoy refers was co-published by Pfizer, the company that markets celecoxib (6). A rapid Medline search via PubMed shows that several papers co-authored by Professor Dougados involve work funded by a variety of pharmaceutical companies, such as Pharmacia (now part of Pfizer), Boehringer, Negma, and MSD-Chibret (7-10). One of these publications, suggesting that the risk of cardiovascular thromboembolism in patients taking rofecoxib is similar to that of the general population, explicitly states that Dr. Bannwarth, Dr. Ravaud and Dr. Dougados received research support, grants, honoraria and/or consultancy fees from MSD-Chibret France (the company that marketed rofecoxib) (10).

Different experts, different opinions. Do the opinions of experts who have worked for the pharmaceutical industry differ from those of other experts? The answer is a resounding "yes", as was recently shown by a New York Times survey of voting patterns on FDA expert committees that discussed the Cox-2 inhibitors in February 2005: the 10 members who had recently worked for the companies concerned voted in favour of keeping rofecoxib and valdecoxib on the market. Without these votes the results would have been against keeping them on the market (11).

Scientific and "non commercial" articles missed by Prescrire's literature search? Bernard Duquesnoy sent us four articles. We needed to go no further than the first page of the first article to note that one of the authors is a Pharmacia employee (1). Three of the authors of the second article (including the first author) received funding from Pfizer (2). The third and fourth papers

suggest that, rofecoxib has greater cardiac risks than classical NSAIDs, but celecoxib does not. The results of the fourth paper were described in issue 256 of *la revue Prescrire* (based on a more detailed study report than the one sent by Bernard Duquesnoy) (3,4,12).

Does Prescrire withhold information? We explained the "real medical reasons" for the premature termination of the APPROVe trial and the market withdrawal of rofecoxib to our subscribers in early 2005, as soon as possible after detailed publication of the data by the Food and Drug Administration and the *New England Journal of Medicine* (11).

Bernard Duquesnoy's mail fails to mention these reasons. Does *Prescrire* lie by omission? This is a serious accusation, but one that is easy to refute. The *Prescrire* staff sifts through available information and evaluates its quality in order to spare subscribers and patients confusion and unjustified therapeutic choices based on useless, biased and weak data. We use totally transparent procedures, provide precise references to support all claims made in our review articles, and make the references available to our subscribers for 5 years. We publish corrections of any mistakes pointed out to us that slip through our quality control procedure.

We prefer to let our readers judge for themselves, by comparing our analyses with those of other publications or "opinion leaders".

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- 1- White WB et al. "Comparison of thromboembolic events in patients treated with celecoxib, a cyclooxygenase-2 specific inhibitor, versus ibuprofen or diclofenac" *Am J Cardiol* 2002; **89**: 425-430.
- 2- Solomon DH et al. "Relationship between selective cyclooxygenase-2 inhibitors and acute myocardial infarction in older adults" *Circulation* 2004; **109**: 2068-2073.
- 3- Mamdani M et al. "Cyclo-oxygenase-2 inhibitors versus non-selective non-steroidal anti-inflammatory drugs and congestive heart failure outcomes in elderly patients: a population-based cohort study" *Lancet* 2004; **363**: 1751-1756.
- 4- Graham DJ et al. "Risk of acute myocardial infarction and sudden cardiac death with use of Cox-2 selective and non-selective NSAIDs": 6 pages.
- 5- Agence française de sécurité sanitaire des produits de santé "Les déclarations d'intérêts des membres des conseils, commissions et groupes de travail 2003". Website <http://afssaps.sante.fr>
- 6- Dougados M et al. "Arthrose en 100 questions" Assistance Publique des Hôpitaux de Paris, in partnership with Searle Pfizer, 2000: 64 pages.
- 7- Leirisalo-Repo M et al. "Combination therapy in early rheumatoid arthritis: a randomised, controlled, double blind 52-week clinical trial of sulphasalazine and methotrexate compared with the single components" *Ann Rheum Dis* 1999; **58**: 220-225.

8- Maillefert JF et al. "Relevant change in radiological progression in patients with hip osteoarthritis. 1. Determination using predictive validity for total hip arthroplasty" *Rheumatology* 2002; **41**: 142-147.
9- Calin A et al. "Defining disease activity in ankylosing spondylitis: is a combination of variables (Bath ankylosing spondylitis disease activity index) an appropriate instrument?" *Rheumatology* 1999; **38**: 878-882.

10- Bannwarth B et al. "Cardiovascular thrombotic events and COX-2 inhibitors: results in patients with osteoarthritis receiving rofecoxib" *J Rheumatol* 2003; **30** (2): 421-422.
11- Prescrire Rédaction "Coxibs, suite: demi-mesures et maintien sur le marché" *Rev Prescrire* 2005; **25** (260): 281.
12- Prescrire Rédaction "Rofécoxib: arrêt de commercialisation (suite)" *Rev Prescrire*; **24** (256): 835.

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Internet addresses: just how reliable are they?

As a medical student, I studied the recent growth in the number of internet addresses used as references for biomedical publications (a). I wondered just how reliable these references were in comparison to traditional 'paper' references, and decided to verify how many of these addresses were 'operational' at the time of publication and how long they remained so.

Methods. In order to evaluate the quality and lifespan of internet addresses published in the reference sections of articles published in biomedical journals, I systematically checked whether those listed as references in the January 2002, January 2003, January 2004 and March 2004 issues of two English-language journals (*The Lancet* and the *Canadian Family Physician*) remained functional in April 2004. I also checked those listed in the January 2002, January 2003, January 2004 and June 2004 issues of *la revue Prescrire*.

First, I assembled the internet addresses listed in each issue (4 to 5 issues per month for *The Lancet*, and one issue per month for the *Canadian Family Physician* and *la revue Prescrire*), and tested each one using an internet connection. I classified the results as follows: -successful, if I immediately obtained the relevant document;
 -semi-successful, if I found the document, but with difficulty;
 -semi-failure, if I obtained a different document from the one mentioned in the reference;
 -complete failure, if I obtained an error message.

I limited the search time for each reference to 5 minutes; if I did not find the document within this time period, I considered the search to be a failure.

Results. I compared the results for the three journals and for the different time periods, with the last period corresponding to the immediate validity of the references.

The Lancet: (2000 electronic references per month on average): in January 2002 the success rate was relatively low (44%), but it increased over the years to 75% in January and March 2004. The average monthly rate of complete failure was 18%.

Canadian Family Physician: (about 200 electronic references per month): here too the success rate increased over the years, from 65% in January 2002 to 80% in March 2004. The rate of complete failure was 14% on average.

La revue Prescrire: (the number of electronic references fluctuated from between 160 to 460 per issue). The average success rate was 65%, except for January 2003 (semi-failure rate 56%). The complete failure rate was 4% on average.

Discussion. Regardless of the journal, the average success rate never exceeded 75% for any time period. The immediate validity tests done in March and June 2004 included failures and semi-failures for some references at the time of publication.

In comparison to the other two journals, the electronic addresses given in *la revue Prescrire* were often incomplete, leading only to the home page rather than directly to the document concerned, making it necessary for the reader to complete the search. This may explain the lower failure rate I obtained for *la revue Prescrire*, as the other two journals usually gave addresses leading directly to the document in question.

These results suggest that biomedical journal editors should pay more attention to the reliability and accuracy of electronic references, so that they offer the same guarantees as traditional paper references.

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a- See: Prescrire Rédaction: "Glossaire de la recherche de documents électroniques dans le domaine de la santé" *Rev Prescrire* 2003; **23** (245 suppl. Se documenter): 899-900.

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