A concern that drug companies cannot ignore

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A report by the House of Commons Health Committee into the influence of the UK pharmaceutical industry has recommended that companies should publish the results of all their trials and follow guidelines for responsible publication practice.¹ Cynics may argue that such reports rarely have much influence over powerful commercial companies and that governments usually ignore their recommendations unless they support existing policies. But this call for greater transparency and responsibility echoes similar calls which, taken together, form a crescendo that is hard to ignore.

Earlier events that may have focused the minds of drug companies and made them more receptive to the latest recommendations include the fine of \$240 million plus \$152 million damages awarded against Pfizer/Warner-Lambert in May 2004 for promoting off-label use of its anticonvulsant gabapentin.² Promotional activities criticized by the US court included having a publication strategy that encouraged the production and dissemination of anecdotal reports of dubious scientific value and the use of ghost-writers to prepare favourable articles which appeared under the names of opinion leaders.

Less than a month later, the New York Attorney General accused GlaxoSmithKline of failing to publish safety data about its antidepressant paroxetine. This case was settled out of court but the company agreed to post results from all its clinical trials on its website.³ Several other companies have followed suit,⁴ and the Pharmaceutical Research Manufacturers of America (the US industry association) has set up a website for this purpose.⁵

Later in 2004, the International Committee of Medical Journal Editors announced that, from mid-2005, journals edited by the 12 committee members would consider papers for publication only if the trial had been registered.⁶ Other journals have now adopted similar policies.⁷ In the USA, registration of trials in serious and life-threatening conditions has been required by the Food and Drug Administration for a few years, but the system has not been policed particularly thoroughly and it is not clear what happens if companies do not comply or provide incomplete information. In contrast, the journal editors' announcement

not only included a sanction that companies would respect (i.e. the threat of not being able to publish in several prestigious journals) but has also been followed by clarification about the type of information required and warnings that journals will check companies' compliance.⁸

Support for trial registration and complete publication is also found in the latest revision of the Declaration of Helsinki which calls for the design of studies to be made available prospectively and for both negative and positive results to be published.⁹ Picking up these themes, the House of Commons report presents cogent arguments why publication bias, and, in particular, the suppression of negative findings, is harmful and supports demands for trial registration.

The question of ghost-writing has also received attention in both medical journals and newspapers for some time.^{10,11} Once again, the House of Commons Committee has added its voice to the debate by calling on companies to behave responsibly. The report refers to the guidelines issued recently by the European Medical Writers Association which seek to abolish ghost-writing by encouraging proper acknowledgement of medical writers' contributions to articles and their source of funding.¹²

One problem with the discussion over ghost-writing has been confusion over exactly what is meant by the term. In this respect, the House of Commons report is helpful in recognizing that it is acceptable for professional medical writers to help doctors write up their research but in condemning the practice of preparing articles with insufficient input from named authors and of covering-up the role of writers or funding companies. This distinction between the legitimate role of professional writers and authorship abuses by pharmaceutical companies has also been emphasized in a recent position statement from the World Association of Medical Editors (WAME).^{13,14} The statement recommends that journals should make clear in their information for authors that medical writers can be legitimate contributors but that their roles and affiliations should be acknowledged.

The issues raised by the involvement of professional writers are also covered in the Good Publication Practice (GPP) guidelines which are strongly endorsed by the parliamentary Committee's report.¹⁵ These guidelines were developed in response to concerns that drug companies were skewing the medical literature by failing to publish

unfavourable findings and by publishing positive results repeatedly. The GPP guidelines therefore call on companies to endeavour to publish results of all trials of marketed products. This suggestion is taken up by the report which calls on companies to make results of all trials available 'at launch as a condition of the marketing licence'. If the UK regulatory authorities act on this it might ensure the implementation of such codes which have, until now, been voluntary. However, European drug regulation is highly centralized, and it is unlikely that the UK would take unilateral action especially over a measure that might be resented by the industry.

The Committee also suggests that research ethics committees should 'require applicants to prove' that a proposed trial 'does not duplicate previous research' and to ensure 'that results will be published in full'. However, similar ideas were proposed over a decade ago,¹⁶ and have been aired more recently,¹⁷ suggesting that ethics committees are unable or unwilling to take on this extra burden.

While many of the recommendations relating to trial registration and publication simply echo or amplify statements from other groups, the Committee took a more radical approach to the drug licensing process. It was particularly critical of the Medicines and Healthcare products Regulatory Agency (MHRA—the UK drug licensing authority), calling for a 'fundamental review' in view of its (unspecified) 'failings'. The report urges the MHRA to publish material submitted by companies to support licensing applications. This would be an important change from the current situation where such information is considered confidential. However, the secrecy of drug licensing and the lack of information available to prescribers about new products has been criticized for many years by other commentators,¹⁸ so it will be interesting to see whether this House of Commons Committee wields more influence.

Some of the reforms proposed by the Committee could constrain prescribing freedom, since it favours a system of limiting the prescribing of new products to hospital specialists and calls for increased monitoring of nurse and pharmacist prescribing. The report concludes that 'it is extraordinary that there are stricter controls on hospital specialists prescribing than on GPs' and recommends that 'tougher restrictions' should be placed 'on what non-specialists can prescribe' with 'greater vigilance to guard against excessive or inappropriate prescribing'. If these recommendations are followed, the UK might move to a system like that in the Republic of Ireland, where certain drugs may be prescribed only by specialists. I suspect that, if such prescribing restrictions are viewed as ways to reduce spending on new products (which tend to be costlier than old ones) the recommendations

might win support from the Department of Health. However, they may be resisted by doctors' organizations. The report could also strengthen the role of the National Institute for Clinical Excellence (NICE) which would presumably be responsible for reassessing products after their probationary period and recommending whether their licenses should be renewed and prescribing restrictions lifted.

This need for support in implementation underlies the inherent toothlessness of House of Commons Committees, whose recommendations tend to be adopted only if they find powerful champions. I therefore suspect that the Committee's calls for reforming the MHRA will be resisted unless a major drug safety scandal forces action. However, if the Department of Health and NICE back the Committee's proposals for restricting the prescribing of new drugs, this could come into force. In the case of the calls for increased transparency for clinical trial results and for trial registration, several powerful groups are already forcing companies in this direction—the report simply adds to the groundswell. Drug companies are increasingly realizing that irresponsible publication practices can generate negative publicity, and are therefore responding to pressure from journal editors and regulatory authorities to clean up their act. They are also starting to realize that lack of diligence over publications could affect their profits, which usually provides the most powerful motive for change and might mean that some of the Committee's recommendations are enacted.

Competing interests I am a co-author of *Good Publication Practice* for pharmaceutical companies and the EMWA guidelines on the role of medical writers in developing peer-reviewed publications.

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