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Good publication practice for pharmaceutical companies

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SUMMARY

Guidelines on Good Publication Practice (GPP) for pharmaceutical companies are presented. The aim of the guidelines is to ensure that clinical trials sponsored by pharmaceutical companies are published in a responsible and ethical manner. The guidelines cover companies' responsibility to endeavour to publish results of all studies, companies' relations with investigators, measures to prevent redundant or premature publication, methods to improve trial identification and the role of professional medical writers. Our aim in publishing the GPP guidelines, which are the first to be developed by and for those working on publications in the pharmaceutical industry, 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 arising from sponsored clinical trials will endorse the guidelines.

Introduction

Pharmaceutical companies' relations with clinicians, academics, medical journals and the public have often been characterised 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 organised 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 publicised 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 Research & Manufacturers of America (PhRMA) 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. Approval was also delayed or made difficult because of company mergers. For 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. We are publishing the GPP guidelines in the hope that they will be discussed further and that 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 behaviour 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 recognise 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].

The scope of the guidelines

The GPP guidelines apply to publications arising from industry-funded clinical studies of marketed products. 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 organisations, 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[11,20]. Therefore we hope that other funding bodies, academic institutions and perhaps research review boards/ethics committees[21] 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[22] 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 recognise 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 recognise 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.

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APPENDIX

Good publication practice: guidelines for pharmaceutical companies

Aim

The aim of these guidelines is to ensure that publications are produced in a responsible and ethical manner. They are designed to be applied in conjunction with other guidelines such as those from the International Committee of Medical Journal Editors[1], the CONSORT group[2], and individual journals. In addition, they may be incorporated into the more detailed operating procedures of individual companies.

Scope

These guidelines are designed for use by pharmaceutical companies, other commercial organizations that sponsor clinical trials and any companies or individuals who work on industry-sponsored publications (e.g. freelance writers, contract research organizations and communications companies). For simplicity, the terms 'company' and 'employee' are used in these guidelines, but they should be taken to include all of these parties.

These guidelines cover publications in biomedical journals, including both traditional print and electronic journals and oral/audiovisual presentations at scientific meetings. They cover peer-reviewed publications (such as original research articles, review articles, sponsored supplements and abstracts), and non-peer-reviewed scientific communications (such as posters, lectures, book chapters and conference proceedings). However, they do not cover promotional materials, which are regulated by specific national codes and legislation.

Publication Standards

Companies should endeavour to publish the results from all of their clinical trials of marketed products. These publications should present the results of the research accurately, objectively and in a balanced fashion. Anyone working on company publications should follow relevant external guidance such as the 'Uniform Requirements for Submission of Manuscripts to Biomedical Journals' issued by the International Committee of Medical Journal Editors (ICMJE)[1] and the CONSORT statement[2]. Additional guidelines relating to publications from company-sponsored research are outlined below.

Relationship between the Company and External Investigators

The contractual relationship between companies and external investigators or consultants should be set out in a written agreement. This should cover publication policies and ownership of data.

Companies should be responsible for coordinating the publication of multicentre trials to ensure that they are reported in a responsible and coherent manner (i.e. results from data subsets should not be published in advance of or without clear reference to the primary paper and should not constitute redundant or prior publication). Therefore, companies should maintain the right to be informed of any plans for publication and to review any resulting manuscripts before they are submitted. Companies should not suppress or veto publications; however, it may be appropriate to delay publications to protect intellectual property.

All authors, external and internal, should have access to the statistical reports and tables supporting each publication. When differences about the presentation or interpretation of findings arise between company scientists and external investigators, both parties should work to find a mutually acceptable solution through honest scientific debate.

Premature Publication

While it is acceptable to present abstracts, posters or lectures at biomedical conferences before the full publication of results, care should be taken to avoid premature or inappropriate publication (e.g. through press releases). Most journals provide guidelines on what constitutes prior publication and impose embargoes on contact with the press before publication. These are also outlined in the ICMJE guidelines[1]. In the case of findings with major implications for public health or of great commercial sensitivity, it may be helpful to discuss with the journal editor the timing of publication and proposed approaches to the media.

Duplicate/Redundant Publication/Multiple Submissions

Most peer-reviewed journals will consider only papers that have not appeared or been accepted for publication in full elsewhere. Presentation at scientific meetings does not constitute full publication, so prior publication of abstracts or posters does not affect the consideration of full papers. These conditions are set out in journals' instructions to authors and the ICMJE guidelines[1], which should be followed in all cases. Because journals do not accept duplicate publications and because they

do not want to waste the time of their reviewers, it is not acceptable to submit a paper to more than one journal at a time.

Companies should avoid duplicate publication of the primary results of a study in peer-reviewed journals. Cases in which secondary publications might be acceptable include symposium proceedings, results of significant and scientifically sound alternative analyses or grouping of data from more than one study. However, such publications should not precede the original publication, should reference the original publication and should include a unique study identifier as described below. Full peer-reviewed publications should contain references to all previous presentations of the data (e.g. abstracts). Translations of papers into different languages are usually acceptable as long as the original source of the publication is clearly acknowledged.

Many major biomedical meetings discourage repeat presentations of findings that have previously been presented to substantial audiences; the guidelines for each individual meeting should be observed. However, there is no absolute rule against submitting several abstracts presenting the results of a single study to several conferences unless this breaches the guidelines of the individual meetings. Closed presentations to inform investigators of results should not jeopardize publication or wider presentation of results at public meetings.

Identification of Studies

Identification of clinical trials by the use of a study, trial registry or protocol number helps readers and those performing systematic reviews by making it clear when data from the same patients are being presented in different publications (e.g. in abstracts and then a full paper or when interim or long-term follow-up findings or secondary analyses are presented). A unique study identifier should therefore be included in all publications.

Authorship

The ICMJE guidelines[1] are a good starting point for determining who qualifies to be an author, but they do not provide detailed guidance applicable to all situations. Furthermore, some journals have adopted a system of listing contributors rather than authors. Therefore, the individual requirements of different journals should be respected. Whatever criterion for listing is used, it should be applied in the same way to both external investigators and company employees. Companies should ensure that all authors fulfil the relevant criteria and that no authors who meet the criteria are omitted from the submitted manuscript. The order in which authors/contributors appear on a publication should be negotiated between all authors/contributors. It may be helpful for companies to outline authorship policies in the investigators' agreement.

Acknowledgments Section

The Acknowledgments section of a paper should list those people who made a significant contribution to the study but do not qualify as authors. It should also be used to acknowledge the study's funding and the company's involvement in the analysis of the data or preparation of the publication unless this is apparent from the list of contributors/authors.

The Role of Professional Medical Writers

The scientists, healthcare professionals and statisticians who were involved with the design, conduct and interpretation of a study (either as company employees or external investigators) should participate in the preparation of publications arising from the data. However, since these people may lack the time, expertise or language skills to produce high-quality and timely manuscripts, companies may wish to employ professional medical writers to facilitate the publication process. The writer may provide publication expertise and assistance with writing, editing or preparing manuscripts or collating comments from contributors. When a professional medical writer is involved with a publication, the following guidelines should be followed to ensure that the opinions of all authors are fully represented in the publication.

- The named author(s)/contributors must determine the content of the publication and retain responsibility for it.
- The medical writer should begin drafting the manuscript after consultation and discussion with the named author(s)/contributors. It is often helpful if the author(s)/contributors and the medical writer agree on an outline of the paper before detailed writing begins.
- The named author(s)/contributors should be given adequate time to comment on an early draft of the manuscript.
- The medical writer should remain in close and frequent contact with the author(s)/contributors throughout the development of the manuscript.
- The named author(s)/contributors should approve the final version of the manuscript before it is submitted.
- The lead author should be responsible for submitting the manuscript to the journal and acting as the primary contact for interactions with the journal editor.
- The contribution of the medical writer should be acknowledged.

The use of professional writers may be particularly helpful when companies publish the results from large, multicentre studies involving many contributors. The

formation of a writing committee involving the medical writer may facilitate this process. While it is acceptable for professional writers or authors' editors to assist authors who have written editorials or opinion pieces (e.g. to improve the written style of authors whose first language is not English), it is not usually appropriate for them to prepare the first draft of such articles.

Responsibility for Implementing the Guidelines

Company employees who are involved with publications and people who are hired by companies to work in this area should be familiar with these guidelines. Companies should ensure that appropriate management structures are in place to implement the guidelines. Company procedures for the review of manuscripts should ensure that approval for submission is given in a timely manner. (Most companies have a procedure in place for medical/legal review or 'copy approval' and it may be helpful to append details of this here.)

Acknowledgements

These guidelines on Good Publication Practice for Pharmaceutical Companies have been actively discussed and incorporated into company practice by several pharmaceutical companies. A number of contract research and communications companies have also agreed to recommend the Good Publication Practice guidelines to their clients. Current endorsing and supporting companies are listed at www.gpp-guidelines.org. Employees of Eli Lilly, EMD Pharmaceuticals, Glaxo Wellcome (now GlaxoSmithKline), Hoechst Marion Roussel (now Aventis) and Merck contributed to the development of the Good Publication Practice document at various stages. However, the current guidelines may not necessarily represent the policies of these companies.

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