

Regulatory writing basics

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Editorial

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The role of a regulatory writer is to produce regulatory documents (usually taken to refer to documents that are submitted in some form to the health authorities). These documents should adhere to the relevant guidance and be fit for purpose, meaning that they transmit the necessary information accurately, transparently, and clearly to the target audience (usually reviewers at the health agencies but readers might also be investigators or members of ethics committees).

In the Internet era, regulatory writers have instant and complete access to almost all the necessary guidelines governing these documents (and Raquel Billiones has gone to the trouble of compiling these guidelines; see p84). Yet there is actually rather little information in the public domain on how these guidelines should be applied and interpreted in practice. Some books are available on medical writing, but these have relatively little if anything to say about regulatory writing and focus on research articles and other aspects of medical communications. A quick search on the Amazon website revealed one book dedicated to regulatory writing.¹ The book was published in 2008, but guidance changes and clarifications are issued in the form of Questions and Answers documents to address contradictory or ambiguous aspects of the guidance.² So while the core skills needed for regulatory writing remain fairly constant, the details may change and the regulatory environment evolves.

This issue of *Medical Writing*, entitled *Regulatory writing basics*, is an attempt to fill, at least partially, the void of information on the subject and provide a useful reference guide for regulatory writers. (Here, I feel compelled to acknowledge that the original idea for this issue did not come from me but rather from Phil Leventhal, the regular *Medical Writing* editor). Regulatory writing is a wide field and so the scope of the articles has been limited to the types of document that an entry level regulatory

writer is likely to encounter. It is also limited to pre-approval documents associated with drug development. The December 2014 issue of *Medical Writing* will be dedicated to the topic of post-approval.

At some point early in their careers, most entry-level regulatory writers will work on a Clinical Study Report (CSR), which is covered in depth by Sam Hamilton (p86). For the most part, the guidelines covering the CSR are detailed and well developed, although they have occasionally been interpreted too literally. For example, the table of contents of the guidelines was interpreted by many companies as a template for their CSRs, resulting in the somewhat absurd situation of having the title page of the CSR listed as Section 1. This is a good example of the pitfalls of unthinking and rather slavish application of guidelines and also, I think, the desire of many companies to be as compliant as possible with the perceived letter of the guidelines while perhaps losing sight of their intent. A necessary skill of a regulatory writer is knowing when to treat guidance as set in stone and when it is appropriate to deviate from the letter of the guidance to ensure clarity and readability.

The Protocol is another document that writers may be involved in at some point in their careers. As Walther Seiler explains though (see p93), despite its obvious importance, the far-from-comprehensive guidelines and varied audience provide unique challenges and also interesting opportunities for regulatory writers. Like the protocol, the Investigator's Brochure (IB), comprehensively covered by Douglas Fiebig on p96, has a varied audience and can be used for a variety of purposes. The IB includes information from the entire drug development process, from preclinical studies through to the latest clinical studies and needs to be updated at least once a year. The coordination of input from such a wide variety of sources may be challenging, particularly as an IB update should be kept to a reasonable length. An update should not merely be a case of simply adding new data; decisions about which data to retain will need to be made and perhaps justified and discussed within a team, with the writer acting as a facilitator and arbiter.

The goal of drug development is to get approval for a drug. An issue about regulatory writing would therefore seem incomplete without reference to the centrepiece of an approval process, the Common Technical Document (CTD). This document binds together the existing documentation from drug development (quality, pre-clinical, and clinical) and also includes dedicated summary documents and a discussion of the data (overviews). Debbie Jordan takes us through the different components of the CTD, with special reference to the clinical modules, such as the clinical summaries and clinical overview, where the services of a medical writer are most likely to be employed (see p101). Regulatory writers will often have to make judgement calls about what is appropriate content for the clinical overview and what should be included in the summaries, although convincing the teams not to put too much detailed data in the overview, for example, is not always easy.

This issue also includes three articles intended to give some useful background for regulatory writers. First, Anga Abed, a medical writer at the European Medicines agency gives an overview and history of drug approval in the European Union (see p117). She explains how the fragmented approval processes in place 20 years ago has given way to a centralised, more efficient system. In addition to changes in the approval process, the conduct of clinical research has also been thoroughly overhauled, as discussed by Gabi Berghammer in her article on Good Clinical Practice (GCP), which also touches on the International Conference for Harmonisation (ICH) (see p106). The concept of GCP now permeates all levels of clinical research, and an awareness of GCP principles will be of great help to regulatory writers. The document types discussed in this issue are subject to ICH guidelines, so an understanding of the ICH and its unifying intent (as well as knowledge of the individual guidelines) is important. ICH has been with us for almost 20 years now, and its profound impact can be

appreciated if, for whatever reason, you have cause to read pre-ICH documents. These can appear chaotic and incomplete, and extracting information from them can be time consuming. Safety is a fundamental aspect of the risk-benefit assessment of a new drug (and hence whether it will be approved). Safety reporting is much more homogeneous than efficacy reporting and is largely based on analysis of adverse events. Like the drug approval processes and clinical research conduct, safety reporting has also undergone marked changes over the last 20 years. In the ICH era, use of the Medical Dictionary for Regulatory Activities (MedDRA) is now mandated for reporting of adverse events and an article on the subject has also been included in this issue (see p113).

While it is hoped that this collection of articles can serve as a useful guide for regulatory writers, especially those in the early stages of their career, merely reading about regulatory writing will not be enough. Regulatory writing is more than just adhering to the regulations (which may be contradictory anyway). A common theme of the articles included here is that regulatory writers often have to act as negotiators and facilitators, finding a solution that is acceptable to different team members with very different agendas. The soft skills needed to deal with these situations are ones that a regulatory writer would be wise to develop. Attending conferences such as EMWA and exchanging experience with established writers will undoubtedly help, but there really is no substitute for direct experience, preferably with a mentor available to advise and guide you in tricky situations.

References

1. Wood LF, Foote MA, editor. Targeted regulatory writing techniques: clinical documents for drugs and biologics. Basel, Switzerland: Birkhäuser; 2009.
2. See for example: ICH E3 guideline: structure and content of clinical study reports questions & answers (R1); 2012 Jul 6. Available from: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E3/E3_QAs_R1_Step4.pdf.