Good Publication Practice: why we need another set of guidelines

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Introduction

Pharmaceutical companies' relations with clinicians, academics, medical journals, and the public have often been characterized by conflicting interests and tensions, and these negative aspects have received considerable attention [1,2] . Yet these different constituencies often work closely together, especially during clinical trials, and successful collaboration is critical to the development of new medicines. While the conduct of the clinical trials themselves is heavily regulated, until recently much less attention has been paid to the process of publishing their findings.

The evolution of GPP

In November 1998, journal editors, academics / investigators and pharmaceutical company employees involved with publications took part in a retreat organized by the Council of Biology Editors (now Council of Science Editors) [3]. Over the course of the meeting it became clear that there was a lack of understanding about the ways in which the different constituencies operated and concern about the ways in which publications arising from company-sponsored research were sometimes developed. Those of us present from within the industry and closely involved with the publication of company-sponsored clinical trials agreed that it would be helpful to identify some principles and common standards to address the concerns about publication practices. We set up a Working Group that drafted 'Good Publication Practice: Guidelines for Pharmaceutical Companies' (or GPP, see Appendix). These guidelines are designed to increase the transparency of the processes involved in the publication of industry-sponsored trials and to establish standards for these. Although they predate the most recent statements by the International Committee of Medical Journal Editors (ICMJE) [1] we believe that they remain timely and pertinent to them.

We consulted widely within our several companies and eventually agreed on a document that addressed the important issues. During 2000 we sent this document to 70 major pharmaceutical companies and publicized its existence in several journals [4-7]. Although we believed that GPP would have the greatest

impact if it was adopted by individual companies, we also discussed the guidelines with the Pharmaceutical Manufacturers Association (PhRMA) in the United States, and the Association of the British Pharmaceutical Industry (ABPI). The guidelines have also been presented at meetings of the Council of Science Editors, European Association for Science Editors, the American Medical Writers Association and the Cochrane Collaboration.

Since the initial meeting in 1998, the membership of the Working Group has evolved as members changed jobs or companies. It is probably typical of current patterns of employment in the pharmaceutical industry that, of the six original members of the group who signed the letter in JAMA [4], three have moved to new companies, one has changed responsibility within the company, one has gone freelance and one has retired. Approval was also delayed or made difficult because of company mergers, which have occurred in three of our six original employing companies. For all these reasons, we (the current members of the Working Group) have decided to publish the guidelines in our individual capacities rather than as representatives of any particular companies, but we acknowledge the support of our various employers over this period, the contributions of previous members of the group, and the numerous other people who have contributed to the development of the guidelines. With this publication, we hope that the GPP guidelines will be discussed further and many companies will wish to endorse them.

Why do we need more guidelines?

Publication in peer-reviewed journals is an integral part of biomedical research. While it is not immune from inappropriate behavior and even malpractice, it is less heavily regulated than other aspects of the process. Many of the issues addressed by the GPP guidelines, such as failure to publish results from negative or disappointing studies and inappropriate allocation of authorship, are not unique to pharmaceutical-industry sponsored trials. However, responsible companies cannot ignore them and are often in a good position to address them. Documents such as the CONSORT statement [8], the ICMJE's Uniform Requirements [9], and journals' instructions to authors are helpful, but none was designed specifically for company sponsors of large trials, and they do not address all the concerns that have been raised.

What issues do the GPP guidelines seek to address?

The two main themes of the GPP guidelines are publication bias and the relationship between pharmaceutical companies and academic investigators.

Publication bias may result from either the non-publication of inconclusive or unfavourable findings or by redundant publication of positive findings. These problems, which are not unique to industry-sponsored trials, may be caused by a number of factors [10] but are well documented [11-13]. The GPP guidelines aim to reduce publication bias in three ways. They encourage companies to endeavour to publish results from all their studies and to avoid redundant publication. However, they recognize that results may legitimately be presented at several scientific conferences, and that secondary analyses or follow-ups may be appropriate. The guidelines therefore recommend the inclusion of unique trial identifiers in all publications to increase transparency and facilitate the preparation of systematic reviews.

The successful conduct and publication of large-scale clinical trials require close collaboration and partnership between clinicians and company scientists. Suggestions that companies should have less involvement in preparing papers [1,2] go against the greater transparency that has been achieved by the contributorship approach to listing authors [14,15] and prevents recognition of the important intellectual and scientific contributions of company employees [16].

The role of professional writers working for pharmaceutical companies is dealt with in detail. This has been an area of particular concern, and some have suggested that the practice should be discouraged altogether [17, 18] . However, we believe that preventing professional writers from assisting with publications would exacerbate the problems of non-publication and delayed publication and that, when such writers are an integral part of the publication process, openly acknowledged, and working within the guidelines, they can improve both the quality and the timeliness of publications [19, 20].

The scope of the guidelines

The GPP guidelines apply to publications arising from industry-funded clinical studies. This includes trials used to support licensing applications (Phase II and III) and those funded by manufacturers after products are approved (Phase IV). The guidelines do not cover studies performed and published independently by investigators (even when these involve some company support, e.g. supply of drugs), although we hope the principles may still be helpful in those cases. The GPP guidelines also apply to other types of publication that are initiated by companies, such as review articles and secondary papers.

The GPP guidelines are designed to be followed by pharmaceutical companies and any company or individual working on their behalf, such as contract research organizations, communications agencies and freelance contractors. They also set out some of the responsibilities of healthcare professionals working with companies as investigators or authors of publications.

How should the GPP guidelines be applied?

We hope that companies will base policies and procedures on the guidelines and devise their own ways of ensuring that they are followed. Therefore we have aimed to set out principles rather than dictate specific procedures or mechanisms. Since these are voluntary guidelines, the language is that of recommendation rather than an imperative (i.e. they set out what companies *should* do rather than what individuals *must* do).

The GPP guidelines for pharmaceutical companies do not aim to replace existing documents such as CONSORT [8] or the ICMJE recommendations [9], and we hope that companies will also consult these and incorporate them into their policies and practices.

What next?

Although the guidelines were written with pharmaceutical companies in mind, many of the issues they address occur in other sectors. In particular, publication bias caused by under-publication of negative or disappointing findings is known to affect studies regardless of the source of their funding [11, 21] . Therefore we hope that other funding bodies, academic institutions and perhaps research review boards / ethics committees [22] might seek to ensure that results from all studies are published. This principle is now included in the latest version of the Declaration of Helsinki [23] which may encourage individual clinicians to take responsibility for this.

Our aim in publishing the GPP guidelines is to stimulate discussion between journals, investigators and trial sponsors and to provide guidance to those who

seek it. We also hope that pharmaceutical companies and others involved in developing publications will endorse them. However, we recognize that developing guidelines is an iterative process, and it is never possible to consult with everybody who might have something useful to contribute. We also recognize that experience of implementing the guidelines in different companies may raise points that require clarification or expansion. Therefore we plan to review the document at regular intervals. Ideally such a review would take place at a forum in which the different constituencies are equally represented, perhaps along the lines of the initial retreat, with a similar small Working Group convened to act on any recommendations.

We hope that the GPP guidelines represent a first step in establishing a common standard for the publication of industry-sponsored studies, and that regular review and discussion will lead to continually rising standards.

References

1. Davidoff F, DeAngelis C, Drazen JM, Hoey J, Højgaard L, Horton R et al. Sponsorship, authorship, and accountability. Ann Int Med 2001;135:463-6.

2. Bodenheimer T. Uneasy alliance. Clinical investigators and the pharmaceutical industry. N Engl J Med 2000;342:1539-44.

3. Wager E. Common aims / different languages: increasing understanding among medical journals, academia and industry. CBE Views 1999;22:41-2.

4. Wager E, Tumas JA, Field EA, Glazer NB, Schulz G, Grossman L. Improving the conduct and reporting of clinical trials. JAMA 2000;283: 2788-9

5. Wager E, Tumas JA, Field EA, Glazer NB, Schulz G, Grossman L. Improving the conduct and reporting of clinical trials. Can J Gastroenterol 2000; 14: 749.

6. Wager E, Tumas JA, Field EA, Glazer NB, Schulz G, Grossman L. Good publication practice. Ned Tijdschr Geneeskd 2000; 144:399-400.

7. Sharp D. Drug industry code proposed on 'ghost' writing. Lancet 2000; 355:1084.

8. Begg C, Cho M, Eastwood S, Horton R, Moher D, Olkin I et al. Improving the quality and reporting of randomized controlled trials. JAMA 1996;276:637-9.

9.International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. www.icmje.org. Accessed 25th March 2003.

10. Gibbs TG, Wager E. Realities of trial registration: the Glaxo Wellcome experience. International Journal of Pharmaceutical Medicine 2000;14:203-5.

11. Easterbrook PJ, Berlin JA, Gopalan R, Matthews DR. Publication bias in clinical research. Lancet 1991;337:867-72.

12. Dickersin K. The existence of publication bias and risk factors for its occurrence. JAMA 1990;263:1385-9.

13. Stern JM, Simes RJ. Publication bias: evidence of delayed publicatoin in a cohort study of clinical research papers. BMJ. 1997;315:640-5.

14. Davidoff F. News from the International Committee of Medical Journal Editors. Ann Intern Med 2000;133:229-231.

15. Rennie D, Flanagin A, Yank V. The contributions of authors. JAMA 2000;284:89-91.

16. Wager E. Drug industry is increasingly allowing employees to be named as authors (letter). BMJ. 1996;312:1423.

17. Reed CR, Camargo CA. Recent trends and controversies in industry-sponsored clinical trials. Academic Emergency Medicine 1999;6:833-9.

18. Committee on Publication Ethics. The COPE Report 2000: Annual Report of the Committee on Publication Ethics. London: BMJ Books; 2000.

19. Grossman L. Ghostwriting (letter). Lancet 1998;351:1741.

20. Wager E. Ghostwriting (letter). Lancet 1998;351:1741.

21. Blumenthal D, Campbell EG, Anderson MS, Causino N, Seashore Lewis K. Witholding research results in academic life science. JAMA 1997;277:1224-8.

22. Antes G, Chalmers I. Under-reporting of clinical trials is unethical. Lancet 2003;361:978-9.

23. World Medical Association. Declaration of Helsinki. Ethical principles for medical research involving human subjects. 2000. 52nd WMA General Assembly, Edinburgh, Scotland, October 2000.