

Bias, conflict of interest and publishing

Concern continues to be expressed about the objectivity of physicians and biomedical researchers owing to the involvement of the pharmaceutical industry in promoting and marketing its products, as discussed in an article by Marcia Angell, a previous Editor of the *New England Journal of Medicine* (Angell, M. *The New York Review of Books*, volume 56, number 1, January 15 [2009]). That the pharmaceutical industry spends huge sums of money to develop and market products is unquestionable. That pharmaceutical companies design pivotal trials, perform the data analysis and greatly influence the publication of the results is also clear. Finally, the likelihood that some physicians have personally profited from their relationship with pharmaceutical companies, and might have hidden their financial conflicts of interest, also seems to be quite likely.

The claim made by Angell that “the pharmaceutical industry has gained enormous control over how doctors evaluate and use its products”, however, does not seem to be evidence-based. For example, at the latest Annual Scientific Meeting of the American College of Rheumatology and Association of Rheumatology Health Professionals, two trials that were supported by the pharmaceutical industry but presented by American College of Rheumatology members (Sundy, J. S. *et al.* [2008] *Arthritis Rheum.* 56 [Suppl.], S400; Weinblatt, M. *et al.* [2008] *Arthritis Rheum.* 56 [Suppl.], S610) emphasized the adverse events of the products being studied, resulting in precipitous and drastic drops in the share prices of the companies involved. Certainly, in these two examples, the supposed control exerted by the companies on the clinical researchers was not sufficient to stop them from reporting the data as they saw fit, despite the detrimental effect on the companies involved. Another example is the development of anakinra, the IL-1 receptor antagonist, which was approved by the FDA for the treatment of rheumatoid arthritis because of its excellent biologic rationale and sufficiently positive clinical data; however, the clinical experience of rheumatologists suggested that the benefit:risk ratio was too low to achieve widespread acceptance of this agent. Thus, despite intensive marketing efforts by the company involved, the agent is rarely used for treating rheumatoid arthritis today. In rheumatology, therefore, it is not clear that the efforts of the pharmaceutical companies have achieved “enormous control” of how physicians evaluate and use their products.

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This in no way obviates the problem of the pharmaceutical companies’ involvement in every step of drug development and marketing, nor the willingness of some rheumatologists to avail themselves of the pharmaceutical companies’ largesse. The extent to which the pharmaceutical companies have actually exerted widespread influence on the objectivity of rheumatologists is, however, not clear, and it is important to document this before the entire profession is condemned as corrupt. The problems of conflict of interest and personal enrichment from the pharmaceutical industry, and their possible impact on

clinical research and patient care, are extremely important, and must be dealt with in a fair and comprehensive manner. It is vital that this does not interfere with the timely development of new products for rheumatic diseases, some of which have not had new therapies approved for many years. The contention of Angell that “It is simply no longer possible to believe much of the clinical research that is published or to rely on the judgment of trusted physicians or authoritative medical guidelines”, however, is just not supported by the evidence in the field of rheumatology.

When looking for whom to blame, there are many players: the pharmaceutical companies themselves (although dismissed by Angell as merely doing their primary job of furthering the interests of their investors), and members of the medical profession. Angell focuses on the medical profession, and suggests that “as reprehensible as many industry practices are, I believe that the behavior of much of the medical profession is even more culpable”. Her solution is that the entire medical profession should “wean itself from industry money itself almost entirely”. She dismisses efforts to regulate conflict of interest as “a desire to eliminate the smell of corruption, while keeping the money”. In Angell’s article in *The New York Review of Books*, a remarkable series of generalizations are made, without any effort to actually gauge the extent of the problem and the impact of pharmaceutical company interactions on the objectivity and judgment of clinicians and researchers, or the effect of the many sincere efforts to document and limit conflict of interest. A recent report in the *New York Times* highlights the serious efforts that have been made at one medical school to address this issue (Wilson, D. *New York Times*, 3 March 2009).

Notably, Angell sees no role for medical publishers in this problem. This, despite the fact that she notes that company employees often “write the papers”, that “negative

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results are not published”, “positive results are repeatedly published”, “a positive spin is put on even negative results”, and that “it is not unusual for a published paper to shift the focus from the drug’s intended effect to a secondary effect that seems more favorable”. Medical publishers certainly have some role in these practices. Moreover, they are for-profit companies that prosper greatly from their interactions with the pharmaceutical industry by selling advertising and reprints of articles. Publishers of medical journals also foster their own prominence and often that of specific products by holding press conferences to market the articles published within their pages. Even though journals are viewed as objective, the possibility that financial conflicts of interest might be a factor in the selection of articles that are published should not be ignored.

The editorial team of *Nature Reviews Rheumatology* realizes that we cannot address the broader issues of potential conflict of interest in the development and marketing of drugs; however, we can examine our own publishing practices to try to determine whether we are truly objective. We have an obligation to be completely unbiased in the material we select to highlight, in the balance of our News & Views articles, and in the

objectivity of our Reviews. Topics to be covered are selected by a multistep process involving individuals whose only criterion is perceived importance to the field. Potential authors are subjected to PubMed searches, seeking not only evidence of expertise, but also absence of previously published bias, and they are asked to declare any potential conflicts of interest. Reviews are rigorously peer-reviewed to ensure they provide a comprehensive and fair compilation of the available data. Finally, all articles are extensively edited to ensure that the text is lucid and free from spin or marketing catch phrases.

We recognize that the issue of conflict of interest is vitally important, and threatens the integrity of the entire field of clinical research and patient care. We firmly believe, however, that a calm and objective analysis of the problem and a willingness of all participants, including medical publishers, to examine their domain of responsibility carefully and enact procedures that would mitigate conflict of interest and ensure open reporting of any possible conflict, would go a long way toward addressing the problem and restoring confidence in the medical profession.

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