European
Medical Writers
Association

The Write Stuff

The Journal of the **European Medical Writers Association**

Vol. 15, No. 1, 2006

Clinical trials

Journal insights

The *Write Stuff* is the official publication of the European Medical Writers Association. It is issued 3 times a year and aims to provide EMWA members with relevant, informative and interesting articles and news addressing issues relating to the broad arena of medical writing. We are open to contributions from anyone whose ideas can complement these aims.

Articles or ideas should be submitted to the Editor-in-Chief (see back cover) or another member of the Editorial Board.

Subscriptions

Subscriptions are included in EMWA membership fees. Non-members can subscribe at an annual rate of:

– €35 within Europe
– €50 outside Europe

Instructions for contributors

– The *Write Stuff* typically publishes articles of 700–2800 words although longer pieces or those with tables or graphics will be considered.
– All articles are subject to editing and revision by the Editorial Board. Any changes will be discussed with the author before publication.
– Submissions should include the full address of the author, including the telephone and fax numbers and email address. Suitable quotes for side boxes can be indicated or they can be selected by the Editorial Board.
– Material should be submitted electronically on computer diskette or by email as an MS Word file using Times New Roman (or equivalent), 10 point size, and single spacing.
– Published articles generally include a recent photograph of the author (portrait picture, CV or passport style).

Back issues

Subject to availability, previous issues of The *Write Stuff* can be obtained for the cost of mailing by contacting the EMWA Head Office (see back cover for address).

Advertising rates (in euros, €)

Corporate		Private / Freelance members only	
– Full page	**€1000**	– Full page	**€200**
– Half page	**€500**	– Half page	**€100**

Behind the press

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Cover picture

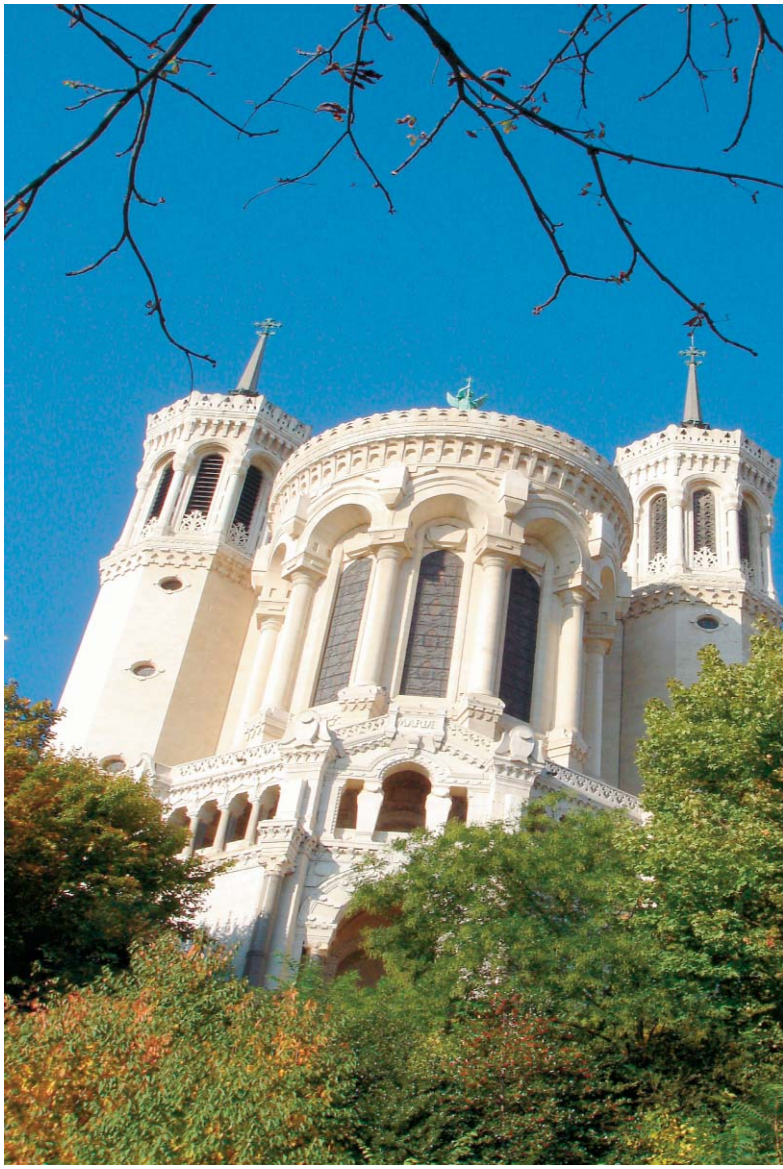
The cover picture is a proposed design for a brochure to promote EMWA. Members are asked for their opinions in a questionnaire enclosed with this issue.

European Medical Writers Association

EMWA 15th Annual Conference

Congrés de Palais, Lyon, France,
Tuesday 2 May to Saturday 6 May 2006

The Executive Committee invites you to attend EMWA's 15th Annual Conference, which will be held in Lyon, France. The venue for our conference is the Congrés de Palais situated in parkland just outside the city centre.



This year sees the introduction of a theme to our conference, which for 2006 is electronic submissions. In addition to the workshops, the conference will include presentations, lectures and discussion forums on the latest advances in electronic submissions, advances that are likely to affect many of our members.

As for the training programme, 42 workshops are available, 33 of which are approved for credit towards the EMWA Professional Development Programme (EPDP). This year will also build on the successful introduction of the advanced curriculum in Malta, and includes some exciting new workshops and discussion forums of interest for medical writers.

Once again, this will be an opportunity to benefit from excellent value-for-money training.

See you there!

Ian Metcalfe

EMWA Vice President

Call for lunchtime discussion leaders

The conference in Lyon will see the return of the popular 'Networking lunches'. For those who haven't been to these before, small discussion groups are arranged to discuss topics of interest to medical writers over lunch. Previous themes for discussion tables have included subjects as diverse as 'Clinical study reports are not boring', 'The medical writer-statistician interface', and 'Medical writing and the meaning of life'. We are looking for volunteers to lead discussions in Lyon. If you would like to lead a discussion, please get in touch with Adam Jacobs (ajacobs@dianthus.co.uk). If you have an idea for a topic, that's great, but don't worry if you are stuck for ideas because we have plenty of suggestions.

From the editor's desk:

Clinical trials – old but not benign

By Elise Langdon-Neuner

The theme of this issue is clinical trials. Clinical trials are as old as the hills or at least the Old Testament according to Susanna Dodgson's article on their evolution published in this issue. Nevertheless today some interventions still remain unevaluated. Take for example parachutes. Gordon Smith and Jill Pell were unable to identify a single trial in their systematic review of randomised controlled trials to determine whether parachutes are effective in preventing major trauma related to gravitational challenge. Alarmed by this oversight, they called for volunteers to participate in a clinical trial to assess the effect of jumping out of a plane with a parachute as against the placebo of 'no parachute' [1]. Although that article was designed to snipe at protagonists of evidence-based medicine, the integrity of evidence secured by clinical trials and of its reporting is of paramount importance to everyone's health.

In clinical trials the new product being tested needs to be tested against something, perhaps logically against no intervention, i.e. no parachute. The idea would then be that the placebo has no effect—however, the matter is not quite so simple. For example, in a clinical trial of dapoxetine (a therapy to increase time to ejaculation), men receiving placebo doubled their time to ejaculation, and did not suffer the side effect of nausea experienced by 20% of the men who received the highest dose of dapoxetine [2]. This is just one example of the well-known "placebo effect", which is one of the more important reasons for today's standard of double-blind, randomised, placebo-controlled trials. Most medical writers will be able to think of a long list of medications that were stunningly successful in open trials and failed miserably against placebo.

Care must be taken to ensure that clinical trials measure what needs to be measured. For example, in testing for lead poisoning, volunteers breathed and swallowed lead in large quantities. Measuring lead in their urine and faeces gave a negative result—not surprisingly, because lead is dangerous precisely because it is not excreted, but accumulates in bones and blood [3]. Failures of clinical trials to detect long-term consequences are increasingly causing pharmaceutical companies to move centre stage, in a gathering storm of lawsuits costing companies hundreds of millions of dollars in payment of claims brought by patients [4].

Not only do we need to know that to be an effective protection for patients clinical trials are properly designed but we also need to know that they are conducted on interventions that patients actually need. Do women need the seven new products for sexual dysfunction (a disease not all experts agree exists) currently being developed? [5]. Why have no entirely new antibiotics been invented since the 1970s? Perhaps the answer is something noted in James Surowiecki's article in the New Yorker, "given the choice between developing antibiotics that people will take every day for two weeks and developing antidepressants that people will take every day for ever, drug companies opt for the latter" [6]. I have heard the same argument applied between vaccines against bird flu and Viagra.

Clinical trials are therefore not without controversies and these affect medical writers too. Medical writers' responsibilities are in the reporting of data from clinical trials to regulatory authorities and to the public. Clarity has not been promoted by the great restrictions that have traditionally been placed upon the divulgence of information to the public about the clinical trials. To combat this problem, the registration of clinical trials was proposed. Two articles in this issue of TWS look into the registration of clinical trials and ask what the medical writer needs to know about registration. Medical journals are reacting to what they see as their manipulation by the industry by dismissing industry-sponsored research with the serious danger that drugs that may help patients are not being prescribed [7]. Accusations frequently mention the inappropriate use of medical writers as ghostwriters of manuscripts submitted to journals. EMWA has tried to bridge the gap between the role of medical writers and medical journals by issuing guidelines (see box on page 5)

Articles in this issue which should further help medical writers in their everyday work include an article that asks whether experience with non-clinical drug development is important for medical writers, another article that gives some intriguing hints on how to do battle with clinical submissions and yet another on how to cope with the electronic Common Technical Document (eCTD). The eCDT is targeted for Europe-wide use by 2009 and is also the theme of the forthcoming EMWA conference in Lyon.

The Write Stuff welcomes suggestions. One has been that we should have more articles about English usage and grammar. In future a greater effort will be made to include at least one article on this topic in each issue. In this issue, we present the first of several articles in which Alistair Reeves will investigate English language myths.

Myths of another kind are explored in Ursula Schoenberg's

From the editor's desk

"codes and quips" article. When I read 'don't let the bedbugs bite' my thoughts rambled on with the quip my children said back to me: 'and if they do, squeeze them tight – they won't come another night'. The article got me thinking about sayings from my own childhood such as 'When one door closes another one opens' and one from an old gardener 'You have to eat a bit of dirt before you die'. As a child, I thought this meant that I shouldn't worry as much about getting dirty as my mother would have done. Now, it seems more like a moral in immunology. I hope that Ursula's article will evoke many reminiscences and favourite sayings to publish in future issues.

Finally, I should like to mention that the authors in this issue come from no fewer than seven countries: Sweden, Switzerland, the USA, the UK, Germany, Austria and Australia. But this is not unusual for TWS, except that the last is the result of a new co-operation with the Australian Medical Writers' Association (AMWA). I am particularly delighted to have received this article. The next issue, in June, promises even more international variety, with its theme of non-native English speakers and translation. Contributions on this topic are very welcome.

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"What should journal editors consider before they publish studies involving animal research ?"

This question was considered in a plenary session at a seminar given by COPE (Committee on Publication Ethics, www.publicationethics.org.uk) in March this year. There is no international standard like the Helsinki agreement applicable to animals. As Angela Turner explained in her article on animal experimental regulations published in TWS (Vol. 13, No. 2, 2004, pages 43-45) researchers submitting papers to a journal are expected to have complied with their own national and local laws, and to have had their work reviewed by the local ethics committee where relevant. Often these regulations will be based on the '3 Rs'

- refinement of experimental techniques to reduce suffering
- reduction of numbers of animals used
- replacement of animals with non-animal methods.

Cultural attitudes towards treatment of animals however varies. The pallet ranges from the French (not the British) who are apparently the most sympathetic towards animal welfare among EU nationals and the Chinese who do not have national regulations for animal welfare.

Journal editors are faced with a problem when manuscripts are received from another country describing experiments conducted on animals in a manner acceptable for that country but unacceptable for the country where the editor resides. An example was given at the seminar where rats had been left to die after experiments had been completed rather than being killed immediately after the experiment. The editor refused to publish this research. The conclusion reached at the COPE seminar was that editors should judge experiments by their own ethics standards when deciding whether to publish. But they may face the dilemma that publication of these experiments could be valuable in furthering research in humans. A point was also raised as to whether society owes a debt to those who partake in trials to publish the study results. The point is probably more applicable to human trial participants in negative trials but is one that is not currently taken into account in publication ethics.

Medical writers might not be party to decisions relating to methods used in experiments involving animals but we do have some control over words that appear in documents reporting the experiments. Here attempts at euphemisms can be deceitful and distasteful.

The word 'sacrifice' was widely used to describe the killing of animals after an experiment until stylebooks bitterly protested against it. Neville Goodman and Martin Edwards in their book *Medical Writing a Prescription for Clarity* write "A sacrifice is a religious rite, or (*COD*) the giving up of a valued thing for the sake of another that is more worthy or more important or more urgent. Do not use sacrifice when you mean kill. A similar debasement is likely to happen to assassinate if the media persist in applying it to the murder of hoodlums and terrorists". I have yet to come across assassinated rats in the documents I edit but 'euthanasia' has crept in. Webster's dictionary defines 'euthanasia' as "the act or practice of killing or permitting the death of hopelessly sick or injured individuals in a relatively painless way for reasons of mercy". The spirit of this definition is hardly that the person responsible for the euthanasia also caused the sickness or injury. The truth is that animals are killed and this is the word to use. Murder and homicide only relate to humans and slaughter is to kill animals for food or to kill in a bloody and violent manner.

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Message from the President

by Michelle Derbyshire

If you have never been to an EMWA conference you are definitely missing out. This year Lyon is set to be our biggest conference yet, with our first venture into a conference centre. The conference theme is the electronic Common Technical Document, a hot topic for any medical writer at the moment and definitely not one to miss! This year we are also expanding what we offer outside of the workshops, including discussion forums and guest speakers. To maintain the great value that EMWA constantly hopes to offer to its members these extra offerings are all included in your registration fee.

You will definitely learn a lot if you join us in Lyon. EMWA conferences are always great places to network, and of course fun too. You just have to book yourself onto a sedate boat trip around a quiet harbour to find that life with EMWA can be an adventure although I'm assured that this year the planned boat trip is harmless-I'm certainly going to give it another go.

What is most impressive about EMWA is its vitality (everybody actually survived the boat trip in Malta) and in this issue of TWS members are encouraged to take a more active part in EMWA. The Executive Committee recognises that your input is continually needed to preserve this vitality by bringing in new ideas and maintaining the association's success. Read Ian Metcalf's 'Itching to play a role' article, …and give it a shot.

I'm afraid that I'm going to have to keep my message short and sweet this time as I have a very demanding new member of the family taking up rather a large amount of my time.

I hope to see you in Lyon.

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Journal instructions to authors are linking EMWA Guidelines

www.emwa.org is not the only place in the Internet where you can find EMWA's guidelines on the role of medical writers in peer-reviewed publications. Journals are beginning to recognise EMWA as a responsible professional body by linking our guidelines on the role of medical writers in developing peer-reviewed publications to their instructions to authors on the Internet.

The BMJ [1] states

"The role of professional medical writers must be transparent. Please name any professional medical writer among the list of contributors to any article for the BMJ (not only original research papers), and specify in the formal funding statement for the article who paid the writer. Writers and authors must have access to relevant data while writing papers. Medical writers have professional responsibilities to ensure that the papers they write are scientifically valid and are written in accordance with generally accepted ethical standards." A link to the guidelines is given [2].

Arthritis Research & Therapy [3], which is an open access BioMed Central publication, has an in-text link and states

"The involvement of medical writers or anyone else who assisted with the preparation of the manuscript content should be acknowledged, along with their source of funding, as described in the European Medical Writers Association (EMWA) guidelines on the role of medical writers in developing peer-reviewed publications. If medical writers are not listed among the authors, it is important that their role be acknowledged explicitly. We suggest wording such as 'We thank Jane Doe who provided medical writing services on behalf of XYZ Pharmaceuticals Ltd.'"

To add credibility to my status as a medical writer I now add 'member of the European Medical Writers Association' in parentheses after my name in the acknowledgements section of manuscripts I submit to journals on behalf of authors. This makes journals aware of our association and its good intentions. I would be interested to receive members' views on mentioning EMWA in this context (please write to me at langdoe@baxter.com).

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Templates: Taking the first step towards eCTD submissions in Europe

by Peggy Boe

The Common Technical Document (CTD) has been the mandatory marketing application format for submissions in the European Union (EU) since 2003. At a recent Drug Information Association (DIA) conference in the United States, a representative of the European Medicines Agency (EMEA) announced plans to accept submissions in the electronic Common Technical Document (eCTD) format without accompanying paper beginning late in the 4th quarter of 2006 [1]. While there are several national authorities in Europe accepting eCTDs, most still require paper as the archival format. With this in mind, sponsors should continue to carefully discuss submission format with the appropriate regulatory authority before finalizing any decisions on whether to submit in paper or to take the next step and submit electronically [1]. Europe has targeted late 2009 for all regulatory authorities to have the capability of accepting "paperless" electronic submissions.

"e" stands for more than just "electronic"; it represents inclusion of a backbone based on the extensible mark-up language (XML).

There is a substantial difference between the eCTD and the paper CTD beyond what most people think of as an electronic submission. In the case of the eCTD, the "e" stands for more than just "electronic"; it represents inclusion of a backbone (similar to an overall submission table of contents [TOC]) that is based on the extensible mark-up language (XML). Creation of the XML backbone requires special skills or use of software typically beyond the scope of regulatory and medical writers. More often than not, sponsors are using publishing groups (either internal or outsourced), who are most knowledgeable in the eCTD software, to import final submission documents into the appropriate place in the XML backbone. Writers may be called upon to assist in determining the appropriate placement of individual documents based on content. Also, writers can facilitate the electronic-publishing process overall by standardizing the way documents are formatted, to make them ready for publishing. Ultimately, every narrative document in the submission (with the exception of original signature pages and certain labelling documents) needs to be submitted in PDF format with extensive navigational aids included (fully hyperlinked and bookmarked). Writers should understand what can be done to make life easier for themselves and others who process the documents.

The first and most important step any regulatory submission writer can take towards preparing documents for an eCTD is to use a submission-compliant template to create each document. But what exactly is a template? According to the Merriam-Webster Online Dictionary, a template is defined as, among other things, "something that establishes or serves as a pattern" [2]. In the case of a word-processed document, a template could be a basic outline for the writer to complete, which helps with content but does nothing to support compliance with format specifications. As a general international guideline, "the display of information should be unambiguous and transparent, in order to facilitate the review of the basic data and to help a reviewer become quickly oriented to the application contents. Text and tables should be prepared using margins that allow the document to be printed on both A4 paper (EU and Japan) and 8.5 x 11 papers (United States [US]). The left-hand margin should be sufficiently large that information is not obscured by the method of binding. Font sizes for text and tables should be of a style and size that are large enough to be easily legible, even after photocopying. Times New Roman 12-point font is recommended for narrative text. Every page should be numbered, according to the granularity document"[3]. Those recommendations apply to paper or electronic submissions, because even with electronic submissions reviewers want the option of printing and binding portions of the submission.

Submission-compliant templates for creating each document are important for a medical writer in preparing documents for an eCTD.

US guidance offers more specifics on format; for example, they recommend using nothing smaller than 9-point font in in-text tables, and settings are specified for the PDF conversions [4]. without standards, the format of a document is largely dependent on personal preference and can vary widely from one document to another, depending on the writer. What is not transparent to the writer is that MS Word applies its own "Normal.dot" file to every document. The Normal.dot file applies three unnumbered heading styles

>>>

>>> Templates for eCTD submissions

and a paragraph text style (also called "Normal"), pre-programmed for the writer to use consistently (.dot is the file extension for the Word Document Template associated with MS Word for Windows). Working within a Normal.dot template requires a writer to build additional styles from scratch, using whatever font sizes and styles, margins, indents, list styles, etc, that the writer prefers. Depending on the settings, MS Word may arbitrarily create new styles for the writer. Additional styles are frequently imported from other documents whenever the writer copies and pastes from another source; thus, the format of documents generated by different writers may vary immensely. MS Word will also "help" the writer format the document whether help is wanted or not, in ways that add significant time and effort to the writing and quality control processes as the writer tries to "fix" what MS Word has done automatically.

MS Word applies its own "Normal.dot" file to every document.

Document styles are important for reasons other than aesthetics and compliance with font and margin specifications. To be electronic-submission compliant, hyperlinks and bookmarks are required for the entire TOC and elsewhere. If inserted correctly, heading styles will automatically generate the TOC and automatically create the TOC hyperlinks and bookmarks when the document is converted to PDF. If inserted incorrectly, those hyperlinks and bookmarks must be created manually by the publishing group. Therefore, an outline alone with the Normal.dot template supplied by MS Word does not suffice to ensure compliance with submission-ready formatting specifications and results in a lot of extra work for the writer or publishing team.

Sponsors should use a set of templates programmed to conform to agency specifications to resolve MS Word problems.

The solution to this problem is for sponsors to adopt a policy of using a set of templates that are programmed to conform to agency specifications. These templates could be developed in-house, but that requires a significant amount of time and effort. Therefore, many sponsors are opting to use software and service providers who have already developed templates and who will maintain the templates as guidances and regulatory requirements change. Such customized .dot templates can supply guidance-compliant styles and additional goodies, such as tools to prevent MS Word from automatically changing numbered lists, to repair unwanted styles, to facilitate printing on either 8.5 x 11 inch letter size or A4 paper without shifting the text on any pages, and to automatically populate repeatable text. If a sponsor does decide to purchase a set of templates, the features and help aids should be evaluated to see whether they include adequate features to make the writing process easier.

Templates can also assist with creating guidance-compliant content by keeping writers informed of recommended text for inclusion in various sections of the CTD. The inclusion of writing aids, such as instructional text, can help ensure inclusion of appropriate content. In some templates, instructional text can be deleted or hidden, either totally or in pieces as a writer completes each section. As an additional bonus, templates can help writers prepare content according to the required CTD granularity. International Conference on Harmonisation (ICH) guidelines describe options for CTD granularity, and sponsors are encouraged to submit documents using finer levels of granularity when transitioning from paper to eCTD submissions to benefit from the advantages of submission lifecycles. One ICH guideline specifies that "when relevant information is changed at any point in the product's lifecycle, replacements of complete documents/files should be provided in the CTD and eCTD." Furthermore, a document is defined as "…a set of pages, numbered sequentially and divided from other documents by a tab" (for a paper submission), and "a document can be equated to a file for an electronic submission. The granularity of the paper and electronic submissions should be equivalent…In an electronic submission, a new file starts at the same point at which, in a paper submission, a tab divides the documents"[5]. Therefore, the replacement process is simplified if sponsors take advantage of using the highest level of granularity with the initial submission, and templates provided in full granularity ease the writer's burden of determining the breakdown of once-familiar larger documents.

Depending on settings, MS Word may arbitrarily create new styles for the writer.

Another granularity specification that writers should be aware of includes a difference between paper and eCTD TOCs: the various TOCs for each CTD module (Modules 2 to 5) are necessary in a paper submission but are not required in an eCTD. The XML backbone replaces the need for TOCs in those modules. Be careful not to misinterpret that point; eliminating modular TOCs does not mean that individual documents do not require TOCs. Some common sense should prevail when generating any document. There is no formal definition of what constitutes the need for a TOC. In general, if a document has multiple sections and spans more than a couple of pages, including a TOC may be a good idea. Always keep the reviewer in mind and simplify the reviewer's ability to navigate through an individual document. Under no circumstances should a large document be submitted without a TOC; a refusal to file might result.

Templates for eCTD submissions

Templates available on the market today may or may not include TOCs for various documents. This is an example of how a sponsor's internal regulatory knowledge (and again, common sense) is important when implementing templates for part or all of the submission documents. The other knowledge-based factor that cannot be included in any package of templates is the decision process appropriate for what content to include (and in what granularity) for a particular product, development programme, and type of submission. By no means should templates be considered the replacement for a sponsor's internal regulatory affairs knowledge base.

In conclusion, templates can improve document quality through consistent, regulatory-compliant formatting, can add to the understanding of recommended content, and can decrease the amount of time normally spent on formatting and quality control, thereby allowing writers to focus on the science and interpretation of data. eCTD submissions begin with document generation and preparation; document generation and preparation begin with a solid template.

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Peggy Boe

has been in the industry for almost 9 years and participates as a presenter with the DIA Medical Writing programs and as a core-credit workshop leader with AMWA. Peggy will present a 3-hour non-credit workshop on the eCTD as well as a 1.5-hour open session on "Templates, Technology, and Document Granularity" at this year's annual EMWA Conference in Lyons, France. In addition, as a primary sponsor of the conference, Image Solutions, Inc. (ISI) has been invited to provide an open session demonstration of templates and other eCTD technology following Peggy's session. Please join them for this wonderful opportunity to learn how you can ease the process of transitioning to the eCTD.

Some English scientific words?

Starting simply.

Chasing a chimera

Greek (chimaira): a creature that merges features of more than one beast. The mythical Greek Chimera had the head of a lion, body of a goat and hindquarters of a dragon. Because the uncertainty of her form made her difficult to paint she has come to represent an impossible idea or hope.
English scientific: a chimera is an organism comprising tissues of two or more genotypes.
NB a chimere (not chimer) is a bishop's upper robe.

Almost as mythical is the dodo.

As dead as a dodo

Portuguese (doido): fool or mad in modern Portuguese. In archaic Portuguese it was the name for a "simpleton".
Scientific English: a common name for the extinct bird *Didus ineptus*. Although Dutch settlers were responsible for the dodo's extinction Portuguese sailors were the first to visit Mauritius in 1505. By sometime between between 1681 and 1693 not one dodo was left, except a stuffed one at the Ashmolean Museum in Oxford. But only until 1755 when the museum director decided it was a bit tatty and had it thrown on a bonfire. An employee tried to rescue it from the fire but was only able to save its head and part of a limb. Hence we know little about this flightless pigeon and had it not been brought to fame by a character in Lewis Carroll's *Alice's Adventures in Wonderland* probably none of us would be saying "as dead as a Dodo" today. All is no longer lost since Dutch geologists found a cache of dodo remains in December 2005 raising hopes of reconstructing the bird and its habitat.

And really quite confusing is chow.

Chow

Chinese (chiao): dough filled with meat. Chow Chow (*Chau-chau*): a Chinese dog with a tail curved over its back. Chow-chow (pidgin English): a Chinese mixed preserve.
Scientific English: John Kirkman in an article in the BMJ (1996;313:1321-3), which urged contributors to medical journals to confine themselves to forms of English that are easily understood, wondered whether a Frenchman would understand "All animals were fed standard laboratory chow". The Frenchman's initial dictionary searches would lead him to conclude the animals were eating British English grub or nosh (with deeper searches he would find the French equivalent bouffe). A British soldier might be even more confused though as chow is a military synonym for cat.

And with that thought 'chow' as the Italians would say.

Battling with clinical submissions: War rooms and other tricks of the trade

by Julia Forjanic Klapproth

Among the gamut of documentation one works on as a medical writer, I would argue that a submission dossier is one of the most interesting – and the most challenging. The summary documentation reflects a compilation of a broad spectrum of data and information and culminates in the clinical overview (CO). In this 30-page report, the author has the task of condensing many different messages from numerous studies, and often years of research, into a single, concisely written document with a consistent take-home message. The CO is supported by two broader summary documents, the summary of clinical efficacy (SCE) and the summary of clinical safety (SCS). These provide a comprehensive summary of all data that is being provided in the dossier, looking at the results both on a study-by-study basis as well as in an integrated, across-study manner (in as far as this is possible). But preparing a dossier is rarely just a writing task: it is a multifaceted activity often requiring skills in diplomacy, team management and project planning.

Preparing a dossier is rarely just a writing task

A writer working on a submission project is frequently faced with project teams of individuals from different functions and departments, each with a slightly different agenda. Although it would seem obvious that everyone is working towards a common goal, in the midst of the game, one often wonders if these individuals are all on the same team! And as the writer your job is to cull the necessary information and messages from each of these functions and prepare a document with a unified message. More often than not it falls to the medical writer to mediate and bring the people together in some way – to find agreement on what needs to be communicated.

Every team I have worked with has started by plunking down a perfectly designed time line

As someone who basically goes from one submission dossier to the next, and on more than one occasion has a couple of submission projects running in parallel, I've developed a few survival techniques for making a smooth ride out of what could otherwise be a bumpy one. It isn't really magic to figure these things out. It is more a matter of learning from experience and understanding human nature.

The first hurdle to overcome often presents itself at the very first meeting with a project team, and comes in the form of the project plan. Every team I've ever worked with has always started by plunking down a perfectly designed time line for preparing the dossier in question, and they sit about and stare at it somewhat like a mother at her newborn infant. It is a holy thing, and they are incapable of even imagining that there might be any kind of slippage in that preciously formed plan! But there will be. There is always slippage in every plan. And as the person who is going to be expected to meet deadlines at the end of that plan when it starts jumping around like a cat on hot coals, you'll be doing yourself a favour to point this out to the team right at the beginning. Now don't get me wrong. Don't get all holier-than-thou about the issue or be too dogmatic. Just make it a point to gently suggest to the team that there should be contingency plans in place for adjustments to the plan when things start slipping. Be ready to smooth down ruffled feathers and wipe away some of the spittle as people have a knee-jerk reaction to your suggestions, but hold your ground. The team will respect you for it later when the slippage sets in.

It makes sense to develop the framework of the SCE and SCS before preparing the CO

So, now that you've managed to develop a plan that is still wildly unrealistic, but with a little more breathing room, it's time to get writing. Where do you start? Generally it makes good sense to begin by developing the framework of the SCE and SCS before preparing the CO. This may seem obvious to some of you, but you would be surprised how many teams I have encountered who actually think I should finalise (yes, finish!) the CO before starting with the SCE and SCS. The rationale for doing it as I suggest is that the CO not only condenses the story, it is the place where we're meant to discuss and highlight points of contention in the data or clinical programme. And it is very frequently in the course of writing the SCE and SCS that these points come to light. In the process of comparing data across studies, patterns arise or discrepancies become apparent (which of course is exactly the purpose of looking at the data this way). It is only then, as the team debates how to present these data in the SCE or SCS and what exactly they need to communicate about them, that the foundation is laid for what will be presented and discussed in the CO. So do yourself a favour. To save yourself from having to rewrite the CO, advise the

Clinical submissions: Tricks of the trade

team that they should begin with the SCE and SCS and then distill the CO from those documents afterward.

OK, so you've put all your data together into your summaries and it's time to start crafting the CO. One of the first things you should do is find out if there are any guidelines from the authorities to whom you will be submitting the dossier on your particular indication or treatment regimen. Just go to the website of the agency in question and do a search for your therapy and the indication. If there are any guidelines, these need to be addressed in the CO, referring to how the clinical programme either did (or did not) comply with these. Then, make a bulleted list of the risks and the benefits of your compound or device. This will help you to make decisions on what data need to be presented in the CO directly, and how to present it all as a succinct, cohesive story. Remember, this is where you pull the information together to tell the story. Each of the pieces needs to fit together to make a complete picture. By taking the time to define up front what pieces you have, you can more effectively slot them into place as you develop the story.

There is no requirement to list all adverse events

Lastly, make sure you have a copy of the most recent version of the product label that the company is intending to submit. All claims and statements in the label need to be supported by statements in the CO. Now, don't misunderstand this to mean you need to have all the data itself in the CO. This is one of the few fights I do choose to pick (I pick them carefully) with a project team. Don't be surprised if you encounter a member of the team from pharmacovigilance or regulatory departments who insist that it is a requirement to list all adverse events in the CO because these are given in the label. This is not a requirement. As long as the main statement supporting the claim in the label is made in the CO with a cross-reference to where the complete data can be found in the SCE or SCS, nothing more is needed. And to be quite honest, there isn't space in the CO for more than that.

Right, so now you have pretty well-developed drafts of the different parts of your dossier. It's time to finalise them and get that puppy off to the agency. To do that, however, you will need buy-in from each different function on the team. Have you ever tried getting a bunch of people to review a document and come to agreement on the final wording by email? It can be at worst a nightmare, and at best a long, drawn-out procedure. Enter the "war room" strategy, a concept taken from US President Bill Clinton's election campaign "rapid-reaction centre".

Basically, you bring the key decision makers from each function on your team and you lock them in a room until they come to agreement on every line in the file. Rule Number one is that once they agree on what is final, there is no changing their minds after they leave the room. This sounds more gruelling than it is. Essentially, this boils down to human nature. The most efficient way to resolve points of contention is to have the people involved discuss it face-to-face. By bringing the team together, everyone has the opportunity to present their perspective on any outstanding issues and the group can come to a decision together. The primary advantage of this is that you as the writer are not left with a collection of conflicting opinions and having to find a way to implement them while making everyone happy. As the team is responsible for the final content and message of these documents, they need to agree among themselves on how to resolve these conflicts. And sitting around a table together is the best way to make it happen.

You lock the key decision makers on your team into a room until they come to an agreement

So there you have it: a few key things to keep in mind when preparing a clinical submission dossier. Obviously when you get deeper into the nuts and bolts of these documents there are numerous possible pitfalls. But in general it all boils down to keeping your head, standing your ground and being pragmatic. Only pick the fights that matter, so think about what it would mean if you don't get your way on a given point before you dig in your heels. And don't forget to have fun.

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Why does The Write Stuff look different?

Every so often journals need a makeover. The Write Stuff is no exception. There are two reasons for the new design you have encountered on opening this issue. The first reason is that The Write Stuff was beginning to look quaint or, less kindly, jaded. This is an inaccurate representation of EMWA's work and its membership. We are a dynamic organisation, continually moving forward and keeping medical writers at the forefront in the rapidly changing field of their work. The second is that the old design was wasteful of space. More space is needed to print all the good articles that are being received and for information relevant to medical writing and EMWA.

Some readers will like the new design. Others will prefer the old one or think the new one could be improved further. Whatever you think your views and suggestions are valued. I look forward to receiving an email with your feedback at **langdoe@baxter.com**.

Experience of nonclinical drug development – is it important for a medical writer?

by Carin Larsson-Backström

An EMWA workshop not only gives you valuable knowledge in the workshop topic. The exercise as a practicing component included in most of the workshops also gives you a possibility to learn more about the other participants. Recently, I attended the workshop on "The Investigator`s Brochure" (IB). The participant profile was medical writers with at least 1 year of experience in the pharmaceutical industry. The exercise consisted of the preparation of a mini-brochure based on actual data given out as a pre-course assignment. During the workshop, we worked in teams to decide about the salient findings to present in an IB. From the comments made by some of the participants within my team, it was obvious that for those who did not have very much experience in nonclinical drug development, it would be difficult to fulfil the obligations stipulated by the International Conference on Harmonisation (ICH) guidelines.

Experience with nonclinical as well as clinical R&D makes it easier to pick out what the investigator needs to know

According to the ICH guidelines [1], the IB should highlight the significant physical, chemical, pharmaceutical, pharmacological, toxicological, pharmacokinetic (PK), metabolic, and clinical information available that is relevant to the stage of clinical development of the investigational product. In regard of the nonclinical studies, the summary should address the methodology used, the results, and a discussion of the relevance of the findings to the investigated therapeutic, and the possible unfavourable and unintended effects, in human. Furthermore, the relevance of the nonclinical information to the proposed human dosing should be addressed, and comparisons should be made in terms of blood/tissue levels rather than on an mg/kg basis. For those of us having experience of several years from nonclinical as well as clinical Research & Development in the pharmaceutical industry, it is not very difficult to pick out things that an investigator needs to know.

Experience of nonclinical drug development is valuable for a medical writer in quite a lot of similar situations. Certainly it should help when writing the Nonclinical Overview and Summary incorporating the new Common Technical Document (CTD) format. The Nonclinical Overview should present an integrated and critical assessment of the pharmacologic, PK, and toxicologic evaluation of the pharmaceutical [2, 3]. Any deviation from existing relevant guidelines [4, 5] on the conduct of the studies should be discussed and justified. The Good Laboratory Practice (GLP) status of the studies submitted should be commented. Studies conducted to establish the pharmacodynamic (PD), PK and toxicokinetic effects, the mode of action, and potential side effects, should be evaluated and consideration given to the significance of any issues that arise. The Integrated Overview and Conclusions should arrive at logical, well-argued conclusions supporting the safety of the product for the intended clinical use. The same ICH guidance [3] also assists the author in the preparation of written summaries of nonclinical pharmacology, PK, and toxicology in an acceptable format. However, no guideline can cover all eventualities, and common sense and a clear focus on the need of the regulatory authority assessor are the best guides to constructing an acceptable document.

The preparation of a Clinical Development Plan (CDP) also involves many considerations concerning the nonclinical drug development. The CDP describes a schedule of studies designed to obtain a product licence and should follow the directions described in the ICH guideline (E8), "General considerations for clinical trials" [6]. To develop new drugs efficiently, it is essential to identify characteristics of the investigational medicine in the early stages of development and to plan an appropriate development based on this profile. Before any clinical trial is carried out, results of nonclinical investigations or previous human studies should be sufficient to indicate that the drug is acceptably safe for the proposed investigation in humans. Important considerations for determining the timing of nonclinical studies with respect to clinical trials include: the proposed duration and total exposure in individual patients, characteristics of the drug (e.g. long half-life), disease or condition targeted for treatment, use in special populations (e.g. women of childbearing potential), and route of administration. The selection of the initial human dose and safe duration of exposure should be sup-

No guideline can cover all eventualities but common sense and a clear focus on the assessor's needs are essential

ported by sufficient information from early nonclinical studies, which also should provide information about physiological and toxicological effects of a new drug. The basis and direction of the clinical exploration and development rests on the nonclinical PK and pharmacology profile, including information such as mechanism of action, dose-response or concentration-response relationships and duration of action, routes of administration, systemic general pharmacology and studies on absorption, distribution, metabolism and excretion. It seems to me obvious that, although most of these considerations will be executed in the Nonclinical Overview, it will help a great deal for a medical writer to have experience and understanding in the preclinical drug development when preparing a CDP.

Quite a lot of knowledge of PD and PK is required for optimal reporting of these studies

Similar considerations concerning the nonclinical drug development as discussed for the CDP are also of importance for the planning, i.e. writing the study protocol [1], and reporting of the clinical studies [7] to be conducted according to the CDP. The variables of concern include:

- the selection and timing of dose,
- duration of exposure,
- route and mode of administration,
- methods of measurements of drug concentrations,
- the specific efficacy and safety variables to be assessed and laboratory tests to be conducted,
- their schedule (days of study, time of day, relation to meals, and the timing of critical measures in relation to test drug administration),
- the methods of measuring them and the appropriateness of the measurements.

These concerns are related in particular to the phase I, human pharmacology studies, starting with the initial administration of an investigational new drug into humans. The analytical methods used, the PK models and the derived parameters should be similar to those used in the nonclinical studies. Reporting the human pharmacology studies requires, however, pharmacological, and in particular, PK experience not only in the consideration of the nonclinical results but also of those from the phase I studies. For the correct reporting of the results and to draw the most correct conclusions of the PD and PK studies, and studies relating drug blood levels to response (PK/PD), requires quite a lot of knowledge of, and preferably some experience in, these specialities.

It helps to have experience in nonclinical drug development also when linking to the nonclinical issues relevant for humans, on writing the CTD Clinical Overview and Summary [8]. Similar considerations are valid when preparing the Summary of Product Characteristics (SPC; 9), which should be based on the Clinical Overview.

Experience of nonclinical drug development, including knowledge and preferably experience of PD and PK, is therefore important for a medical writer. It is definitely of help when writing all the documents mentioned: the IB, the nonclinical and clinical overviews and summaries incorporating the CTD format, the nonclinical and clinical study reports, the CDP and the SPC. When writing these documents, it is important for any medical writer, and in particular for those with no or only limited experience in nonclinical drug development, to establish team building early, and to decide the role for the medical writer. Why not also use the network of the many talented members that EMWA provides, to establish collaboration between the EMWA members?

Why not use the EMWA network to establish collaboration between members?

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Language Quiz

In which of the following counties is Roman writing the official form of writing and why?

- Korea
- Vietnam
- Thailand
- Japan

Answer in box on page 21

Trial registration: What do writers need to know?

by Elizabeth Wager

Trial registration: the current situation

The International Committee of Medical Journal Editors (ICMJE), which comprises the editors of some of the world's most influential medical journals, have added an extra hurdle for publication. Since September 2005, they have refused to publish trials in their journals unless they have registered. This policy was announced in late 2004 together with criteria for suitable registers [1]. Up to mid-2005 there was a grace period during which trials could be registered retrospectively, i.e. after they had started. But trials that started recruiting patients since mid-2005 must now be registered prospectively, i.e. before recruitment begins, to meet the editors' criteria.

The World Health Organization (WHO) has brought together editors and registration experts to agree a minimum data set required for registration [2, 3]. However, pharmaceutical companies have raised objections about certain items they consider sensitive and would prefer not to release at trial initiation. It would have been tidier if the editors had agreed on what information they required before making registration compulsory — but, for the moment, companies must do their best and hope that their registrations will be deemed adequate if they choose to submit results to the ICMJE member journals.

How did we get here?

The idea of trial registration was proposed around 20 years ago [4]. The main proponents were people compiling systematic reviews who were concerned that these would be biased if some trials remained unpublished. It was even suggested that underpublication of results constituted research misconduct [5]. In the 1990s one or two pharmaceutical companies and other organizations established voluntary trial registers [6], but few others followed their example and, up to the early 2000s, the US industry association, PhRMA, opposed registration despite US legislation calling for registration of trials in serious and life-threatening conditions. However, growing public concern about systematic nonpublication of unfavourable findings and legal action against Glaxo SmithKline focusing on nonpublication of safety data about its antidepressant Seroxat (which was settled out of court), increased the stakes. The demands of the ICMJE editors were the first to be accompanied by a sanction companies really feared, namely exclusion from the world's most respected medical journals.

What register should I use?

At present, two registers meet the editors' criteria: ClinicalTrials.gov and the ISRCTN (International Standardized Randomized Clinical Trial Numbering) scheme. Clinicaltrials.gov is run by the US National Library of Medicine. It was initially established in response to legislation requiring the registration of US trials into serious and life-threatening conditions. When the editors' first announcement appeared, there was some consternation that ClinicalTrials.gov would accept only trials of products being considered by the FDA. Companies that had not applied for a US licence, or investigators studying other kinds of interventions, could not register their trials. ClinicalTrials.gov quickly relaxed its entry criteria, but this has not entirely allayed concerns that it is funded by the US government and there is no guarantee over its future policies or funding.

The ISRCTN system also caused debate when the editors first published their criteria, since these stated that acceptable registers could not be run by commercial companies. The BMJ was concerned that this requirement ruled out the ISRCTN since it was then owned by the Current Science group (a commercial publishing company). The BMJ therefore issued a slightly different statement from the rest of the ICMJE [7]. However, since then, the ISRCTN has been transferred to a not-for-profit organization. Since ISRCTN is independent and self-financing, it charges a fee for registration, but this may be waived in cases of hardship and for trials from resource-poor areas. An attempt was made to secure EU funding for the ISRCTN system, but it failed.

The European Medicines Evaluation Agency (EMEA) registers all trials submitted as part of licensing applications, but these data are kept confidential so the so-called EuDRACT database does not meet the editors' requirements [8].

Which journals are affected?

Initially, the requirement applied only to the journals edited by the ICMJE committee members (not to all journals that endorse the ICMJE Uniform Requirements). However, other journals are now following suit [9]. Anybody involved with publication strategies should keep a watchful eye on journals in their area.

Why do we need trial registration?

The main aim of registering trials is to ensure they are published responsibly. Findings that are statistically significant or that favour the sponsor's product are more likely to be published than negative ones, and such publication bias can skew the results of meta-analyses as can undetected redundant publication [10]. Unambiguous study identification should reduce these effects and make it easier to call companies to account for unpublished studies. Another possible benefit of public trial registers is that they can help patients identify studies for which they might be eligible and thus help recruitment. WHO is also encouraging national trial registers as a means for countries to develop local health research infrastructure. Public access to details of trial design such as primary endpoints should also raise reporting standards and prevent selective or biased reporting. The EMWA guidelines already suggest that writers should have access to the protocol when preparing reports [11], and trial registration should make such key information readily available to journal reviewers and interested readers.

Another argument in favour of registers is that they will allow researchers to see what other trials are underway and therefore avoid duplication. However, others argue that knowledge of development plans and full details of trial designs could reduce competitive advantage. Commercial companies and academic institutions may therefore be reluctant to make full details available at an early stage. This had led to discussions about a lock-box system under which sensitive details of trial design are entered at the start of the study but only made public later. This proposal seems unlikely to find favour from the journal editors and WHO, but it may be a useful compromise if companies refuse to release full details.

What about trial results?

Trial registration should not be confused with posting results on websites, although these are often discussed together. To achieve its goal of preventing under-publication, registration must be accompanied by a commitment to publish results of all trials [12]. Some companies, and the US industry association PhRMA, have already established websites for this. However, it is not yet clear whether journals will regard such postings as prior publication — so this route may be reserved for studies that are not being submitted to peer-reviewed journals. It seems likely that the ICMJE will agree that posting a summary (e.g. using the ICH E3 summary format from clinical trial reports) is analogous to conference abstracts and therefore will not affect full publication in their journals. However, companies do need to be cautious until the editors issue a definitive statement. On a brighter note, preparing the website summaries has created opportunities for writers in at least one company which decided not to use summaries from existing reports.

Conclusions

Trial registration is now a fact of life for anyone hoping to publish a clinical trial in one of the major medical journals. It is likely to spread to other journals. To achieve its aims, trial registration needs to be linked to a commitment to publish results. Registration may raise the standard of reporting clinical trials and might even create a few extra jobs for medical writers!

Affiliations / Competing interests

Liz Wager is a member of the WHO Scientific Advisory Group on trial registration. She has also served on an advisory board for ISRCTN. She used to work for Glaxo Wellcome, which was the first company to establish its own trial register. She has also advised various companies about trial registration strategies.

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What are your FOMs?

A FOM is a frequently used word that we always misspell (FOM = frequent occurrence misspelling). Most of us will have five to seven of these and according to Richard Bell they will account for 60% of our spelling mistakes (*Writing Magazine* Christmas 1993). What about a spellchecker? You say. Richard Bell is not very enthusiastic about spellcheckers partly because throughout a travel article he had written his checker endeavoured to persuade him to change Eiffel Tower to offal Tower. A solution recommended by some American researchers is to carry around a prompt list but Bell thinks you might feel rather foolish flourishing your list in front of colleagues. One alternative he suggests is to memorise a phrase like "accidents occur on occasions" to help you spell each of these words with a double c. Another is to read more so that you visualise the words on a page and recognise the word's odd shape when it is misspelled.

Transparency in disclosure of clinical trial information

By Ruth O'Halloran

Unfortunately we live in a society where loss of trust is a recurring theme: loss of trust in government, religion, the law… In terms of conduct of clinical research, loss of trust is not surprising considering recent scandals associated with the pharmaceutical industry, which have also resulted in a loss of trust in government agencies such as the Food and Drug Administration (FDA). During 2005 tremendous change was instigated to affect a significant improvement in transparency and accountability of how clinical research is conducted and reported.

Background

Evidence-based healthcare is dependent upon published research—where else would decision or policy makers get their information? However, we constantly read that medical literature is distorted by publication bias. Publication bias arises from differential reporting of study results depending on the direction and strength of the findings; therefore, entire studies may fail to reach publication, or specific results within a study may not be reported (selective reporting) because of the nature of the findings. Often there are reasons why results from clinical research may fail to reach publication, some of which include: null results; not an important result; unfavourable results; sponsor has control of data; analysis incomplete; study incomplete; rejection from journals. This results in publication bias, which has negative effects on science (redundant publication of positive findings; wasteful duplication of research) and medical practice (review articles may be misleading when they are only based on some of the evidence). Moreover, entities conducting clinical research have an ethical responsibility to trial participants to report the findings from their research.

Change: why now?

In recent years numerous guidelines have been developed in an attempt to improve the quality of publications and promote good publication practice [1-3]. In September 2004, the International Committee of Medical Journal Editors (ICMJE), which comprises the world's most influential journals (see Table 1), stated that, as a condition of consideration for publication, they will require proof that all clinically directive trials (primarily phase 3, excludes phase 1) were registered in a public trials registry prior to when the first subject was enrolled [4]. What can perhaps be counted as the most significant event on the road to eliminating publication bias occurred when this became a mandatory requirement for manuscripts submitted to ICMJE member journals for clinical trials starting on or after 1 July 2005. All clinical trials ongoing on this date were required to be registered on or before 13 September 2005. While this requirement is only for ICMJE member journals, there is little doubt that other journals will follow suit.

Clinical trial registries

The rationale for registries was to increase subject recruitment (inform patients and clinicians about recruiting trials), to complete the evidence base by eliminating publication bias, and to reduce duplication of effort in research.

In the influential September 2004 statement, the ICMJE endorsed the US National Library of Medicine sponsored registry: www.clinicaltrials.gov. In their July 2005 follow up statement [5], the ICMJE insisted that registration of a clinical trial should comply with the World Health Organisation (WHO) minimal data set, which contains 20 fields [see www.who.int/ictrp/en for details].

Currently there are only two registries accepted by the ICMJE: www.clinicaltrials.gov and www.isrctn.com (the

Table 1: International Committee of Medical Journal Editors (ICMJE) Member Journals

ICMJE Member Journals
Annals of Internal Medicine
British Medical Journal
Canadian Medical Association Journal
Croatian Medical Journal
Journal of the American Medical Association
Nederlands Tijdschrift voor Geneeskunde (The Dutch Medical Journal)
New England Journal of Medicine
New Zealand Medical Journal
The Lancet
The Medical Journal of Australia
Tidsskrift for Den Norske Llegeforening
Ugeskrift for Laeger (Journal of the Danish Medical Association)

International Standardised Randomised Clinical Trial Numbering scheme). However, it seems that every region, country, state and company have developed or started to develop their own registry. To date the number of active registries is enormous, some of these include: Australian Clinical Trial Registry (ACTR) [www.actr.org.au]; Canadian registry (www.canadatrials.com); European clinical trials database (EudraCT) [www.eudract.emea.eu.int: to be incorporated into the proposed EUROPHARM database]; Japan Pharmaceutical Information Center (JAPIC) [www.japic.or.jp]; South African National Research Register (SANRR) [www.sanrr.gov.za]; UK National Research Register (NRR) [www.nrr.nhs.uk]. In February 2005 new legislation (Fair Access to Clinical Trials Act) was introduced to US congress stipulating mandatory registration of clinical trials and mandatory reporting of clinical trial results. Now there are 22 states in the US with proposed legislation for registries. In addition, there are >300 commercial and disease specific registries available, not to mention a large number of company specific registries.

This explosion of growth in the number of registries raises problems such as: How many registries is enough? Which registry to choose? What about certification of registries? How will unique trial identification numbers be assured? How will compliance be monitored? What about the quality of the data entered?

Thankfully the WHO has taken a leadership role and developed an International Clinical Trials Registry Platform (ICTRP) [www.who.int/ictrp/en], through which all WHO certified registries will be accessible. It is planned that this will be an internationally accepted centralised repository for clinical trial information (registries and results), and fully functional by 2008. Clinical trials will be unambiguously identified using uniform standards. The WHO will also provide certification of acceptable registries and promote compliance.

As the ICMJE imposed deadlines passed, interested parties kept a watchful eye on compliance in registering trials and also on the quality of the data entered. A review of trial registration at www.clinicaltrials.gov during the interval May to October 2005 showed that there was a 73 per cent increase in the number of trials registered during this time (note: this time interval incorporated the final ICMJE deadline of September 2005) [6]. The authors concluded that, although data records were more complete than trials registered previously, there is still room for improvement.

Pharmaceutical industry response

The pharmaceutical industry (see Table 2 for member associations) released a joint position statement in January 2005 recognising the public health benefit of registries [7]. In addition, the pharmaceutical industry committed to posting clinical trial results to a free, publicly accessible results database, regardless of the outcome. Results will be posted within one year after a drug is first approved and commercially available, or one year after trial completion. Summary information will be presented in an objective, scientific format (non-promotional and in accordance with the International Conference on Harmonisation [ICH] E3 guideline [8]) and fully report study findings including all primary and secondary outcomes, and safety. These summaries are not intended to replace patient-physician interaction, the comprehensive nature of the product label or be a substitute to a peer-reviewed publication, nor should they be a barrier to peer-reviewed publication. A number of companies are using the Pharmaceutical Research and Manufacturers of America (PhRMA) sponsored website www.clinicalstudyresults.gov, while others are using their own company websites. Recently, the Federation of Pharmaceutical Manufacturers and Associations (IFPMA) established a portal enabling access to all industry sponsored websites [www.ifpma.org/clinicaltrials.html].

Currently there is no mandate for disclosure of clinical trial results; it is voluntary. However, the WHO has indicated that they will establish results disclosure standards. As we move forward, there will need to be a traceable link between registration and results reporting, as well as consistency—meaning that either trialists or the WHO will need to exercise due diligence to ensure registries and results databases are kept up to date.

Conclusion

Future success of the above initiatives will be dependent upon, and primarily driven by, the WHO taking a leadership role in providing globally harmonised standards and processes. Many challenges lie ahead for management, compliance and consolidation of the numerous registries and results databases that have emerged. Issues still needing consensus include: creating a genuine balance between transparency and intellectual property; addressing the number of registries, including their credibility and quality; defining roles and responsibilities; establishing globally harmonised standards and processes.

There is no arguing that the combined effort from all trialists over the last year has resulted in a positive step forward toward improving transparency in disclosure of clinical trial information, albeit with lots of room for further improvement…

Table 2: Pharmaceutical Industry Associations

Pharmaceutical Industry Associations
Federation of Pharmaceutical Manufacturers and Associations (IFPMA)
European Federation of Pharmaceutical Industries and Associations (EFPIA)
Japanese Pharmaceutical Manufacturers Association (JPMA)
Pharmaceutical Research and Manufacturers of America (PhRMA).

>>>

>>> Disclosure of clinical trial information

Affiliations/Competing interests

Ruth O'Halloran is an employee of Pfizer Worldwide Development Operations, Sydney, Australia. Ruth is involved with registration and results database activities for Pfizer clinical trials in the Asia region and has presented regularly on this topic. This article has been submitted by Ruth on behalf of the Australasian Medical Writers Association.

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Authorship, accountability and communication professionals

As the world recovered from the South Korean stem cell fraud [1], the American senior author of one of the articles retracted from the journal Science was being investigated to elucidate his possible role "in the fabrication and falsification of the data" [2]. The investigation disclosed authorship practices that EMWA members may find unusual.

Dr Schatten was not involved in data acquisition, analysis or oversight despite his role as senior and corresponding author, but his disengagement is hard to infer from the authorship and funding information in footnote 32 (reproduced in the University of Pittsburgh panel's report) of the Science article. He did not fulfil the criteria for authorship [3,4], and although he accepted "the responsibility that all authors [...] have seen and approved the manuscript, its content, and its submission to Science" [5] it was later discovered that many authors had not read the paper until after it was published. However, he participated enthusiastically in the "reputational enhancement" that followed publication, and may have been instrumental in getting the paper accepted for publication [6,7]. Later he abruptly dissociated himself from the study when ethical problems came to light.

Would a communication professional have claimed authorship and then tried to evade responsibility when serious ethical problems were identified? Not if he or she espoused the Good Publication Practice recommendations [8] and EMWA's professional code of practice [9]. The latter notes that "by agreeing to be listed as an author, the medical writer takes public responsibility for the research." Public claims of authorship credit bring public accountability for the content, both for researchers and for the communication professionals who aid them. Schatten, a researcher, was apparently paid large sums of money by lead author Hwang and was also rewarded with senior authorship. Yet had he been a medical writer instead of a researcher, his behaviour would be considered unprofessional and unethical, not merely "misbehavior" [2,6].

The incident shows that the roles of authors and communication professionals need to be carefully distinguished, and that all contributors regardless of their role need to be held publicly accountable for their input.

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Medical writers in drug development and marketing

by Keith Dawes and Katherine Kauper

To be a successful medical writer there are a number of 'prerequisites', often contained in job descriptions: a life science academic education, flawless English language skills, the ability to express medical data accurately, customer focus, a commitment to quality, an ability to be flexible and highly organised, team skills, a familiarity with industry standards, and the ability to work to tight deadlines. These are all valuable skills, but let us go further and explore where medical writers can contribute and hopefully provide some useful advice along the way.…..Read on!

Functions of medical writers

Most medical writers are employed by pharmaceutical companies, contract research organisations (CROs) or communications agencies. There are also freelance medical writers, and medical journalists (or regular contributors to scientific journals) who can be broadly classified as medical writers. The tasks of individual medical writers will vary, as those who work for CROs and the pharmaceutical industry are often employed in the preparation of regulatory documents, whereas communications agencies often prepare promotional/marketing related items. However irrespective of their working environment the role of professional medical writers in preparing and contributing to a finished document is often pivotal.

A well-organised medical writing department, as for a large pharmaceutical company, will have numerous functions. Predominantly these will involve input into scientific documentation, which can be at all levels of drug development (see Box). Consultancy is also a key role for medical writers, clients and colleagues often ask for advice on issues ranging from document templates or regulatory requirements, information for a protocol, style or branding for a product, quality control and marketing messages for a product or presentation. Medical writers also contribute to discussions on development programmes, trial designs, data analysis, product launch and marketing activities and should be proactive in ensuring clarity in wording, document quality, marketing messages and construction of scientific arguments. Effective interaction with team members, external consultants, clients and investigators is also a necessary role of medical writers.

Typically medical writers will be responsible for handling multiple activities within a given project, with back up support from designated team members. If this is not daunting enough, medical writers often work in multiple indications with different drug classes. Experienced medical writers with a broad knowledge of numerous therapeutic areas, drug development, marketing and sales can be seen as an encyclopaedic figure, a 'jack of all trades' and a master of communication.

Product lifecycle: examples where medical writers can contribute during a product lifecycle. For the successful development, launch and maintenance of a product, planned deliverables are interdependent.

1. Identification of target molecules
2. Scrutiny of drug candidates: product development plans
3. Clinical studies (Phase I - Phase IV): regulatory documents, investigator brochures, protocols, newsletters, analysis plans, safety reports, study reports
4. Submission/launch: submission dossier, launch manuals
   The product: branding guidelines, product monographs, Q&A documents, strategic publication planning/manuscripts
   The company: product resource documents, staff workshops, internal newsletters, competitor assessments, launch meetings
   The market place: product sales materials, slide kits, advisory boards, websites/multimedia, opinion leader development, external newsletters
   Congresses/events: expert's meetings, regional/global meetings, abstract books
   Public relations (PR)/press releases: media monitoring, PR manual, PR communiqués, core press materials, publicity campaigns, press releases
5. Life-cycle management/new indications: maintaining product awareness (both through marketing activities and customer education)
6. Patent expiry: strategic market assessments

Team skills for medical writers

Medical writers interact with a variety of people, each with a particular investment in a project, and good team skills are a key prerequisite for employees. Medical writers who are not natural team members (who avoid the telephone in favour of e-mail) or are ineffectual in face-to-face meetings will find their working lives more difficult. Managers will also be required to spend extra time focusing their efforts to complete projects successfully. Hence team skills need to be developed and maintained. This can be done through appropriate training, assigning projects correctly and by nurturing staff to participate more openly. Professional training programmes also instil confidence in new medical writers.

Dealing with different perspectives or stakeholders in a project can also be difficult for a medical writer (see Box). The potential for conflict needs to be minimised. Notably marketing and clinical perspectives clash or marketing and

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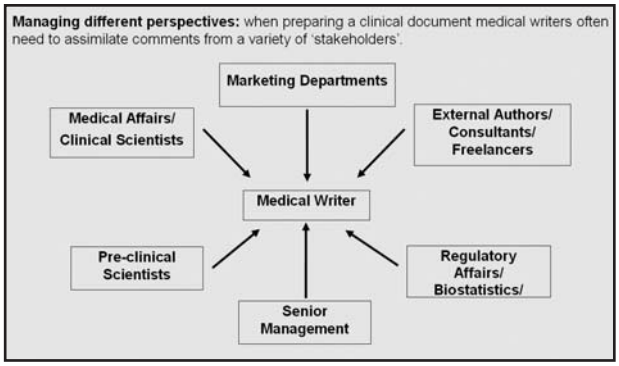
>>> Drug development and marketing

sales may have different ideas (or country affiliates). It is often necessary for the medical writer to facilitate pragmatic discussion between groups to prevent project delays, or to ensure the consistent delivery of product messages. If there is a key deadline to be kept it may be necessary to force issues into the open to get a resolution. Clashes between marketing and external authors are also common. Again open communication along with maintenance of scientific rigor is the best way to resolve these conflicts.



Managing different perspectives: when preparing a clinical document medical writers often need to assimilate comments from a variety of 'stakeholders'.

Effective use of a medical writing department also requires planning as the ability to identify potential bottlenecks and plan contingencies is a key skill in any team effort. Assigning a study report to be drafted and controlled by a medical writer at the start of a project can alleviate other members of an unwelcome burden, and can prevent team members from becoming 'too close' with the potential for delays and team conflict. The medical writer in conjunction with the project leader will be responsible for fielding all input into a document and for chairing appropriate meetings to resolve any issues. If there are a wide variety of opinions, closed, one-on-one meetings should be avoided as issues need to be discussed openly with all team members.

Managing medical writers

Medical writing can be stressful and employees can also feel isolated and unappreciated. Commonly these feelings are increased in small medical writing departments or if line management is inadequate. Hence effective management processes should be in place.

Clear job descriptions need to be written so that employees know what is expected of them (including a list of core skills). Training programmes should be established to allow medical writers to obtain their core skills and to gain new skills, and there should be regular appraisals and professional mentoring. A clear career structure should be established, which must be transparent and based on achieving set goals (outlined in appraisals). Clear line management needs to be established and administrative support should be available. Managers may need to act as internal advocates to enhance the profile of a medical writing department, and medical writers should be considered as experienced professionals who can contribute at all levels of a project. Work variety, new challenges and fair work distribution will also help team building and motivation. Ultimately the aim for an employer should be to train, maintain, develop and retain medical writers.

Practical skills for medical writers

A medical writer's list of skills could also include knowledge of scientific publishing and the requirements of the publishing industry (and also a basic statistical training). Medical writers also need some practical skills to be effective including computing, proofreading and editing skills. For new medical writers the importance of acquiring good proofreading and editing skills cannot be overlooked.

For non-medical writers proofreading is often thought of as a brief review to find and highlight errors, but professional proofreading has a different meaning and is separate to editing. For professionals proofreading is comparison either between two versions of the same document (e.g. a word copy and a typeset copy) or within the document to find inconsistencies and errors. Editing is correcting and improving a document (e.g. correcting grammar, improving sentence construction) for readability, to adhere to a specified editorial style, and to prepare the document for the next step in the process. Often this clear distinction between editing and proofreading becomes blurred for medical writers. However, as document quality should be a primary focus of any medical writing department efforts need to be made to encourage a 'proofreading/editorial reflex' in all new medical writers. Additionally consistency and quality can be ensured through established operating procedures, the use of style sheets/checklists and by ensuring clear review processes for draft documents.

In summary medical writers play a vital role during drug development and post product launch. Moreover experienced medical writers have a number of skills that increase their value to a company, knowledge of different indications and drugs, an understanding of all stages of drug development, launch and marketing, the ability to help pragmatic decision making, and a thorough understanding of quality. Their success is dependent on personality, team skills, effective management, appropriate training and use of practical skills. Companies should be proactive in training, mentoring and retaining these valuable employees.

The authors acknowledge their professional colleagues who over the years have provided the basis for this article through discussion and practical advice.

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Recommended reading for medical writers:

The Chicago Manual of Style: The Essential Guide for Writers, Editors, and Publishers (15th Ed). University of Chicago Press, 2003. ISBN 0226104044.
The Science Editors' Handbook. Maisonneuve H, Enckell PH, Polderman AKS, Thapa R, Vekony M (Eds). Published by EASE, the European Association of Science Editors, 2003. ISBN 0-905988-13-2.
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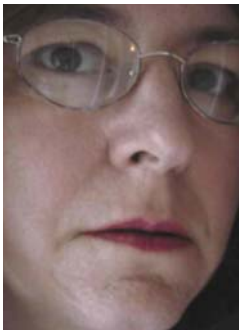
The CONSORT statement. Comprising a checklist and flow diagram to help improve the quality of reports of randomised controlled trials. (http://www.consort-statement.org).



The evolution of clinical trials

by Susanna J Dodgson

According to the US government website ClinicalTrials.gov a clinical trial is "a research study in human volunteers to answer specific health questions" [1]. Clinical trials so defined have been the tools for determining whether a therapy works better than nothing for decades, perhaps for millennia. The first recorded clinical trial was of the biblical Daniel testing the effects of a diet of pulses rather than meat (see Box).

> "In the third year of the reign of Jehoiakim king of Judah came Nebuchadnezzar king of Babylon unto Jerusalem, and besieged it…And the king appointed [4 children] a daily provision of the king's meat, and of the wine which he drank: so nourishing them three years, that at the end thereof they might stand before the king… But Daniel purposed in his heart that he would not defile himself with the portion of the king's meat, nor with the wine which he drank [and said to the king]… Prove thy servants, I beseech thee, ten days; and let them give us pulse to eat, and water to drink. Then let our countenances be looked upon before thee, and the countenance of the children that eat of the portion of the king's meat: and as thou seest, deal with thy servants. So he consented to them in this matter, and proved them ten days. And at the end of ten days their countenances appeared fairer and fatter in flesh than all the children which did eat the portion of the king's meat. Thus Melzar took away the portion of their meat, and the wine that they should drink; and gave them pulse."
>
> ***(King James Bible, Daniel Ch1).***

Daniel's requirement for food that differed from the munificent diet given by King Nebuchadnezzar follows the requirements for open-label clinical trials and was far more successful than most modern clinical trials. The results were clear cut and did not require imported specialist statisticians to prove that the sponsor's therapy was better than standard care as I observed in a single phase 3 clinical trial for a cancer therapy. This therapy did not impress the US regulatory body, the Food and Drug Administration (FDA), and the sponsor's new drug application (NDA) for marketing authorization was rejected.

I wanted to know how clinical trials progressed from being odd things that biblical heroes dabbled in to impress potentates to being complex and legal mechanisms by which all therapies and devices are tested. The James Lind Library, launched in 2003 by The Royal College of Physicians of Edinburgh, is an online resource for tracking clinical trials [2]. The first recorded clinical trial they report is the biblical Daniel's, the second was from 11th century China and the third from 16th century France. But the Edinburgh surgeon James Lind (1716-94) who investigated the best treatment for scurvy and from whom the library takes its name was probably the first person to have conducted a controlled clinical trial of the modern era (see Box).

> "On the 20th of May 1747, I selected twelve patients in the scurvy, on board the Salisbury at sea. Their cases were as similar as I could have them. They all in general had putrid gums, the spots and lassitude, with weakness of the knees. They lay together in one place, being a proper apartment for the sick in the fore-hold; and had one diet common to all, viz. water gruel sweetened with sugar in the morning; fresh mutton-broth often times for dinner; at other times light puddings, boiled biscuit with sugar, etc., and for supper, barley and raisins, rice and currants, sago and wine or the like. Two were ordered each a quart of cyder a day. Two others took twenty-five drops of elixir vitriol three times a day ... Two others took two spoonfuls of vinegar three times a day ... Two of the worst patients were put on a course of sea-water ... Two others had each two oranges and one lemon given them every day ... The two remaining patients, took ... an electary recommended by a hospital surgeon ... The consequence was, that the most sudden and visible good effects were perceived from the use of oranges and lemons; one of those who had taken them, being at the end of six days fit for duty ... The other was the best recovered of any in his condition; and ... was appointed to attend the rest of the sick. Next to the oranges, I thought the cyder had the best effects ...".
>
> ***Taken from Dr James Lind's "Treatise on Scurvy" published in Edinburgh in 1753, and quoted by Dr Peter Dunn (1997;76;64-65 Arch. Dis. Child. Fetal Neonatal Ed)***

Dr Lind was the most modern of scientists; he reacted to a problem which had not been in existence before improvement in sail engineering enabled ships to leave land and sail oceans and seas without landing for months. However, like many modern scientists, his interpretation of his clinical trial results was way off the mark; he concluded that citrus fruits cured scurvy because of their action on the

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>>> The evolution of clinical trials

digestive processes. How Dr Lind interpreted his results is irrelevant; after a lag of 50 years, directly because of James Lind, British sailors' rations included citrus fruits [5].

After the report of this scurvy trial in 1753, the number of reports of clinical trials increased. The number of clinical trials reported in journals indexed by the US National Library of Medicine has steadily increased since 1950, when "A controlled investigation of streptomycin treatment in tuberculosis" was reported [6]. During 1974, 175 papers had "clinical trial" in the title and "controlled" in the keywords, this had increased to 215 during 1984, 715 during 1994, and 1945 during 2004.

James Lind. Published with kind permission from The James Lind Library, www.jameslindlibrary.org.

Clinical trials started to become embodied in legislature as governing authorities began recognizing a need for regulating pills, potions and ointments in the early 20th century. The FDA was founded in 1862 as a scientific institution and became a law enforcement organization after the US Congress passed the Food and Drugs Act in 1906. After that, legislation progressively demanded greater accountability for marketing food and drugs and the need for testing drugs in clinical trials increased. "A drug tragedy in Europe, the births of thousands of deformed infants whose mothers had taken the new sedative thalidomide, focused public attention on pending US legislation to further strengthen the Federal Food, Drug, and Cosmetic Act. The Drug Amendments of 1962, passed unanimously by the Congress, tightened control over prescription drugs, new drugs, and investigational drugs. It was recognized that no drug is truly safe unless it is also effective, and effectiveness was required to be established prior to marketing ….. Drug firms were required to send adverse reaction reports to the FDA, and drug advertising in medical journals was required to provide complete information to the doctor — the risks as well as the benefits."[7]. The changes in the law are known as the Kefauver-Harris Drug Amendments 1962.

The increase in clinical trial data has led to the increasing number of jobs for medical writers in the pharmaceutical industry. The downside of the increase in clinical trial data has been the lack of control of how these data are reported; I have in a previous article described the practice of guest authorship in which healthcare professionals claim authorship credit for medical journal articles for which they neither wrote nor analyzed the data [8]. This article attracted the attention of a journalist from the Wall Street Journal, and an example I quoted was given in a recent article which she wrote [7]. The dialogue continues as clinical trials generate increasingly greater amounts of data. My hope is that medical writers will take control of clinical trials, have the understanding and the scientific background to design clinical trials, and be increasingly recognized as clinical science professionals.

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The Story Of The Laws Behind The Labels

A series of articles on the FDA's website provide further interesting information about the history of the FDA and laws governing the marketing of food and drugs. www.cfsan.fda.gov/~lrd/history1.html

Language Quiz

The answer to the language quiz on page 12 is Vietnam. The official Roman writing was established by missionaries.

Myths about English

by Alistair Reeves

Theodore Bernstein, well-known among writers for his entertaining and pragmatic publication 'The Careful Writer' [1], published 'Miss Thistlebottom's hobgoblins: the careful writer's guide to the taboos, bugbears, and outmoded rules of English usage' in 1971 [2]. Miss Thistlebottom was a school teacher who had rigidly taught the same for her entire professional life, had some outdated ideas, knew absolutely everything about the English language, and knew how to enforce this knowledge—assertively.

Most British (and, I think, American) people carry with them in the back of their minds the spectre of such a fearsome but caring, probably bespectacled, most likely not made up, sensible flat-shoe-wearing, impassioned and learned Miss Thistlebottom expounding on English grammar at the front of the classroom and rapping them on the knuckles with a blackboard duster for putting a comma before 'and', or some other unforgivable grammatical transgression. My Miss Thistlebottom was actually called Mrs Whitfield in York many years ago (she fulfilled all attributes, except she wore very high heels), and I fell in love with her when I was 8 because she taught us French and English and I was captivated from the word 'Go' by her enthusiasm for language. I have rejected or modified many of her rules since my primary school days, but if Mrs Whitfield hadn't existed, I wouldn't be writing this now. Mrs Whitfield ensured that these rules hovered over me like the sword of Damocles for many years—and it even still pricks me in the back of the neck now and again. But (Mrs Whitfield: "Alistair! Never start a sentence with but!") she was also a splendid teacher and encouraged us even at that age to form our own opinions and defend them—not, however, about commas before 'and'.

You enter the world of writing and find that many writers appear to have successfully shaken off the spectre of their Miss Thistlebottom (although that blackboard duster does still hover in the background), were never subject to 'Close-Encounters-Of-The-Miss-Thistlebottom-Kind', apparently learned rules that you never heard of from a 'reliable' source, or are just very laid back about the whole thing. Sometimes I think that the laid back attitude is the best as far as English is concerned: provided you remain consistent and true to your own convictions—although these may change (see Myth 2 below)—this is all right. One thing I can assure you of: ask native-English-speaking writers, and they will tell you they are glad that they never had to learn English as a foreign language.

It's all a matter of building the confidence within yourself to listen to the different possibilities, decide—if you have the choice—what you want to do, remain consistent, and retain the necessary flexibility to stay out of any time-wasting and ultimately frustrating discussions on whether, for example, 'in vivo' should be italicised or not—unless you win, which you probably won't.

The 4 myths below are amongst the most common questions I receive about English in our context. Almost all are 'agree-to-differ' issues, where gaining consensus is practically impossible. It's not worth making enemies or losing your job about any of them. I make no claims to being a Miss Thistlebottom and hope what I have to say helps you in your daily work.

The points are problematic because:

– It is often claimed that they are governed by rules, and they are not. Conventions do exist, but the thing about conventions is that they—like guidelines—are not rules, and depending on where you are in the world or which style guide you consult, different conventions prevail.
– Because they are not governed by rules, they are also subject to personal preference. Frequent usage of a formulation often makes it 'sound right'.
– They are often not apparent when speaking. Many liberties with language can be taken when speaking, but there is a great gap between the spoken and written word, as reflected by Georges Louis Leclerc in his inaugural address on being received into the Académie Française in 1753 [3]: "…ceux qui écrivent comme ils parlent, quoiqu'ils parlent très bien, écrivent mal".[1]

My approach is always to pick the easiest option to make writing (and checking my texts) easier for me and, I hope, to make reading easier for the reader.

Myth 1: You should never start a sentence with digits

I would like to banish the myth entirely that this is governed by rules. There is no rule that states that numbers at the beginning of sentences have to be written out as words (e.g. 'Fifteen subjects were enrolled'). Likewise, there is

1 "...those who write as they speak—although they may speak very well—write badly".

>>>

>>> Myths about English

no rule that elsewhere in text, numbers smaller than 10 (or 11 or 12) should be written out and that digits should be used for greater numbers. There are conventions. These vary according to company, style guide, publishing house, personal preference and—like many things as far as language is concerned—mood.

We all have our personal preferences, and this is one area where my preference is difficult to suppress, because I think that the choice I have made makes writing easier and helps maintain consistency. If I have my own choice, I always use only digits, whether at the beginning of a sentence or in text. There is absolutely no reason in medical and scientific writing why you should not, with two exceptions: 'one' often looks better than '1' (but no other digits); and when digits immediately follow one another and there is potential for confusion.

Consider the following:

'1 23-year-old man was withdrawn from the study because of …'. Here you have the choice of saying 'A 23-year-old man…' if the reader has no previous knowledge of this man. If the statement '1 23-year-old man…' is preceded, for example, by '3 subjects discontinued because of adverse events:', i.e. the reader knows that the man in question was 1 of 3, then you have to say '1' because the indefinite article would not be appropriate because you are enumerating. In this case, it is clearly better to say 'One 23-year-old man…', to avoid the '1' and the '23' being read together, even if reaching the age of 123 years is still unlikely.

And consider the following:

' … was poured into 2 5-mL tubes.' Even despite the hyphen (which I think is unnecessary) and the space between the '2' and the '5', eyes scanning a page may read this as '25-mL' tubes or '2.5-mL' tubes, so it is clearly better to write '…two 5(-)mL tubes'.

It is possible to think of quite a few other rare situations where potential for misunderstandings may occur. This is always the case. Face those situations as you come to them and find a common-sense solution.

We are in the business of getting the message across, so consider the following:

Two hundred and twenty-seven subjects were enrolled.

OR

227 subjects were enrolled.

Which hits you in the eye better? And don't you dare be tempted to put 'A total of' before '227' (see below).

Message: if you are an employee, do what your company wants. Depending on your employer, you may be able to do what you want. If you are a freelancer, do what your client wants (one of mine wants everything below 13 written out—so what! At least I know what they want). If you have the choice, do what you want and follow the golden rule: be consistent. But be aware: if you write out digits up to a certain number, you will have to do an awful lot of checking that you have done it consistently.

It is worth mentioning here that the misconception that a sentence should not start with digits has led to the widespread use of at least 3 of the greatest redundancies in writing in general to start sentences: 'a total of', 'in total' and 'overall'. 'A total of' might be justifiable in the following sentence: '45 patients were enrolled in study 1, 43 in study 2, 41 in study 3, and 6 in study 4; thus, a total of 135 patients were treated'. But I would still far rather read: '135 patients were treated: 45 in study 1, 43 in study 2, 41 in study 3, and 6 in study 4'. Get rid of 'a total of'!

Myth 2: There is never a comma before 'and' in lists with more than 2 elements

Oh yes, there is! In English, you almost always have choices. Here you have 4 (or more?) choices and good arguments can be presented for all. I do express a preference below—for my usual prime reason: to make writing easy and maintain consistency, without endless checking—but you should form your own opinion.

Choice 1. Never put a comma before 'and' in lists with more than 2 elements.

Choice 2. Always put a comma before 'and' in lists with more than 2 elements. This is called using the 'serial comma'.

Choice 3. Put a comma before 'and' in lists with more than 2 long elements; do not put a comma before 'and' in lists with more than 2 short elements.

Choice 4. Use a semicolon like the serial comma in lists with more than 2 long elements, including before 'and'; use the serial comma or do not put a comma before 'and' in lists with short elements.

After starting out in life with Choice 1, Choice 3 was my preference for a long time, but recently I have switched to Choice 2 and feel very happy about this. Why? First, because it took me a long time to shake off the spectre of Mrs Whitfield. Second, because now I never have to clutter my thoughts with this irksome question, it makes things dead easy, and it is much easier to remain consistent. The serial comma has its origins in American English. I think it's great! Despite this, if you opt for Choice 1, you will also have an easy life remaining consistent. With Choice 4, you will create much work and decision-making for yourself as far as being consistent is concerned, but if you manage to be consistent, you deserve only praise.

Myth 3: Adding 'in order' before an infinitive sometimes adds meaning which would otherwise be lost

Forget it. Feel free to use 'in order' before an infinitive all the time when you are speaking or when you write emails. Scrutinise texts from others and texts you write, step back into objective mode, and see if you think that 'in order' adds any additional meaning. I am sure that you will decide that it does not.

Does the first sentence here really tell you more?

1) In order to harmonise procedures across studies, a 90-day censoring rule was applied in all.
2) To harmonise procedures across studies, a 90-day censoring rule was applied in all.

Or the first here?

1) This review of the literature by Barnes and Mitchell gives an overview of important findings concerning sex differences in order to assist clinicians in treating women with bipolar disorder.
2) This review of the literature by Barnes and Mitchell gives an overview of important findings concerning sex differences to assist clinicians in treating women with bipolar disorder.

Eradicate it from your formal writing entirely. It adds nothing. Don't worry: you'll get used to it.

Myth 4: Plurals of Latin and Greek words should be retained as in the original language

The only difference between Latin and classical Greek and other languages is that they are amongst the languages that are still in use but are no longer spoken. When was the last time you used 'scenari' and 'fiaschi', the Italian plurals of 'scenario' and 'fiasco'? Chance has it that the plural of most of the French and Spanish words we use in English is the same as in English, except for those ending in 'eau', but these days 'gateaus' is just as acceptable as 'gateaux'. The uninflected plural of 'guru' in Hindi is 'guru', but I think most of us would choose to use 'gurus'.

I quote Edith Schwager from 'Medical English Usage and Abusage' [4]: "Most Latin words that have been thoroughly integrated into English can be pluralized perfectly legitimately by simply adding an 's' (or 'es' in my opinion) to the singular form: *stadiums, memorandums, curriculums*. Using *stadia, memoranda, curricula* … probably fulfils an honest human need—the need to appear learned". 'Addenda' is another example. For me, this also applies to Greek words, and my resolve to use the usual English plural was strengthened on seeing 'pig pancreata' in a report on the preparation of insulin. Times have changed, and most of us lack the solid grounding in Latin or Greek required to confidently use the correct plural, so one thing is certain: if you want to use the Latin or Greek plural, you should always look it up (you can't rely on the Internet for this) and not just assume that they all end in 'a' or 'ae': for example, the plural of 'locum tenens' is 'locum tenentes. It's a jolly sight easier to use 's' or 'es'.

Formulas or formulae? For me, of course, always formulas. For some words, you will find that dictionaries allow different plurals depending on meaning. Specifically for formula, those I have consulted say 'either-or' or that the 'ae' ending is *preferred* for the mathematical or chemical use of the word, not that it is right and 's' is wrong.

I have no doubt that the above points and many more will remain controversial. Next time you are standing in awkward silence looking for a good topic for small talk in the company of writers, pick any of the above points and innocently ask your companions: "What do you think about …?". Make sure you have a firm opinion on the point chosen before you start and be prepared for vehement disagreement and a catalogue of conflicting 'rules', some of which will certainly make you scratch your head or sense that blackboard duster hovering above your knuckles. I guarantee that the silence will be broken and that 'big talk' will ensue: these actually trivial niceties of the English language cause more discussion, controversy and argument than they are worth!

Look out for more myths in the next issue!

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3. Georges Louis Leclerc (Comte de Buffon) (1753) *Discours sur le style* (prononcé à l'Académie Française par M. de Buffon le jour de sa réception le 25 août 1753)
4. E Schwager (1991) *Medical English Usage and Abusage* Oryx Press.

Access to data

Medical writers might have been following Dr Aubrey Blumsohn's accusations of 'unethical' secrecy made against Procter and Gamble, in which he claimed that research was published by the company in his name when he had not been given full access to the data it was based on. The report had been written by a ghost writer employed by Procter and Gamble (see http://observer.guardian.co.uk/uk_news/story/0,6903,1657302,00.html).

This exemplifies a growing problem in relations between pharmaceutical companies and investigators in academia. It is a problem that the International Committee of Medical Journal Editors had already turned their attention to in 2003 when they updated The Uniform Requirements for Manuscripts Submitted to Biomedical Journals (www.icmje.org). In the updated version the section "Project-Specific Industry Support for Research" became section "II.D.2 Potential Conflicts of Interest Related to Project Support". In it the stipulations for authors in academia working with industry were expanded from "scientists should not enter into agreements that interfere with their control over the decision to publish the papers they write" to "researchers should not enter into agreements that interfere with their access to the data and their ability to analyze it independently, to prepare manuscripts, and to publish them. Authors should describe the role of the study sponsor(s), if any, in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the report for publication". (This wording is retained in current icmje which were updated in February 2006.)

Dating made easy...

by Alistair Reeves

Writers often ask me: 'What is the correct way to write the date?', or say '…so that's the right way to write the date in British English, then'. Like many things in English, there are plenty of ways to do it wrong, but there is no one way to do it right. On top of this, there is the well-known US-UK difference of transposition of the days and months, with other countries following one or the other. There are also myriad formats in Microsoft Word in the date field options.

When I was at school in England, we were taught the following formats:

– July 23rd, 1965.
– 23/7/65.

These are still correct. The slash is still the correct separator in US and UK English and not the full stop or period (but the slash is not sacred). 23rd July 1965 and 23rd July, 1965 are also acceptable, but there is no need to write 23rd of July 1965, even if you always say it when speaking.

Now I write:

– 23 July 1965.
– 23/07/65 (very rarely).

Sometimes even 23JUL(19)65 or 23 JUL (19)65 (or sometimes Jul).

And we also see

– 23-JUL-(19)65 (sometimes Jul).
– 23.07.65.

Why?

Ordinal suffixes 'st', 'nd', 'rd' and 'th': I have entirely dispensed with these in the date, in both private and professional writing. This is perfectly acceptable and is gaining widespread acceptance because it cannot be misunderstood when numbers are part of a date, and it makes it very easy to be consistent. When speaking, you still say 'first of' for '1', 'second of' for '2' etc. Even if clients want me to use the ordinal suffix, I have turned off the Microsoft Word default rule that makes superscripts out of them, because it is unnecessary, adds nothing, and looks messy. I have clients who assume that because Microsoft Word does something, it must be right. This is not the case. Non-native speakers of English and native speakers living abroad please note: 23. July 1965 (with a full stop or period) does not exist!

23 July 1965 instead of July 23rd, 1965: I now write the number of the day before the month because this avoids the comma between the number of the day and the number of the year. Avoiding superfluous punctuation is always good in English, and makes it much easier to remain consistent. In scientific texts, I always write the month out and do not use a number. If the day written out precedes the number of the day, as in Friday 23 July 1965, I have also dispensed with the comma. Leading zero (07 or just 7 February) or not? I don't like the leading zero, but I use it because it has come into common usage and I am flexible! The 15th Edition of the Chicago Manual of Style [1] was published in 2003. Previous editions recommended the 'British style' which it stated is as follows: 1 July 2003 (!). The 15th Edition, however, recommends writing: July 1, 2003 ("the way everybody does it in real life" in the words of Anita Samen, an editor of the 15th edition [2]). 'Real life', however, is that there are different 'everybodies', so we don't have to agree with this.

23/07/65 instead of 23/7/65: I actually think the zero is also superfluous here for the day or the month, but have suppressed my preference here too, deferred to common usage, and now add a leading zero for the day and month. Apart from anything else, if you have lists of dates in a column, they are all the same width with the zeros there. I do not use this format in formal writing because of the potential for confusion between the day and month, e.g. 07/02/53: 7 Feb 53 or 2 July 53? If there is any chance of confusion with the year, then I use a 4-digit number and remain consistent with this within the same text.

23JUL(19)65, 23 JUL (19)65 or 23-JUL-(19)65 (sometimes Jul): with or without the spaces or hyphens, just be consistent—and also be consistent with the use of upper and lower case. If texts have a lot of dates in them, it is very wearing on the reader to have the month written out all the time, and the slash format cannot be used because of the potential day-month confusion. If you have been used to seeing the day followed by the month for most of your life or vice versa, it is extremely difficult to change this in your mind, even if you are told at the beginning of a text which order is used. Abbreviating the month to 3 letters leaves no room for confusion, but this format is only suitable for study reports, tables, case narratives and summary documentation, not for publications and other text seen by the professional and lay public, where the date should always be written out in full (preferably: 23 July 1965). Each month is abbreviated to its first 3 letters and no full stop/period is needed. Dates generated programmatically

Dating made easy…

are often supplied in one of these formats and often have a 4-digit format for the year as a result of the '2000 problem'. There is no need to go through and change them all by writing out the month! An interesting aside here: according to the Chicago Manual of Style [1], 'JUL' is called 'army style' and 'Jul' is called 'navy style'. So obviously the US Army and US Navy agreed to differ on this one. I don't know if we should learn anything from this or not!

23.07.(19)65: dots instead of slashes is the continental European way of writing the date in this format in many countries, but this is cropping up more and more in English texts I see from native speakers living outside the UK. As long as the writer is consistent, I don't think it really matters because no-one is going to think that 23.07.1965 is not a date (but this does not solve the day-month confusion issue).

Roman numerals: sometimes I still see 23/(.)VII/(.)65 or variants (e.g. vii). If you like date styles of this sort, reserve them for private correspondence.

ISO date format: an ISO date format exists (ISO 8601): YYYY-MM-DD = 1965-07-23 (always 10 keystrokes) for 23 July 1965. It would be great if we could all agree, and on the following website there are good arguments for using this format: http://www.saqqara.demon.co.uk/datefmt.htm ('Campaign to get the Internet world to use the international date format'), the main ones being consistency and avoidance of confusion, which are always worth supporting. However: standardization usually only works if it saves lives, makes life very much easier, becomes law, or is likely to increase income, so I don't think we'll be seeing this format establish itself for a long time to come.

By the way: standard abbreviations for days of the week in English do not exist. Look on the following website: http://www.ego4u.com/en/cram-up/vocabulary/date-/month-day, and it tells you that the abbreviations are Mon, Tue, Wed, Thu, Fri, Sat, Sun. These are the abbreviations I use. But Tues, Thur and Thurs are also common. The days are rarely abbreviated down to 2 letters; this looks strange. Whatever, no full stop is needed.

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Excessive advertising in peer-reviewed journals

In their interesting article, "Excessive and Disproportionate Advertising in Peer-reviewed Journals" Freidman and Richter investigate the ratios of advertisements to editorial content in two general medicine journals and compare these ratios to those in speciality science journals. The results point to a discord between the advertising practices of the two journals, who are important member journals of The International Committee of Medical Journal Editors (icmje), and the ethics guidelines produced by that committee. Recognising that journals need to make a profit to survive, the authors conclude that the icmje guidelines should define standards for excessive and disproportionate adverting[1].The authors also repeat a recommendation they made in a previous article on the relation between conflicts of interest and research results, "Scientists, physicians and editors need to facilitate greater discourse concerning the ethical dilemma of an increasingly commercialized scientific community".

[1]http://www.ijoeh.com/pfds/IJOEH_1201_Friedman.pdf

A cute problem

When I was a managing editor of a diabetes journal I often encountered the phrase 'acute insulin response'. In its instructions to authors my journal specified that Oxford English was to be used in articles. The *Concise Oxford Dictionary* (*COD*) defines 'acute' as

– (of sensation or senses) keen, sharp
– Shrewd, perceptive (an acute critic)
– (of a disease) coming sharply to a crisis, severe, not chronic
– (of a difficulty or controversy) critical, serious

and otherwise as something to do with geometrical angles and sounds.

None of these definitions cover what is intend in the phrase 'acute insulin response'. I was able to trace the phrase back to Professor Daniel Porte who coined it in about 1969 to describe the sudden beta-cell secretion of insulin following a sharp and short stimulation. But an earlier description in 1965 by another researcher used the phrase 'dynamic insulin response' for the same phenomenon.

You might conclude that as Porte was American he looked up 'acute' in *Webster's*. Here he would have found a wider definition than that in the *COD*, e.g. it includes lasting a short time in relation to experiments. If he actually did look up 'acute' he would have found the exact definition to describe his phenomena 'having a sudden onset, sharp rise and short course'. I suppose it would be pernickety to point out that this definition too only relates to disease. Having established that acute is not appropriate to describe a physiological process but accepting that it may be taking on this new meaning is it ok for a professor to excuse his absence from a meeting with "My 90 year old father has acutely been taken into hospital"? Do we also have to accept the 'acutely dead rats' I recently found in a study report? Perhaps I am being unfair. Maybe this is an early sign of reports taking on a more zany flavour, a leaf out of the leaflet slipped through my letterbox by the charity Cats Protection. The charity asked for donations for their Kitten Crisis Appeal, which they describe as an acute (or A cute) problem.

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Meet the EMWA Executive Committee Candidates... 2006

Each year, EMWA members are asked to vote for those posts on the executive committee that have come up for re-election. An election for the post of vice-president is held every year, and other posts are opened for nominations after a maximum of 2 years. This year, the posts due for election are the vice-president and the membership officer. As TWS went to press, only one nomination had been received. Please keep an eye on the EMWA website for any further developments. If you would like to vote and will not be present at the AGM, you may vote by proxy: see the website for details.

There will be a change from the usual procedure this year for filling the post of president. Normally, the post is filled by the previous vice-president. However, our current vice-president, Ian Metcalfe, has reluctantly decided that he is unable to continue in the role. Our current president, Michelle Derbyshire, will therefore be standing for re-election as president. Similarly, Adam Jacobs will be standing for re-election as immediate past president.

For the position of Vice President: Julia Forjanic Klapproth

I like to say that medical writing is a blossoming niche. But when EMWA was founded some 16 years ago, medical writing wasn't even on the map. At that time the idea was to bring together the few, scattered people around Europe who were doing what is now collectively known as medical writing. They wanted to tap into their cumulative experience and provide some kind of a formalized status to the idea of medical writing. EMWA was born from the heart and soul of those few who volunteered their time and experience to begin teaching what they knew to other writers. Today EMWA has a highly respected educational programme and is a professional organization that is recognized around the globe.

Yet, in my opinion it's time to take EMWA to the next stage as an organization. It's time to take EMWA beyond essentially "just" training (gasp!) and move into a broader realm of discourse. As a unified, professional organization, EMWA offers what we as individual writers are unable to realize. Not only does it provide a forum for us to discuss amongst ourselves, but it sits as a respected body from which we can interact with other organizations (such as EMEA or FDA) and thereby develop an important exchange of knowledge. There are so many topics out there that are ripe for discussion and clarification between us as writers and the regulatory authorities… and I have to ask myself, why don't we utilize the recognition EMWA has earned to contact them and ask them about it? By building on the foundation EMWA has already laid, we can develop it into a multifaceted organization that provides a wider scope to its members.

As a candidate for the position as Vice President, I am in a unique position in that I have in fact served in the role as Vice President previously. During that term I dove into the role charged with my passionate enthusiasm for EMWA and the world of medical writing. But at that point in time my focus was different to what it is today. Five years ago EMWA was in need of some consolidation and realignment and I attempted to bring it that. Already then I initiated my idea of bringing more out of the organization than pure training when I organized a 1-day conference focused specifically on the CTD, which at the time had just reared its head and writers everywhere were in need of an opportunity to speak with the authorities and hear their opinions on what to do with this new beast. And exactly that is the type of topical theme that I would like to see become a regular feature of what EMWA offers.

Take for example the eCTD. It's happening right now. It became the mandatory format for submission dossiers in some European countries (e.g. Belgium) in 2005. How many people do you know who really appreciate the implications of how it will affect our work as medical writers? How many companies do you know who are actually already fully capable of even generating a true eCTD? So it seemed to me that it was time for EMWA to address the issue. Hence the targeted focus on the eCTD at this year's annual conference in Lyon. And this is only one of many such important topics (think translation, communications, regulatory oddities) that EMWA could be bringing directly to its members every year.

Which brings me back to my beginnings at EMWA. I started out as the membership officer. It was a position I stood up for because I was impressed by the way EMWA was a relatively unbureaucratic organization that was truly driven by and for its members. I was impressed that as a new writer I was readily accepted into the fold of the membership and that I was able to get as involved as I was willing to be. I was impressed by the way the trainers of the organization were by and large other members who had particular skill sets offering their knowledge to the rest of the members for no pay. It was clear to me that the heart of EMWA is its members, which is why it seemed the best way to really get to know the organization would be to start as membership officer. And thanks to your vote of confidence back then, I was given the opportunity to do just that.

So here I am asking for your vote of confidence one more time. I'm asking you to think about whether or not you think EMWA is ready to move forward. Whether or not it is time to really blossom into our niche and offer a broader palette of opportunities for its membership. EMWA should continue to provide and develop its excellent and essential training programme. But it should also delve into providing a forum for writers to explore and keep pace with the ever-changing world of scientific documentation. I'm ready to take EMWA to the next step. Are you with me?

Itching to play a role?

by Ian Metcalfe

There cannot be a member of EMWA who does not have the phrase "EMWA: run by the members for the members" imprinted on his or her soul or at least written above the office door. But do we all realise how vital members' contributions are to the future of our organisation?

Out of the many key factors involved in keeping our organisation alive and kicking our two committees, the EMWA Professional Development Committee (EPDC), and the Executive Committee (EC) play principal roles. The EPDC is intrinsic to the high quality workshops that EMWA provides. More is said about it on the EMWA website (www.emwa.org). Here I'd like to give you a bit of background to the EC; it consists of eight elected members and is responsible for the running of EMWA and ensuring that the members' needs are being met whilst maintaining a viable organisation. The eight elected positions on the EC are:

– President
– Vice President
– Immediate Past President
– Secretary
– Treasurer
– Membership Officer
– Public Relations Officer
– Education Officer

Generally these enthusiasts have an urge to be involved in the running of our organisation; a much-quoted phrase is "I just want to give something back".

The EC has been established with fixed tenures of two years for each role to ensure that fresh ideas are continuously brought to the table for discussion. The only exceptions are the roles of Vice President, President, and Immediate Past President; these roles are intertwined and lead on consecutively from each other. This enables a certain level of continuity and consistency on the EC, which is necessary to avoid repetition of concepts and ideas and to give the EC stability.

Every year at our annual conference, during our Annual General Meeting (AGM), there is at least one position vacant on the EC. It is from the membership that the next budding volunteer is sought.[1]

For the past few years, with the notable exception of the election of our Membership Officer last year in Malta, the positions have run uncontested. There could be all sorts of reasons for this but perhaps the main ones are that members are not aware of:

– what the roles involve
– the personal rewards being involved can bring
– the fellowship and fun the EC has running EMWA
– that the EC is eager to welcome new members

I suppose it might also be possible that they think it is too much work.

One of the numerous discussions we've had on the EC has been "how to get more members involved in various aspects of the organisation, without the responsibility of being on one of the committees" (a factor we see as potentially intimidating the numerous members with good ideas from volunteering for the positions on the committees). We have discussed various concepts, such as sub-committees and forums for certain aspects or topics of our work, which we will hopefully have ready for our annual conference in Lyon. A scheme that we hope will show that the running of an organisation such as EMWA is more enjoyable and rewarding than strenuous and time consuming.

On this note I'd like to stress that the EC positions are not as onerous as they may initially appear. While it is true that some positions require more input than others, the make-up and responsibilities of each role are such that they can, and always should, fit in with even the most hectic of schedules; after all we are volunteers.

So what is it that we do on the EC? In a nutshell: we are responsible for the running of the organisation. We take decisions that determine everything from where the next venue for our conference will be to the colour of the new EMWA brochure and everything in-between. We also try to take a lot of factors into consideration for improving the "product offering" that EMWA provides to its members, an important factor for the continuation of EMWA. As you can probably guess, each of the positions on the EC is given responsibility for a specific area of EMWA. These have been nicely presented in the "Would you like to become more involved with EMWA" call on the next page.

A lot of the decision making and discussion of concepts by the EC takes place when we can all gather together. So far during my time on the EC this has been solely during the EC meetings at the spring and autumn conferences (although we do also organise teleconferences). In terms of workload, I have to admit that the conferences and the few

1 One exception being that to be elected Vice President the individual has to have held a position on the EC as a pre-requisite. An important factor as the Vice President is responsible for the following year's conferences and must be used to the needs of the organisation as a whole - and believe me, it also helps to be aware of how the EC functions.

>>>

>>> Itching to play a role

weeks before conferences are rather busy times for EC members. The finalising of many small details and trying to ensure that everything runs smoothly is, as you can probably imagine, very time consuming. Once at the conferences, we do our best to integrate with our fellow members, whilst flitting between meetings and discussion groups; quite exciting times really.

Naturally there is also a fairly continuous stream of emails circulating throughout the year regarding the various discussion points, either raised at the EC meetings or thought of between conferences, but not enough mails to get a company's IT department in a fluster. In addition, to make sure we don't get bored during the inter-conference periods, there is usually a list of tasks related to the EC member's position that should be completed before the next meeting. These tasks are fairly evenly distributed across the board and no one is left alone with too much to do.

To give you specific examples, my duties for our conference in Lyon include securing guest speakers; working with our Education Officer (Virginia Watson) and Head Office in putting together an educational and (hopefully) entertaining programme of events; helping to identify and secure sponsorship for the conference; working with our Public Relations Officer on a new EMWA brochure aimed at the uninitiated; managing EC discussions on the future of EMWA, and last but not least drafting articles for TWS.

While I may have stressed the fact that the duties the EC perform should neither be overly taxing nor interfere too much with earning a living, there are often many things left undone, as even the combined efforts of the eight volunteers on the EC is not quite able to cover everything. This last point is the origin of the thoughts behind this and the "Would you like to become more involved with EMWA" call below.

Through removing some of the smog that may have clouded the role of the EC, I also hope that the articles in this issue of TWS will stimulated some of our members to come forwards and offer help. After all, EMWA is run by the members for the members.

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Would you like to become more involved with EMWA?

EMWA is your membership organisation. As a policy the Executive Committee (EC) continually recruits members to subcommittees for the various activities that serve the membership. The following are examples of areas where volunteers can become involved. Some tasks are simple and take very little time; others are more demanding. All, however, are gratifying, will give you a sense of community within the organisation and experience in areas that can enhance your CV.

Conference Organisation

EC representative: Vice President

- Identifying potential speakers and lecturers for the conferences.
- Identifying and inspecting suitable venues for future conferences.
- Generating ideas for social events.
- Chairing discussion fora.

The Website

EC representative: Website Manager

- Monitoring dialogue pages
- Helping the membership officer to get feedback on the website.

The Write Stuff (TWS)

EC representative: Journal Editor

- Identifying topics and authors for articles.
- Copyediting and proofreading.
- Guest editing an edition of TWS.
- Columnists.

EMWA Professional Development Programme

EC representative: Education Officer

- Identifying and encouraging new workshop leaders.
- Becoming a workshop leader.

Contracts and Legal Interests

EC representative: Secretary

- Reviewing contracts.
- Translating contracts.

Members Interests

EC representative: Membership Officer

- Mentoring conference first-timers.
- Answering questions from potential new members.
- Surveying the membership on how they would like EMWA to change.

Publicity and Sponsorship

EC representative: Public Relations Officer

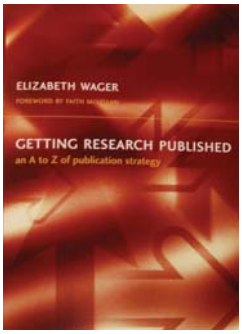
- Identifying and contacting potential sponsors.
- Generating interest in Medical Writing in general and in EMWA in particular.
- Representing EMWA in conferences and meetings

Business Management and Finance

EC representative: Treasurer

- Assisting with preparation of the budgets.
- Helping to monitor expenditure versus income.
- Generating ideas to increase income and lower expenditure.

If you are interested in contributing to EMWA in a subcommittee please contact the appropriate member of the EC. The contact details of all of the members of the EC are provided in every edition of The Write Stuff.



In the Bookstores...

The road to publication success

by Karen Shashok

Elizabeth Wager. Getting research published. An A to Z of publication strategy. Oxford, Seattle: Radcliffe Publishing, 2005. ISBN 1 85775 687 8 (Paperback)

If you work for corporations or institutions that aim to publish their research output efficiently for the widest possible impact, and if you are not already familiar with Wager's earlier writings and EMWA's own efforts to support good publication practices, you should buy this book and read it from start to finish. It condenses almost everything you'll need to know to develop successful publication strategies, bringing together Wager's vast knowledge and the most up-to-date documents that underpin good professional practice for medical writers and other research publication facilitators.

In the section titled "About this book" the author explains to readers how they can use the book to locate the information they seek. Wager is careful to point out the potential limitations of her advice and the pitfalls of taking everything in the book as the last word in publication strategy. Some areas in science publication—notably the responsibilities of authors in complying with document preparation requirements and ethical guidelines, and the roles of research sponsors in clarifying their motives for publishing their results—are evolving rapidly, so changes can be expected and readers will need to keep track of new developments.

The first part of the text proper, titled "Publication strategy—an overview," consists of a few concise chapters that summarize the approaches the author has developed and found useful in the course of her practice. Wager recommends reading this section first if you are new to publication. In-house managers who are thrown into the deep end of corporate publication will also find this section an invaluable guide to understanding what priorities and tasks are involved in developing an effective publication strategy. Another audience for this section is author's editors and other publications consultants who are already familiar with how science journals operate and are preparing to tackle project management and other tasks with broader organizational responsibilities than translating or editing manuscripts for submittal. For author's editors and translators, this section provides valuable guidance on how longer-term publication projects could be set up and run.

The second part of the text is an A-to-Z listing of terms used in research publication. Although many entries are for concepts associated with biomedical publication (e.g. "Big Five," "CONSORT" and "Trial identifier"), other entries can be read and considered in the context of journal publication in other areas of science and technology (e.g. "Anonymous reviewers," "Figures" and "Impact factors"). This coverage makes the book potentially useful to publications planners in areas other than biomedical research.

Leading the way in ethics and good professional practice

In the chapter "Working with a medical writer" the author raises the possibility of conflict between the medical writer and the authors (or their superiors) when the latter find it hard to agree on the content. Wager says, "it is unreasonable to expect the writer to act as arbitrator," and "it is unfair to expect writers to act as mediators in disagreements between sponsors and investigators." It is of course the researchers themselves who must assume responsibility for the data and their interpretation, as the Vancouver (ICMJE) guidelines have made clear for many years. Similar lines of accountability are drawn in EMWA's own guidelines on the role of medical writers, and in the Good Publication Practice (GPP) guidelines for pharmaceutical companies—both conveniently reprinted in Appendix 3 of the book. But once the medical writer has become deeply involved in developing and managing a publication strategy for the client and in facilitating communication between all the players involved in writing, revising and publishing the material, it may be difficult to simply withdraw and let the authors and their sponsor resolve their differences in data interpretation. This makes it important for responsibilities and expectations to be defined at the onset of a project, so that the burden of conflict resolution—a process that may cause delays and missed deadlines—is not placed on the medical writer's shoulders.

Influence of culture and language on publication strategy

For EMWA members who work with authors whose first language is not English, the book contains a few valuable pieces of practical guidance, although future editions could perhaps expand a bit on the increasingly international aspects of scientific-technical-medical communication. In the entry for "Acknowledgements," translators need to be added to the list of professionals who deserve to be named in this part of the publication. The entry for "Names" notes that "[m]ost English language journals are not particularly good at handling Spanish or Chinese names" (how true!), and cautions that particular care is needed with accents and "with multi-part names or those in which the family name appears before the individual name." The entry for "Redundant publication" notes that "[s]econdary analyses, follow-up studies and translations should be clearly labelled as such and should always include a reference to the original study." Unfortunately, there is no entry for sec-

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>>> In the Bookstores...

ondary publication (to make the information more widely accessible to readers in the authors' own language when English is not their first language), and thus there is a lingering (and no doubt unintentional) implication that translation is an ethically distasteful option only to be tolerated under special conditions. In fact, secondary publication is a perfectly legitimate practice as long as the primary publication is clearly referenced and the editors of the primary journal are advised of the authors' intention to publish the same study in another language.

In the entry for "Xenophobia" Wager points out that '[g]eographical bias definitely exists to some degree, and a good strategy therefore needs to take it into consideration." Strategies to offset this bias should probably involve a dispassionate look at what the target journal's readers expect to find in terms of scope, coverage and geographical or epidemiological relevance as well as a consideration of the medical and scientific topics the journal aims to cover. Something as simple as asking the editor before submittal whether the journal would publish a study on a specific problem investigated in a specific population may save time and avoid frustration if the answer is an honest "No." And in these times of declining standards in the use of English and the scarcity of proficient technical editing and copyediting, efforts to ensure that the manuscript as initially submitted is highly readable and meets the target readership's expectations for use of language will probably pay off in enhanced chances of publication.

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What is a defining clause or the curse of the 'ing' form

For some time I have been asking myself whether the difference between 'that' and 'which' or rather the use of commas in relative clauses is taught in English lessons at Austrian schools. If not, which seems likely, then certainly the idea that the 'ing' form can come to the rescue has not escaped Austrian authors who write in English. Take just one example from the manuscript I edited today "A1PI belongs to the family of serpins inhibiting serine proteases." This hardly makes sense but saves worrying about whether it is just that family of serpins that inhibit serine proteases or whether it is all serpins, which inhibit serine proteases. I have also noticed 'what' being used recently as a sort of compromise between 'that' and 'which' as in "These interactions are important for the up-regulation of CD40L on activated T cells what is essential for the co-stimulatory interaction with B cells." I have seen 'what' used like this in manuscripts from American speakers too.

One of the clearest explanations of defining and non-defining clauses that I have read was written by Valerie A. Elliston. She has kindly granted TWS permission to reprint her article, which you can read in the box on this page.

'That' or 'Which'? Relative clauses

The choice between 'that' or 'which' depends upon the type of relative clause involved and is connected with the use of commas.

A relative clause is introduced by 'who', 'which', 'that'. There are two types: defining or non-defining. Do we know enough about the subject of the sentence or do we need to define it with a few more words?

1. The experiments that they reported were successful. (Some)
2. The experiments, which they reported, were successful. (All)

Example 1 implies that there are other experiments, unreported and unsuccessful. The words 'that they reported' form a defining relative clause. It is needed in order to define this particular group of experiments.

Example 2 implies simply that the experiments were successful. The words 'which they reported' placed between a pair of commas, form a non-defining relative clause. The experiments were all successful; the clause 'which they reported' is just extra information.

1. Do not give fluids that are diuretic. (Some)
2. Do not give fluids, which are diuretic. (All)

Example 1 permits administration of fluids but NOT those that are diuretic.

Example 2 forbids ALL fluids because they are ALL diuretic. In this sentence, only one comma is necessary.

Purists insist on the use of 'that' for defining relative clauses, and the use of 'which' as weIl as the comma or commas for non-defining relative clauses. The argument is that this distinction makes it easier to grasp the difference. However, it is now acceptable to use 'that' or 'which' for defining but always 'which' for non-defining.

Another point: 'which' can sometimes relate to a whole clause or sentence, not just to a single word. 'She tore up the letter that upset me.' = She tore up the letter and I was glad because that particular letter upset me. But, 'She tore up the letter, which upset me.' (Comma plus 'which') = The act of tearing up the letter upset me because I wanted to keep it. Therefore, the careless use of 'that' or 'which' and the comma or commas can actually reverse the meaning of a sentence.

Again, these are simple examples. It is not difficult to imagine more serious situations that need more care. In such cases, if the careful distinction between 'that' and 'which' helps to make things clearer, why not draw it?

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Valerie A. Elliston is a registered indexer and former adult education lecturer in English language and literature

Codes, quips and sayings – they're all in the family

by Ursula Schoenberg

The other day I was cuddling my 4-year-old daughter, when she smiled angelically at me and said "May I have a piece of souse?" Imagining a secret listener, this question suddenly brought home to me the wonderful fun and power of language usage in the family. The word "souse" derives from German and means "pickled meat"[1], but in our family it means the lower part of the earlobe, which may be gently nibbled if the question above is answered in the affirmative.

This was one of many expressions and catchphrases my dad handed down to me. Dad grew up on a ranch in the American Southwest and lived through the Crash and the Great Depression. This naturally influenced his outlook on life – he was practical, frugal and very down-to-earth. One of his life's mottos has already been eloquently described by Garrison Keillor when sketching Midwestern men of Scandinavian origin: "Don't buy new if the old still works." The other motto is one that caused me a good deal of time and effort after Dad's death: "Save things, they might come in handy later."

The up side is that Dad is still with me through these sayings, and I mean on an almost daily basis. Being a modern-day mom-cum-chauffeur for my child, I'm often reminded of his quips, many of them automotive in nature. One of my favourites can be used any time a car with a loose muffler or straining engine passes: "If my car sounded like that, I'd be worried." Difficult situations with specific drivers provoke a withering "There's one born every minute," in our car.

Then there is the category I would describe as "practical living advice". I have to be more selective when using these phrases, since many of them are wildly outdated and make people look at me oddly if I use them. "Don't do anything I wouldn't do!" is pretty benign, but when have you last heard the expressions "Don't take any wooden nickels!" or "I wouldn't touch it with a 10-foot pole"? And even though I heard "You drive everybody around you up the wall," quite a lot as a kid, there was also the comforting (?!) "Night night, sleep tight, and don't let the bedbugs bite!" to tuck me into bed at night.

All this drives my husband crazy, who complains that I have to have the last word in every situation (he's wrong, of course). Strangely enough, it hasn't stopped him from adopting some of my dad's expressions as his own, notably SNAFU (a military acronym for "situation normal, all f….. up") and "What a bunch of malarkey!" – an expression whose etymology still remains in the dark[2]. He should have listened to my mom. One of the 'bon mots' from her (German) side of the family is "If you marry a girl from Hornburg (the village my mother's family comes from), you don't need to buy a dog." Forewarned is forearmed.

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See also:
[1] http://www.thefreedictionary.com/souse?p
[2] http://www.worldwidewords.org/qa/qa-mal1.htm

Agatha's secrets should help medical writers

Hopefully all EMWA members have taken on board the research findings of The Agatha Project and are including phrase like "can you keep your eye on this", "more or less", "a day or two" and "something like that" in their regulatory documentation. These should trigger increases in the inspectors' serotonin and endorphin levels and fill them with pleasure and satisfaction when reading your documents. Medical writers' armoury can certainly be enhanced by the findings of the study undertaken by a team of neuro-linguists at the universities of London, Birmingham and Warwick in the UK (ITV1 documentary, 27 December 2005). The researchers subjected Agatha Christie's works to computer analysis and showed that the all-time best-selling novelist's word combinations stimulate higher than usual activity in the brain. Not only this, her secret also lies in the use of a very limited vocabulary so that readers are not distracted and can concentrate on the clues and plot. Writers of regulatory documents have long known this secret, however. And as for Agatha's use of em-dashes–to create a faster-paced, unreflective narrative–these have also been creeping into regulatory documents recently. So much for thinking that em-dashes should be reserved for dramatic effect and are inappropriate for scientific text. Even the opportunity to scorn their substitution for all other forms of punctuation as lazy writing has been denied one, now that a lecturer in English education at King's College London has dismissed the importance of correct punctuation as absurd (*The Daily Telegraph*, 4 March 2006).

Webscout:

The world of drug development and approval

by Joeyn Flauaus

Regulatory writing includes, among other things, preparation of documents to be submitted for drug approval. In the course of drug development a broad spectrum of documents needs to be written, such as clinical study protocols, clinical study reports, investigator brochures, and 'Common Technical Document' (CTD) modules. Generally, the writing of submission dossiers (CTD modules) is the most challenging as all the data gathered in the course of drug development are summarized and discussed.

Because writing regulatory documents is a complex process, some insight into clinical development and regulatory requirements is useful. Medical writers have to make sure documents comply with regulatory or other guidelines for content, format and structure.

Below you will find a selection of links that provide you with detailed information, guidelines and templates that are required in drug development and for drug approval.

http://www.fda.gov/oc/gcp/

Good Clinical Practice (GCP) is a standard for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials. This site provides information on Good Clinical Practice in FDA-Regulated Clinical Trials.

http://www.ich.org/

The regulatory authorities of Europe, Japan and the United States previously had their own processes and requirements for obtaining regulatory approval but a harmonization of these regulatory authorities was required to ensure a more economical use of human, animal and material resources, and reduce unnecessary delay in the global development and availability of new medicines. Hence, the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) was established to co-ordinate and harmonize international regulatory requirements.

http://www.aboutctd.com/index.htm

The CTD, a specification for applications for drug approval, was designed to be used across Europe, Japan and the USA. The CTD is maintained by ICH. This site provides comprehensive and detailed information about the CTD and the Electronic Common Technical Document (eCTD). In the download section, you can find the latest guidelines, templates, and FAQs for various modules.

http://www.clinicaltrials.gov/

This site, a service of the US National Institutes of Health, provides information about clinical studies in human volunteers sponsored by the National Institutes of Health, other federal agencies, and industry. Studies conducted in the US and in over 120 countries are listed in the database by diseases, treatments, locations, and names of researchers.

http://www.wiley.co.uk/genetherapy/clinical/

This site provides information on worldwide gene therapy clinical trials. The database allows a search by continents and countries where trials are being performed, indications addressed, vectors used, and gene types transferred.

Sensationalising science

The Social Market Foundation (SMF), an independent public policy think tank (www.smf.co.uk), has accused the UK media of sensationalising science. Pointing to the MMR vaccine shambles as an example, Claudia Wood of SMF said she thought the media should be cautious in how it gives over scientific evidence, and it should make sure that people understand that there are certain risks to some things but a lot of the time evidence isn't conclusive. The SMF have made several recommendations for improving scientific understanding among the public:

- Newspapers and broadcasters should employ more science graduates
- Scientists and science graduates should be encouraged to undertake media training
- Universities should offer multidisciplinary science degrees, which include issues of ethics
- Policymakers need a better understanding of public perceptions of risk

See: http://news.bbc.co.uk/1/hi/sci/tech/4771154.stm

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Please email me at **joeyn@trilogywriting.com** with any URLs comments or suggestions for the next issue.

Journal watch:

Ghostwriting

by Nancy Milligan

The role of medical writers in the preparation of manuscripts for publication has long been a contentious issue in the literature, and the past few months have been no exception, with a number of articles discussing the issue from a variety of contrasting viewpoints. At one end of the scale, Joyce P Griffin-Sobel, writing in the Clinical Journal of Oncology Nursing (CJON), clearly felt very strongly against the use of medical writers in publications [1]. Griffen-Sobel considered the use of professional writers as fraudulent, particularly if their contribution goes undisclosed. She goes on to suggest that the use of medical writers prevents oncology nurses from developing vital publication skills, and proposes that 'any oncology nurse who takes care of acutely ill patients on a daily basis has every skill needed to write a manuscript'. Who would have thought that those two sets of skills were so interchangeable? As a result, the editorial board of the COJN has proposed to refuse to publish manuscripts with contributions from medical writers or communication agencies.

A recent article by Brennan et al in the Journal of the American Medical Association is less negative [2]. Although the article is primarily concerned with the conflict of interest between a physician's commitment to patient care and the marketing of a product, the subject of ghostwriting is touched upon. The authors suggest that ghostwritten articles should be prohibited; however, it is unclear whether this means the use of medical writers full stop, or just the use of unacknowledged writers.

Finally, an article in the Annals of Internal Medicine gives a much more balanced view of the argument [3]. Although the article is not a glowing review of the contribution of medical writers, the authors do not appear to be totally against them as long as the rules are followed. That is, they suggest that editors should always be entirely upfront about the contributions of medical writers, an issue for which EMWA has been campaigning for some time. In fact, the authors referred to the EMWA guidelines on the role of medical writers in developing peer-reviewed publications [4], but strangely failed to reference them, a matter which was put right by Adam Jacobs in a letter published in a later issue [5].

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4. Jacobs A, Wager E. European Medical Writers Association (EMWA) guidelines on the roles of medical writers in developing peer-reviewed publications. Curr Med Res Opin 2005;21:317–22.
5. Jacobs A. Exorcising ghosts and unwelcome guests [letter]. Ann Intern Med 2006;144(2):149.

This is to be a regular column on articles in the medical literature about professional medical writers, so we would welcome any suggestions for articles to be included in the future. To make a suggestion please e-mail: **journalwatch@dianthus.co.uk.**

Buying prescription drugs on the Internet

Are you greeted in the mornings by a computer screen filled with emails imploring you to buy medications? The pros and cons of ordering drugs online are discussed in a recent article[1]. With Americans paying 60% more for the same medications than the British pay the main advantage is seen as lower prices (but they are not always lower). Other pros are convenience, obviating doctor visits for repeat prescriptions, and anonymity. The disadvantages are that you never quite know what you are getting. The dugs can be counterfeit (>10% of drug sold worldwide according to FDA), passed their expiry date, not approved, or have been taken off the market because of safety concerns. Having passed these hurdles the drug might not be suitable for you. Cyberdoctors are used by many Internet pharmacies to advise purchasers, who complete questionnaires, but few websites give the credentials of the doctors (if not computer entity) giving these services, and advice is not always reliable.

Other concerns are privacy and drug abuse. Privacy would be breached if the pharmacies were to make purchases public or sell information to other companies. Nonmedical use of prescription dugs comes second only to smoking marijuana as the most common illegal drug use. Online pharmacies who do not require prescriptions (about 20%) facilitate such abuse. The article's author advises patients only to use Verified Internet Pharmacy Sites (www.nabp.net/vipps/).

1. Weiss AM. Buying prescription drugs on the internet: promises and pitfalls. *Clev Clin J Med* 2006;73:282-8.

Clinical trials
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