Special Article

"Good Publication Practice for Pharmaceutical Companies": Where Are We Now?

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Abstract and Introduction

Abstract

Eighteen months on from the publication of "Good Publication Practice for Pharmaceutical Companies," one member of the working group that developed these guidelines reflects on what they have achieved and what has changed since they were first developed.

Introduction

Pharmaceutical company publication practices have recently attracted the attention of journal editors, the mass media, and even been the subject of legal proceedings. The issue of the nonpublication of trial results moved from being a largely academic concern to the subject of newspaper headlines when GlaxoSmithKline was sued by the New York Attorney General.[1] The settlement included a commitment to make summaries of trial results available on the company Web site. At around the same time, other companies, such as Eli Lilly, announced similar policies.[2]

Companies may have also been examining their publication policies in the light of the case against Pfizer-Warner-Lambert, which resulted in the company being fined $240 million and ordered to pay $152 million in damages for promoting the off-label use of gabapentin (*Neurontin*).[3] Evidence brought against the company included having "A 'publication strategy' that subsidized the production and dissemination of anecdotal reports favorable to off-label use of *Neurontin* ," which were "of no scientific value." Some news items also mentioned the use of ghostwriters.

It is tempting to believe that a great deal of time, effort, and even money might have been saved if companies had paid more attention to their publication practices. A set of guidelines on Good Publication Practice (GPP) for pharmaceutical companies were published in mid-2003.[4] This article reviews the history of the guidelines in light of the recent developments.

The GPP Guidelines

The GPP guidelines were developed by a group of people working within the pharmaceutical industry who were closely involved with the publication of clinical trials. The spur for establishing guidelines was a retreat organized by the Council of Biology Editors (now the Council of Science Editors) in late 1999, which brought together journal editors, academics, and drug company employees.[5] This meeting highlighted several concerns and some misconceptions about the way in which drug companies reported trial results. Attendees from about half a dozen companies worldwide therefore formed an informal working group and produced the guidelines. Although we sought and received comments from journal editors and academic investigators, our aim was to produce practical guidance from within the industry and for the industry.

The guidelines evolved slowly, following a sometimes tortuous path up and down corporate hierarchies. Seeking approval for the guidelines often resembled the game of "Snakes and Ladders," with progress up one ladder counting for nothing when companies merged and we had to start again at the bottom. After the wording was finally thrashed out, publication was delayed by rejection from 2 journals, whose editors had expressed an interest in the guidelines but whose reviewers believed that the guidelines were not of sufficient interest to readers and not sufficiently novel to warrant publication.

Despite the obstacles, the working group remained determined to publish and seek endorsement for the guidelines, because we believed that they could improve reporting of industry-sponsored clinical trials that would, ultimately, help both prescribers and patients. Because the guidelines focus on peer-reviewed publications, which involve collaboration between companies, editors, and investigators, we did not agree with the journal reviewers who suggested that they should be published in an "industry publication," so

we persisted in getting GPP published in a peer-reviewed journal so that the guidelines would be available for comment and discussion by the entire biomedical community. The guidelines were eventually published in *Current Medical Research and Opinion* in 2003.[4]

Contents of the Guidelines

Publication Bias

The 2 major issues addressed by the guidelines are publication bias and the role of professional medical writers. The medical literature becomes distorted when unfavorable findings are systematically underreported, or when favorable results are published redundantly. Nonpublication of trial results has been classified as a form of research misconduct,[6] and the harmful effects of publication bias have been clearly demonstrated.[7,8] The GPP guidelines therefore call on companies to endeavor to publish the results of all clinical trials of their marketed products.

We used the term "endeavor" because we recognized that, ultimately, journal editors decide what gets published. However, by publication we meant full publication in a peer-reviewed journal, not posting a summary on a corporate Web site. We called on companies to publish findings of clinical trials, ie, those that involve patients, rather than attempt to distinguish "hypothesis-testing" studies from exploratory or "hypothesis-generating" ones. We also resisted suggestions to qualify the statement by phrases, such as "meaningful results," because this raises the question of who decides what is meaningful. "All" is unambiguous and "clinical trials" is a widely recognized term that avoids the industry jargon of study phases that may not be familiar to everybody. This statement was underpinned by a belief that conducting trials with patients carries an ethical responsibility to publish the findings, whether or not they are favorable to the sponsor. However, we appreciated that companies need to set priorities and that, in terms of public health, the most important findings are those relating to marketed (rather than experimental) products.

From our discussion with companies, we soon discovered that this commitment to endeavor to publish the results of all clinical trials was considered a major burden and was probably the reason why so few companies were prepared to publicly endorse the guidelines from the start.

To counter the problem of covert redundant publication, which can also skew the evidence base, the guidelines proposed the simple solution of including a trial identifier (such as a protocol number) on all publications. Although trial registration may carry other benefits, such as informing potential participants about ongoing studies and reducing underpublication, we believed that in 2000, when the guidelines were being developed, few companies were ready to commit to prospective registration. We also believed that registration was meaningless without a commitment to publish findings, and that the aim of eliminating publication bias would therefore be achieved more effectively by getting companies to commit to publishing results of all their clinical trials and to including a trial identifier on all publications.[9] Inclusion of an identifier, such as a protocol number, effectively identifies all publications arising from a single study and, in particular, helps scientists preparing systematic reviews to distinguish primary findings from follow-ups or subgroup analyses. This is important because it prevents data from the same patients being counted more than once in systematic reviews. More recently, many companies have been forced to reconsider trial registration in light of the September 2004 announcement from members of the International Committee of Medical Journal Editors (ICMJE) that registration would be a requirement for publication in their journals from July 2005.[10]

Role of the Sponsor and of Professional Writers in Trial Publications

The GPP guidelines acknowledge that some companies have sought to exert undue influence over trial reporting and have abused their relationships with the investigators/authors through the inappropriate use of ghostwriters. However, the use of professional writers should be distinguished from poor publication practices and undeclared competing interests. Many journal editors and academics now recognize that professional writers may actually improve the reporting of clinical trials and that involvement of a medical writer is not, of itself, unethical.[11] Writers often contribute language skills, familiarity with reporting and journal requirements, and expertise in presenting data that may be lacking among investigators. Professional writers can also offer time uninterrupted by the demands of the clinic or lab, which is essential to producing a good paper within a reasonable time frame.

However, despite anecdotal condemnation of bad practices,[12,13] the existence of medical writers is rarely even acknowledged in journal instructions. We therefore believed that it would be helpful to set out, in detail, a code of practice describing what professional writers should and should not be expected to do. The recommendations also aim to ensure that named authors have sufficient access to results and adequate opportunities to make meaningful contributions to publications.

More recently, the European Medical Writers Association has developed its own guidelines,[14] providing further detail but based on GPP. Both sets of guidelines seek to abolish the practice of ghostwriting, in which the role of writers is hidden, but encourage responsible practice by writers who should, along with their funding sources, be openly acknowledged. Similar principles have been stated by the American Medical Writers Association.[15]

The GPP guidelines focus mainly on the reporting of clinical trials, but the recommendations about the role of writers also cover the preparation of editorials and opinion pieces. Recognizing that this has been particularly open to abuse and inappropriate sponsor influence,[12] the GPP guidelines recommend that editorials should not be ghostwritten (ie, the named author should always prepare the first draft). However, it may be appropriate for professional writers or authors' editors to assist authors at a later stage, for example, if the named author is not a native English speaker. Although not stated explicitly in the guidelines, many nonsystematic

reviews fall into the category of opinion pieces rather than primary research and therefore should be drafted initially by the named author. As with all publications, the role of the sponsor, and of any professional writers involved, should be clearly acknowledged.

The other type of ghosts that the GPP guidelines seek to flush out are deserving company authors whose names are omitted because of sponsors' attempts to play down their involvement with a study or publication.[16] Recognizing that journals have different conventions for listing authors or contributors, the GPP guidelines simply recommend that whatever criteria are used to determine authorship, they should be applied consistently to company employees and external investigators.

Have We Achieved Anything?

Five years after the initial meeting, and 18 months on from the publication of the GPP guidelines, have we achieved anything? Despite the fact that only a handful of pharmaceutical companies have publicly endorsed the guidelines (details available at:

www.gpp-guidelines.org

www.gpp-guidelines.org

), several major companies have based their publication policies on GPP. (For example, Merck acknowledges GPP in the publication policy available on their Web site.[17]) The guidelines have also received support from several communications companies and medical writing agencies that have agreed to encourage their customers to follow GPP and to incorporate the principles into their own procedures.

A member of the GPP working group was also involved in developing the Pharmaceutical Research Manufacturers of America (PhRMA) guidelines,[18] which have many similarities to GPP. Although the PhRMA guidelines are slightly more cautious than GPP (notably, calling for the publication only of "meaningful results of controlled clinical trials of marketed products" and excluding "early-phase or postmarketing" studies "of an exploratory nature"), we appreciate that developing any wording with several parties involves some compromise, and we recognize that, although they do not go as far as GPP, both guidelines are moving in the same direction and adherence by all PhRMA members and would represent a major step toward achieving responsible publishing practices.

The requirement for prospective trial registration by the members of the ICMJE represents an important shift in publication policy.[10] It will be interesting to see how pharmaceutical companies and other journals respond. Although I support any initiative that will reduce publication bias, I am concerned that the issues of registration and reporting may get confused. The GPP guidelines are based on the premise that trials should be reported fully in peer-reviewed journals, and it would be unfortunate if the rush to trial registration (coupled with GlaxoSmithKline's response to the New York case) was to lead companies to concentrate on posting unreviewed summary findings on the Internet at the expense of developing "proper" publications.

After the initial difficulty in getting the guidelines accepted for publication, we have been encouraged by support from journals (eg, the *BMJ* and the suite of journals from *BioMedCentral*) in providing links to the GPP Web site from their instructions to contributors. Our vision is that GPP may become as widely accepted as the Consolidated Standards of Reporting Trial (CONSORT) statement,[19] with medical journals requiring all industry-funded studies to follow the guidelines. (It is, of course, no coincidence that we chose the title GPP to reflect the process of Good Clinical Practice, because we believe that responsible reporting is the necessary last stage of conducting an ethical clinical trial.)

No guidelines are perfect, and practices should evolve to reflect the changing world of biomedical publication and, if we are feeling optimistic, gradually improving practice. It is encouraging to note that, since publication in 2003, the guidelines have been cited 13 times in other publications. We welcome comments and suggestions to improve the guidelines and hope to continue the dialogue between editors, investigators, and people working in or for the drug companies. In the meantime, we encourage companies to endorse the guidelines and hope that editors, investigators, and writers will find them helpful. We also hope that other journals, including *MedGenMed* , will add their support by promoting the guidelines through their instructions to contributors and encouraging greater transparency about the role of commercial companies in the development of publications.

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