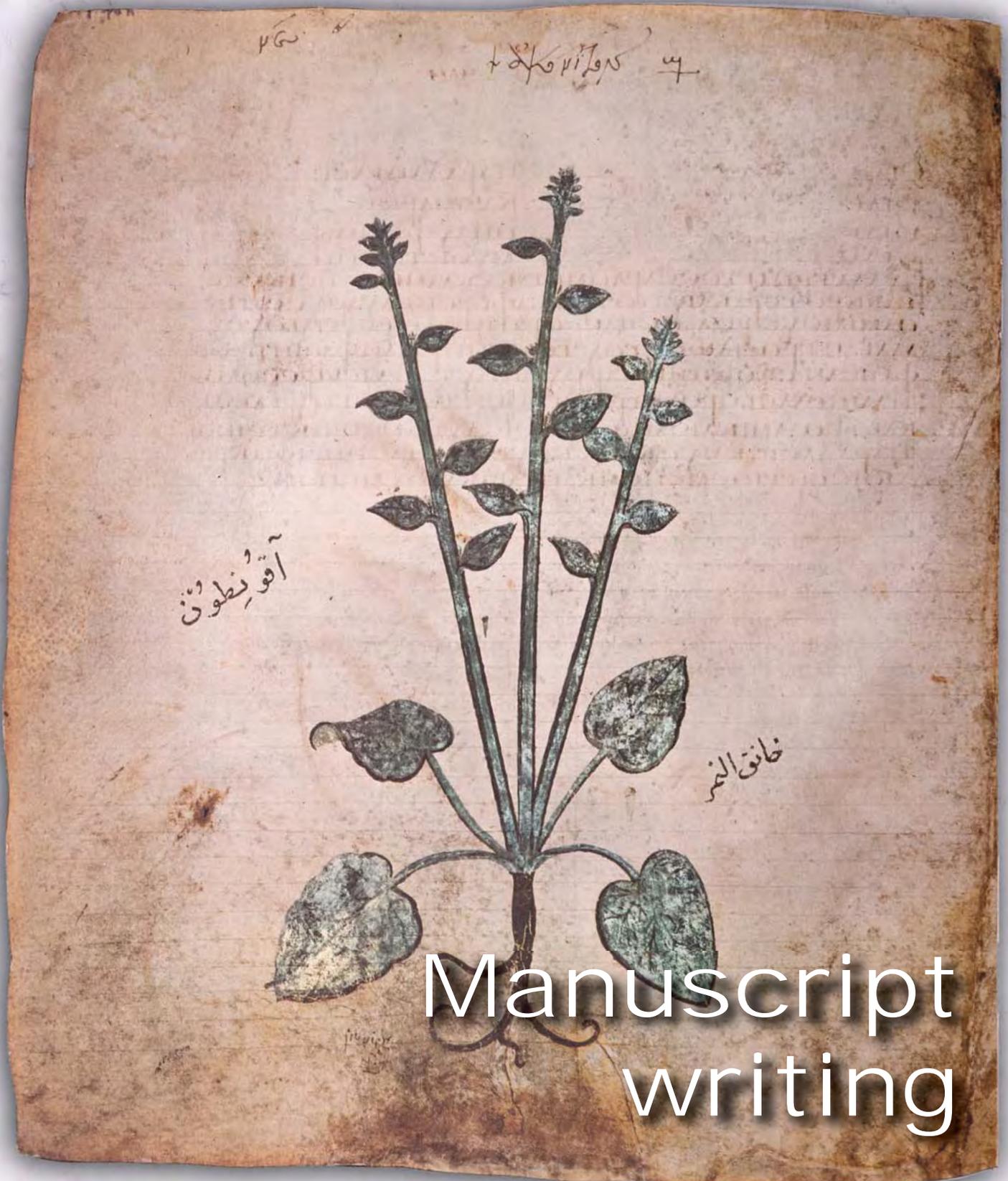


The *Write Stuff*

The Journal for European Medical Writers

Vol. 19, No. 3, 2010, ISSN 1854-8466.



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Journal insights

The *Write Stuff* is the official publication of the European Medical Writers Association. It is issued 4 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, but opinions expressed in individual articles are those of the authors and are not necessarily those held by EMWA as an association.

Articles or ideas should be submitted to the Journal Editor (see below) or another member of the Editorial Board.

Subscriptions

Subscriptions are included in EMWA membership fees. By writing to emwatws@associationhq.com 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 800–2500 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 e-mail address. Suitable quotes for side boxes can be indicated or they can be selected by the Editorial Board.
- Material should be submitted by e-mail 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, min. 360 x 510 pixels).

Timelines

Month distributed	Deadline for receipt of articles	Deadline for receipt of adverts
March	1 st January	15 th February
June	1 st April	15 th May
September	1 st July	15 th August
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Advertising rates (in euro, €)

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Manuscript writing

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■ From the Guest Editor's desk



The joys of... manuscript writing?

by Phil Leventhal

Writing a manuscript can be a daunting task. The pressure is on: the standards for peer review are high and more or less subject to the whims of the referees and editors. And an inability to get a manuscript published can be viewed by some writers (as well as their colleagues and clients) as a personal failure. There are also the difficulties in understanding, selecting, and explaining huge amounts of sometimes disorganised data; writing clear and convincing prose; and working within a team that might include awkward and chaotic members. Added to that is pressure to present the material with exquisite accuracy and to make sure that what is presented meets the highest ethical standards—tasks that should not be left only to a medical writer but often are.

These issues can fill writers with dread—but there are real rewards that make the challenge of manuscript writing worthwhile. There is a true feeling of accomplishment that comes with getting a manuscript published. Also, new projects are often intense intellectual challenges, making them an opportunity to learn new subjects, develop new areas of expertise, and use high-level problem-solving and analytical skills. And because manuscript writing is difficult, success is much appreciated by clients and co-workers.

There are many resources available to help write scientific manuscripts, but few address manuscript writing from the point of view of a professional medical writer. In this issue of *The Write Stuff*, we offer a comprehensive series of articles to help guide medical writers through the various aspects of preparing peer-reviewed manuscripts. For these articles, we included not only European voices but also American ones to get an international perspective.

Writers most often are asked to put together manuscripts based on clinical study reports (CSRs). Converting a CSR into a manuscript can be a monumental task, especially because the goals of these two kinds of document are different. Furthermore, a CSR might be hundreds of pages long with more than 100 tables and figures, whereas a manuscript is usually limited to 3000–5000 words and six or fewer display items. Also, manuscripts are often an afterthought, so additional analysis and information may be needed. Finally, a manuscript must tell a story and be acceptable for publication in a peer-reviewed journal. Fortunately, Jacky Wu (page 172) provides specific ideas to make converting CSRs to manuscripts manageable. For example, getting all involved parties to agree about what

will be included in the manuscript as early as possible in the writing process can save time and avoid a lot of troubles later on. The article also includes specific instructions on exactly what should be in each section of a manuscript based on a CSR, essential information for any writer.

The nuts and bolts of putting together a manuscript are one thing, but how does a medical writer learn to write well...and what does that mean? Some people seem to just have a natural knack for writing good prose, but can this be learned? Amin Bredan (page 175) explains that writing well is simply writing a clear and convincing narrative that leads the reader logically through the findings, rather than a chronological account or checklist, and he gives pointers on how to organise and word the manuscript to accomplish this. Stefan Lang and Marc Esser (page 178) add that, although manuscript and marketing writing differ, comprehensibility in all scientific communications is based on the same main principles: simplicity, structure, brevity, and stimulation.

Another critical soft skill in manuscript writing is effective interpersonal communication. For example, manuscripts are often produced by large multifunctional teams, some of whose members may have different opinions and styles of working. In particular, a disorganised team can create unnecessary complexity and problems. Fortunately, Andrew Walker (page 180) provides practical tools, tips and techniques for working within a multifunctional team producing a manuscript. He describes a logical process that minimises miscommunication, disagreements and delays when working group projects.

Effective communication with the editor and referees during the peer review process is also essential for manuscript writing. To get the manuscript published, emotions need to be mastered and referees' and editors' comments need to be dealt with in an appropriate and effective way. The stress that comes from not knowing how to do this well is what keeps many medical writers away from manuscript writing. Dorothy Pennachio and I (page 188) explain that there are both pragmatic steps and emotional devices that a writer can use to effectively communicate with editors and writers and deal with the peer-review process. The tips we provide can even help a writer use the review process as a way to improve the manuscript and grow as a writer.

Effective communication with the editorial office is important not only after the manuscript is submitted but also before peer review even starts. Elise Langdon-Neuner

From the Guest Editor's desk

(page 184) explains that the cover letter, a part of the manuscript often overlooked, can have an important influence on the editor's decision of whether to send a manuscript out for review. She describes how to put the right information into a cover letter so as to improve the chances of the manuscript being published.

Finally, we medical writers often justify our existence by saying that we improve the quality of published manuscripts, but is it true? And where do we and manuscripts fit in the grand scheme of medical communications? Sometimes they seem to be an afterthought or for advertising purposes only. John Carpenter (page 193) explains that peer-reviewed publications are an essential part of a medical communications strategy, and he describes the vital role they play and how they should be incorporated into the communications plan. Adam Jacobs (page 196) provides some evidence that, at least on the basis of fulfilment of CONSORT guidelines, professional manuscript writers have a positive impact on manuscript quality. So, it seems that we manuscript writers are important! But, of course, only if the job is done well, which is exactly what this issue of *The Write Stuff* is meant to help with.

Phil Leventhal

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Many of the topics discussed in this issue are touched on in the EMWA workshop 'Introduction to Manuscript Writing' (formerly 'Successful Manuscript Writing') co-led by me and Julia Forjanic-Klapproth, which will be given in Nice in November 2010 and in Berlin in May 2011.



'hoping for a hole-in-one'

© Renée Albe

Themes of upcoming issues of *TWS*

Women: The cover of the first 2010 issue of *The Economist* sported the question "What happens when women are over half of the workforce?" The question was prompted by the imminent event of women crossing the 50% threshold to become the majority in the American workforce. As the medical writing profession has long been in this happy situation *TWS* is calling for articles about women and medical writing. Please submit articles (up to 2500 words) and short reports/boxes (up to 100 words) by 1st October.

Medical writing careers: Alison McIntosh is guest editing the March 2011 issue. A broad range of career topics will be covered including getting started, different medical career paths, and the future challenges for medical writing.

Please contact Alison with your suggestions and contributions for this issue at aagmedicalwriting@btinternet.com.

Medical devices: Claudia Frumento will be guest editing the June 2011 issue which will focus on regulatory and communications issues relating to medical devices. Please contact Claudia with your suggestions and contributions for this issue at claudia.frumento@t-online.de.

As always articles or short reports on subjects of interest to medical writers which are outside the themes are also very welcome.

Please send articles, letters to the editor and suggestions for individual articles or future issue themes to me, Elise, at langdoe@baxter.com.

■ Message from the President



Dear Colleagues and Friends,

by Laurence Auffret

I hope you've made the most of the hot summer and found time to relax.

It seems our Lisbon conference took place only 5 minutes ago. A lot has happened for EMWA since then though, and we are already looking forward to the Nice and Berlin meetings.

Closer yet is the Institute of Clinical Research (ICR)-EMWA joint symposium taking place on 14th September in London. This year the event, themed 'Clinical trial documents: Joining the dots', is set to attract delegates from pharmaceutical companies, contract research organisations, medical writing agencies, freelancers, also academic, NHS and ethics committee personnel. There is still time to register, please have a look on the EMWA website for further information.

As discussed during the AGM in Lisbon our new UK constitution is being finalised and strategy plans are evolving. If you weren't able to attend the AGM you can access the minutes of the meeting on the website (About Us > EMWA News > Lisbon AGM minutes). Please let me have your comments as it is crucial for us to gather feedback from all members.

As a growing organisation EMWA needs all its members to act as ambassadors. You can now download a full presentation of the EMWA (see website) that can be used for various purposes:

- Getting a detailed scope of activities and benefits you can access as a member
- Explaining to management why we need to attend EMWA conferences
- Explaining the value of the membership to potential new members

If you use the slides we would love to hear about your experience and we welcome your suggestions. (Write to pr@emwa.org, or use our Facebook and LinkedIn groups).

The TWS has seen great changes in recent weeks as the new online archive has been launched. You can search the archive with keywords and make comments on the articles. This feature is freely accessible from the website for all EMWA members. Just log into the members-only section of the main EMWA website. Non-members can also access the archive at a fee. Once more, feedback is invaluable to help us improve this feature, so feel free to contact

our website manager (webmanager@emwa.org) with your suggestions.

We also had a number of new volunteers offering to help with the multitude of activities. Many thanks for coming forward and offering your skills and experience. We are currently looking for members' input in:

- Communicating with potential members and/or member targets
- Organising the Conference buddy scheme
- Contributing to content on the EMWA website, Facebook and LinkedIn groups.
- Taking and processing photos posted to the EMWA website
- Conducting and annual website review (broken links etc)
- Conducting electronic industry surveys
- Reporting on events of interest for our members
- Other areas of interests you think would help to improve EMWA's running and evolution

Any ideas please get in touch!!

I leave you with this 'Manuscript writing' issue which will guide you through the steps and issues revolving around the theme. Enjoy your reading.

Hope to see you in November in Nice.

Laurence Auffret

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About the cover image

This image is from an illuminated version of *De Materia Medica* produced in about AD 512. *De Materia Medica* is a series of five books on the medicinal properties of plants written by Dioscorides, who lived in northern Cilicia (southeastern Asia Minor) in the first century AD. As the manuscript was passed from one owner to the next, it was annotated in Greek, Arabic, Turkish, Hebrew, and French. It was acquired by Emperor Maximilian II in 1569 for the imperial library in Vienna, which is now the Austrian National Library, where it currently resides. For further information, see http://penelope.uchicago.edu/~grout/encyclopaedia_romana/aconite/materiamedica.html.



Diversifying the EMWA membership base

by Sophie Huggett

The 2010-2013 EMWA Strategic Plan [1] set out four main aims to support the assertion that 'EMWA is the network of professionals that represents, supports and trains medical communicators in Europe'. These aims are to further the profession; build the association; share expertise and grow the membership. Just 3 months on from its first publication, some of these aims are beginning to bear fruit. In this article, we hear from one new EMWA member, Sophie Huggett, about how she came to be interested in medical writing; why she joined EMWA; her first impressions of the association gained through her attendance at the May 2010 Lisbon Conference; and her interesting suggestion on how to appeal to potential members in the student arena. By reaching out to less conventional potential members like Sophie, we begin to appreciate how the overall membership profile can diversify and become further enriched as we move towards fulfilling the goals of the 2010-2013 EMWA Strategic Plan.

Sophie's Story:

European Medical Writers Association—it already sounded as if there was something in it for me. And so there was. I ended up at the EMWA Lisbon conference with my 13,3” Macbook screen full of inspirations. At 23 years of age, I am not exactly the average associate. I am a medical student in my 4th year and am currently working in an immunology laboratory in Hamburg, doing my PhD. I work part-time as a medical translator for a gynaecological review journal distributed within Germany. I am still very new to this field but have always thought about working in medical journalism. I grew up bilingually as my father is South African, then I learnt French and Portuguese and I always felt torn between studying languages or sciences. Thus, working as a medical writer, part- or full-time is something I could very well imagine. I started writing motivation letters for my friends' applications for scholarships and internships and, by chance, ended up working for a gynaecologist who liked my style of writing and asked me whether I wanted to try out translating for his journal.

In spring, I found EMWA by accident on the Internet while looking for medical writing workshops. I decided to give it a try by visiting the conference in Lisbon, an added

attraction, as I had studied there for a year in 2007/2008, which gave me the chance to visit my friends, enjoy *pasteis de nata* and recall my Portuguese. What appealed to me was that the concept and the workshops seemed very professional and so I was willing to pay the money for membership, advanced credits and the workshops. I was brought up in a family where expenses for the children's education were never thought about twice. So here I was, deciding to invest in my own education with a sum of money exceeding two months' earnings. First of all, I knew it would benefit me in my current job; secondly, it represented a realistic professional opportunity for me and a chance to meet those people already involved in an area that is arguably less well-known. My friends, for example, were not familiar with the job of a medical writer and could not possibly imagine what it consisted of.

Unfortunately, a lot of workshops were fully booked at the time I applied for the conference, but in the end I did find a few suitable ones. I attended publication planning, fundamentals of immunology, adverbs and corpus-guided translation. Fundamentals of immunology turned out to be a little too fundamental, but sometimes it is good to step back and see the bigger picture again once you are lost in biochemical signal transduction pathways. Furthermore, I found it interesting to observe what other people find difficult in a subject that I myself have mastered. Publication planning was interesting as it gave me a glimpse of what

My friends were not familiar with the job of a medical writer and could not imagine what it consisted of

working in the pharmaceutical industry might be like. The key question was: what do you have to bear in mind when a new drug comes on the market? The workshop was well done with an example of a drug for which publications and presentations had to be scheduled according to the annual meeting of the society that publish the journal and bearing in mind the dates when the clinical studies would be finished. I found the workshop very interesting. It did not have any specific relevance for my work as a translator, and although I study medicine, pharmaceutical companies are a mystery to me and with my alternative Greenpeace lifestyle, I would have never thought about working in one. However, people I met during the whole conference made me change my mind as they showed me a whole new working field that could be relevant to me once I finally know what to do with my medical degree.

What's news at EMWA

> Corpus-guided translation was a wonderful seminar that managed to answer a lot of my questions concerning the choice of words in a medical article. For those who are not familiar with this term: a corpus is a number of text files (100-200) converted from a pdf, for example, on a medical area. So I could have a corpus on gynaecology and immunology and they would serve as my database when translating a text. Specific programmes designed for corpus-guided translation then search a term or phrase within the text files. All relevant articles are then sorted and show the name of the journal they were published in. This

helps for embedding specific terms and phrases into a text and can quickly answer whether, for example, to use the word 'pathological' or 'pathologic'. I did not know about this fantastic tool before and I have since started using it. Building a corpus takes time, but it is worth it. I not only use it for my translations, but also for editing my own scientific work as it gives examples of good medical English. The last workshop I took was on adverbs, which I found very useful, too. In my opinion, the position of an adverb or an adverbial phrase closely correlates with style. I also did not know of any rules concerning the position, so it was good to underpin my feeling for language with a few basic grammar rules.

However, the EMWA conference does not only consist of the workshops. The lectures were interesting for me as a medical writer, but, coincidentally, also from my perspective as a medical student. For example, I had never used podcasts before and now I have started using them for my studies. I have always enjoyed playing around with new technologies and am very familiar with new Internet tools as I had the chance to grow up with them. To be honest, I cannot imagine studying medicine without the Internet. Even so, the EMWA lectures on Web 2.0 were inspirational in the use of the Web and showed how medical writing and the Web are closely linked. I would have never thought of opening up a pathology laboratory in Second Life, as Dr Anne Cunningham, the plenary lecturer had done, just to give an example.

However, the most relevant part of the conference for me was networking (here, I mean in reality, not in cyberspace). I had very interesting conversations over lunch concerning careers and opportunities as a medical writer but also exchanged philosophies about living and working. When I left the conference I felt that it had opened up an entirely new world for me, with many more doors and pathways to be explored. It was one of those great moments in life where you were courageous enough to try out something completely new, without any expectations and then all of a sudden, you meet the most interesting people and have unique experiences. And it was one of those moments where I understood, that so far, I have been very lucky with turns my life has taken.

I have just one idea on how to improve the conference: open it up for more students, by introducing student fees for the conference. By increasing EMWA's profile in the universities of Europe, it seems to me there is surely an untapped potential membership group—and, I think the inspiration would be mutual.

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'Oh my darling, I do hope they'll take good care of you!'

© Renée Albe

Senator Grassley's report on ghostwriting

Those who follow developments on ghostwriting in the medical literature will be aware that US Senator Charles Grassley has been an outspoken critic of the practice. He has just released a report [1] into his 2 years of inquiries into medical ghostwriting.

On the whole, much of what he writes is sensible, but there do seem to be a few ways in which he has slightly missed the point.

The main thrust of his argument, which I wholeheartedly agree with, is that ghostwriting is a bad thing, particularly when financial relationships are not disclosed. If a drug company pays a ghostwriter to write an article, respected academics sign their names to the paper without reading it, and the involvement of the drug company is not disclosed on the paper, then there is a serious lack of transparency and a worrying potential for bias. Grassley condemns such practices, and rightly so.

Grassley goes further, and points out that even if a medical writer is acknowledged, "it is unclear whether or not the academic expert evaluated the implications of what he was submitting for publication". That's a fair point. Acknowledgement of writing assistance, by itself, is not enough: it is also important to be sure that named authors control the content of the paper. This is a point also made in the EMWA guidelines [2] on the role of medical writers in publications (which I'm pleased to see was cited in Grassley's report).

It is disappointing, however, that Grassley makes no mention of the legitimate role that professional medical writers have when properly acknowledged and when working in a meaningful partnership with the named authors. From reading his report, you could be forgiven for thinking that he wasn't aware that there are ethical medical writers out there who wouldn't dream of the sort of ghostwriting he describes. Given that he's supposedly spent 2 years looking into this, that omission is unforgivable.

A further good point that Grassley makes is that policies and guidelines against ghostwriting need some means of enforcement. However, it is not clear who he believes should take on that role. One hint in that direction is that he does mention a checklist published last year in *PLoS Medicine*, which is designed to allow journals to ensure compliance with good practices in this area [3]. For example, it asks "Did the author(s) make the final decision on the main points to be communicated in the manuscript, particularly in the conclusion?" If journals were to incorporate the checklist in their instructions for authors, it would be far harder to publish papers with inappropriate involvement of medical writers. Sadly, although Grassley mentions the checklist, he doesn't make any recommendation that it be used, which is puzzling given that it is designed specifically to stamp out the very practices he objects to so much. It is also disappointing that *PLoS Medicine*, which has been vocal in condemning ghostwriting, has not incorporated any requirement for authors to complete the checklist in their instructions for authors.

My own opinion on enforcement is that it is probably going to have to be the responsibility of medical journals to police the articles they publish. Granted, most journals lack the resources to do this properly, but I can't see any other realistic way in which it could be done. The ghostwriting checklist was specifically designed to allow journals to take on that policing role with minimal resources. I am sure that if journals were to take a more robust approach to eliminating ghostwriting, it would have a big effect.

There are one or two other strange things in Grassley's report. Some examples of confusing and vague acknowledgements of writing assistance were taken from papers published over 10 years ago, when there were no guidelines for acknowledgement of medical writers. Grassley also states that, despite the publication of many guidelines condemning ghostwriting over the last few years, the prevalence of ghostwriting remains unchanged. He cites a study looking at the prevalence of ghostwriting [4], which concludes "The prevalence of honorary authors has not changed significantly since 1996, but ghost authorship has declined significantly." However, Grassley misreports this, saying that "these numbers did not differ significantly from a 1996 study", and also "the prevalence of ghostwriting remains largely unchanged". He is also confusing "ghostwriting" and "ghost authorship", but that's a discussion for another day.

Not only did the study he cites find that ghost authorship has declined significantly, but my own research also found a decrease in the prevalence of ghostwriting between 2005 and 2008 [5]. Grassley didn't cite that research. Whether that's because he wasn't aware of it or because he ignored it because it didn't fit his story isn't clear. Either way, it calls into question the intellectual rigour of his report.

Anyway, those gripes aside, it's worth reiterating that the main thrust of what Grassley is saying, namely that it is important for medical publications to be prepared in an honest and transparent manner, is entirely sound.

Just one final rather intriguing point: given Grassley's clear disapproval of ghostwriting, it is very odd that the report has Senator Grassley's name on the front, and yet the text refers to him consistently in the third person. I wonder who wrote the report? The writer is not acknowledged.

Adam Jacobs

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This is an edited version of a blog that was previously published on my website.



From clinical study report to journal article: Presenting the science and the message

by Jacqueline Wu

Publication of clinical trial results is an important step in the development and marketing of new drugs and new indications for existing drugs. In the United States, FDA regulations now require the publication of results for all clinical studies of drugs, biologics, and devices, except for Phase 1 trials [1]. The task of reducing a clinical study report (CSR) that can be thousands of pages long, to a manuscript of 5000 words or less is one that frequently falls to the medical writer. This article aims to provide some insight into writing an accurate, well-written, and timely manuscript on the conduct and results of a clinical trial that will be acceptable for publication in a peer-reviewed journal. It is not intended to provide a complete list of what should be included in such a manuscript. Several sets of guidelines are available that provide detailed information on requirements for manuscripts describing clinical trials, including the International Committee of Medical Journal Editors (ICMJE) [2], Consolidated Standards of Reporting Trials (CONSORT) [3, 4], and Good Publication Practice (GPP) guidelines [5].

The medical writer preparing the manuscript—whether as a company employee or as a freelance writer—usually works under the direction of a company publications committee or medical affairs department. With regard to authorship, it is important for the writer to ensure that the ICMJE, CONSORT, and GPP guidelines are carefully followed. However, as a writer, you should remember that even though you prepare the manuscript, the authors are responsible for its content and must be fully involved in its development and review. The topic of manuscript authorship has been extensively discussed in this journal [6, 7, 8] and elsewhere and will not be addressed here.

Before you start writing, remember that a manuscript is not intended to read like a CSR. A CSR contains lengthy and detailed descriptions of the conduct and results of a study, with multiple numbered sections and subsections, and extensive supporting documentation. A manuscript should read more like a narrative summary of the study, with a limited number of sections and all necessary information contained within the text, tables, and figures. In general, try to avoid cutting and pasting text from the CSR. I've found that it's usually easier to write summary text from scratch rather than try to condense the detailed information in the CSR.

First steps

One of the first steps in preparing an article based on a clinical study is to determine which endpoints will be presented. Clinical studies frequently have multiple endpoints and, due to space limitations in the journals, it may not be possible to present all of these in one article. The primary endpoints of a study should always be defined and the results presented, unless they have previously been published elsewhere. Secondary endpoints may be presented in the same article as the primary endpoints, in a separate article, or not at all. If only some of the secondary endpoints are presented, be careful to avoid bias, or even the appearance of bias, in deciding which endpoints to include.

It is important for all involved parties to agree about what will be included in the manuscript as early as possible in the writing process. This can help avoid extensive revisions of the manuscript later on. Everyone involved in reviewing the manuscript should understand the data and what conclusions can be drawn from them. I have worked for clients where a lack of understanding of the data has led people to make exaggerated and inappropriate statements about the study results. This can be avoided by having a full discussion of the data and what conclusions can be drawn from them either during the manuscript kick-off meeting or during the preparation and review of the manuscript outline.

All parties should agree what will be included in the manuscript as early as possible

It is important to decide which journal the manuscript is intended for as early as possible. Most companies have their own procedures for selecting a journal. If possible, selection should be done during the kick-off meeting or when the manuscript outline is reviewed. The manuscript can then be drafted according to the selected journal's guidelines for content, style, and format. Check the journal website for information, including their target audience, the types of articles they publish, and the maximum length of the manuscript. Read articles in recent issues to get a feel for the style of the journal.

Describing the Methods

Once agreement has been reached on what should be included in the manuscript, I usually start by writing the methods section, as I find this is the best way of familiarising

Presenting the science and the message

myself with the study. Condensing the detailed methods in a clinical study report into a concise description for a journal article can be challenging. A good place to start is with the CONSORT checklist [3], which lists the essential items that need to be included.

The methods section should start with a statement about when and where the study was conducted, that Institutional Review Board (IRB) or Ethics Committee approval for the protocol and patient informed consent were obtained before any study procedures were performed, and that the study was conducted in accordance with ICH guidelines for Good Clinical Practice [9].

Important inclusion/exclusion criteria need to be summarised. These should include patient age, stage of the disease being treated, key markers of the disease, the presence of absence of other medical conditions, use of concomitant medications, and important clinical laboratory values.

A description of study design (e.g., prospective, double-blind, randomised, placebo-controlled) should always be provided, as well as information about the test drug (and comparator drug if applicable) and dosing regimen, the duration of treatment and any follow-up period, and the timing of patient evaluations. All endpoints to be presented in the results should be described, together with the methods for measuring them. Describe the primary endpoint first, then any secondary endpoints. This information can be condensed from the CSR by presenting only the relevant facts; for example, when blood samples were collected but not the details of how they were collected, and by summarizing when procedures were performed rather than listing procedures at every study visit (e.g., “blood samples for clinical laboratory measurements were collected every 2 weeks for the first 8 weeks and then every 4 weeks until the end of the study”).

A description of the statistical methods used to compare groups for primary and secondary outcomes, as well as methods for additional analyses such as subgroup analyses must be included. If you're not familiar with the statistical methods used in the CSR, ask the statistician for help to make sure that you're describing them accurately.

Presenting the Results

As with the methods section, condensing the results of a clinical study into an acceptable length for a journal can be challenging. The use of well-constructed tables or figures can provide a concise and effective way of summarizing large amounts of data. Three important areas need to be presented: patient disposition and characteristics, efficacy results, and safety results.

The CONSORT checklist strongly recommends the use of a flow diagram for describing patient enrolment and disposition. You may be able to take this directly from the CSR,

or you can refer to the example flowchart provided on the CONSORT web site [3]. Present patient demographics and baseline characteristics in a table and briefly summarise the data in the text. One way I have found to do this is to present the key information for the overall population in the text and state whether or not there were any notable differences between the treatment groups. Readers can refer to the table for detailed information for each treatment group.

Present efficacy results in tables and figures wherever possible (remember, “a picture paints a thousand words”). However, keep in mind that some journals limit the number of tables and figures that can be included, so less important information (e.g., demographics where there is a single study group) can be presented only in the text. Do not copy tables and figures directly from the CSR, as these are usually more detailed than needed for a manuscript. For example, a CSR table may include detailed statistical results or multiple time points, while for a manuscript, the key data (e.g., mean, standard error or standard deviation, confidence intervals, and p-values) and just one time point may be sufficient. Again, the text should contain a brief summary of these results and should not repeat data presented in the table or figure. Present results for the primary efficacy endpoint first and then present the secondary endpoints in the same order as they were described in the methods.

Safety data usually consist of adverse events and other variables such as clinical laboratory tests and vital signs. Present the more frequent or relevant adverse events in a table and describe key differences between treatment groups in the text. A similar format can be used for laboratory values or vital signs. More detailed information about serious or other important adverse events is best provided as descriptive text.

Writing the Introduction and Discussion

I usually write the introduction and discussion of a manuscript after I have drafted the methods and results section,

as by then I have a better understanding of the conduct and results of the study. The introduction in the CSR can sometimes be used as a starting point for the manuscript.

If you use text and supporting references from the CSR, remember to verify the content and citations of all references to be sure they are being used appropriately. The goal of the introduction is to provide a brief overview of the disease and treatment that are the subjects of your manuscript. A brief review of limitations of current treatments (if applicable) is helpful and can provide a useful transition into presenting the rationale for the study being reported.

The discussion is often the most contentious section of the manuscript, as this is where the final conclusions or ‘messages’ of the study are presented. The objective is to

I find to familiarise myself with the study starting with the methods section is best

The discussion is often the most contentious section of the manuscript

Presenting the science and the message

- > discuss the study results in the context of previously published information about the disease and drug being reported. Include a discussion of the limitations of the study. Do not repeat data presented in the results section, do not cite tables or figures from the results, and do not present new data. Do not write conclusions that are not supported by the data and do not make overt marketing statements; these are likely to be questioned or removed by the journal's reviewers. As mentioned earlier, make sure that everyone involved in reviewing the manuscript understands the data and what conclusions can be drawn from them.

Handling the internal review process

Most companies have a standard review process that defines who reviews the manuscript and when. As a writer, the extent of your involvement in the review process may depend on whether you're a freelance writer or permanent staff member. If you're working as a freelance, you probably won't have a say in who reviews the manuscript, but you should ask to participate in review meetings if possible. This can really help you get a feel for what the reviewers are thinking and may provide insight into their comments. If multiple reviewers are providing comments on your draft

manuscript, ask for someone to consolidate them into one document. This makes incorporating the edits much easier and will also highlight any conflicting comments.

If you're a staff writer, you may have more input into the review process and more direct access to the reviewers. Include as many different viewpoints as necessary early in the review process so that you're not surprised by last-minute comments that may change the entire tone of the manuscript. I usually find that review meetings or conference calls are best for early draft reviews and that subsequent edits can be handled by e-mail unless there are substantial changes.

Again, remember that even though you are writing the manuscript (either as a freelance or a staff writer), the authors are responsible for the final content and must be fully involved in the review process.

Final words

Companies often conduct multiple studies of similar design with a particular drug or will publish different endpoints from the same study in different articles. When this happens, it can be difficult to avoid repeating very similar information in different articles. I usually try to find at least one unique aspect of each study to focus on and make sure this focus is reflected in all sections of the manuscript, especially the introduction and references. In particular, I try to minimise citing the same general references in every manuscript, but make sure I cite all other publications describing the study.

Preparing a succinct account of a clinical trial for a journal article can be challenging but very satisfying. I like to remember that very few people will read an entire CSR, but a well-written manuscript published in a reputable journal may be read by a wide audience; and as writers, isn't that what we all want?

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Science quotations

The following are selected quotes from a great collection of quotes, mainly about science, compiled by Helmut Schütz of BEBAC Consultancy Services for Bioequivalence and Bioavailability Studies. The full list can be accessed at <http://forum.bebac.at/Quotes.html> where the original sources are (mostly) revealed by hovering over the author's name at the end of the quote.

A drug is that substance which, when injected into a rat, will produce a scientific report. Anonymous

Those people who think they know everything are a great annoyance to those of us who do. Isaac Asimov

Pharmacokinetics may be simply defined as what the body does to the drug, as opposed to pharmacodynamics which may be defined as what the drug does to the body. Leslie Z. Benet

Statisticians, like artists, have the bad habit of falling in love with their models. George E.P. Box

To call the statistician after the experiment is done may be no more than asking him to perform a postmortem examination: he may be able to say what the experiment died of. R.A. Fisher

See page 233 for more quotations.



Writing the results and discussion of a research paper

by Amin Bredan

Despite the availability of a wide variety of resources on good science writing and the introduction of science writing courses in many academic institutions, journal editors continue to air their gripes about having to slog through poorly written manuscripts [1]. The journal *Nature* has this to say on its website: “Many papers submitted for publication in a *Nature* journal contain unnecessary technical terminology, unmanageable descriptions of the work that has been done, and convoluted figure legends” [2]. Not all can be blamed on inadequate fluency in English; even manuscripts that are grammatically sound can be unnecessarily difficult to read. The roots of the problem seem to lie deep in ingrained habits transmitted from mentors to protégées. In an article recently published in *Science* [3], the author states that academic language “uses sophisticated words and complex grammatical constructions that can disrupt reading comprehension and block learning” and mentions the “impenetrability of prose constructions.” However, nowhere in the article does the author address the need for improving and simplifying academic writing, and instead suggests that students should be taught better how to deal with the status quo.

Many science papers also have problems in the organisation and presentation of the information in the different sections. In this article I first discuss some important elements in the organisation and presentation of results and the requirements for a scholarly discussion, and I then deal with issues of writing style.

Provide the information where the readers expect it

The research paper has a well-established structure, commonly referred to as IMRAD, though some exceptions exist, such as articles in *Nature* and *Science*. In the IMRAD format, the introduction is succeeded by the methods section, after which come the results, followed by the discussion, though it is quite common to combine results and discussion in one section. If these sections are separate, the results section should recount the results and refrain from interpretations, discussions and reference to previous work. The discussion should provide a brief summary of the important results and discuss them in the context of the aims, but it should not restate the results in detail or repeat the background material provided in the introduction. Also, it should not discuss methods unless it is a methodology paper or there is a specific issue affecting the results.

Keep the readers in mind

Sometimes scientists spend such a long time with their experiments and manuscripts that everything becomes obvious through familiarity. Whether a particular point is

obscure because the authors did not explain it clearly or because they thought it did not need explanation, the result is the same. Authors should be continuously aware of this and keep their readers in mind while writing. They should also try to read their manuscript through the readers’ eyes. It is even better to ask someone who is familiar with the topic but not involved in the work to review the manuscript.

Writing results

Good results speak for themselves, but their eloquence can be stifled by bad writing. One can view the process of writing the results as a continuum through which the laboratory notes are morphed into the final version of the results section of a manuscript. For experienced writers, this process comes naturally. But for younger scientists, it can be a difficult process and the result is not always pleasing. Though writing is not an exact science and there is no magic formula to follow, adhering to some simple rules can reduce the stress and avoid many pitfalls.

Don’t just report results chronologically: Tell a coherent story

There is general agreement among editors and professional science writers that the results section should tell a story and not be a chronological account of the results. Studies can run into difficulties that necessitate backtracking, introduction of new experiments and the tying up of loose ends. Presenting the results in their chronological order in such cases can be disorienting for the reader, who has to invest much effort to follow what was done and why. Readers are not interested in what was done when, but in grasping the overall picture as well as the details as easily as possible.

One way to prepare for writing the results is to collect the various pieces of evidence, be they tables, graphs, gels, micrographs or brief summaries of data, and to place them on a table. Sheets of paper can be easily rearranged to find the best way for presenting the results. That arrangement can then serve as a road map for the actual writing. Alternatively, one can write an outline of the results or draw it diagrammatically. The outline can fit on one page and it can be easily modified. Regardless of which method one adopts, it is always important to prepare a plan ahead of the actual writing, to follow it, and to modify it if necessary.

Hand the results to the readers: Do not drop them in their laps.

The results section should report the results of the experiments without interpreting them or describing the rationale or methodology. Some journals might enforce this policy, but others might have different requirements. For

Writing the results and discussion of a research paper

> example, the instructions to authors on the website of *Infection and Immunity* state that the results section should “include the rationale or design of the experiments as well as the results.” Introductory notes on rationale and methodology orient the readers. This is particularly relevant when the experimental setup is complex or there are many similar experiments. A good example of providing context to results without being intrusive is the following:

“To prove that M2e-tGCN4 is indeed a tetramer, chemical cross-linking experiments were performed with the homobifunctional cross-linkers BS3 and DSP” [4].

However, one should not include references to previous work or interpretation and analysis.

Discussion: Going beyond the results

In the discussion, authors try to explain how they answered the research question and convince the readers of the validity and significance of the results. To this end, authors use several means. They interpret the results by explaining what they mean and by comparing them with published results. If the results contradict published data, the author should try to explain why. Citing only papers that agree with the current work not only shows bias but undermines the authors’ intention to convince. The author should discuss how the results fit with previous hypotheses, and whether existing hypotheses should be modified or new ones proposed. By accurately describing the limitations of the study and how they might affect the results, the author engages in self-criticism and provides evidence for objectivity. Finally, by proposing future lines of work, the author indicates how the current work serves as a stepping stone for greater understanding or development.

Avoid rehashing the results

The basic requirement for a good discussion is not to simply rehash the results with a sprinkling of references to the literature. One should have a strong grasp not only of the results, but also of the relevant literature. As the author is writing a particular result, he or she should be aware of how it relates to the literature. If the author has to repeatedly shuffle through published papers in search of something relevant to insert after a particular result, the discussion is likely to be disjointed.

Should the discussion aim to discuss the research question or the results?

When I asked a few colleagues this question, most of them seemed surprised: To them it was obvious that it should discuss the results. In my opinion, by concentrating on the research question, one discusses the results more effectively because the discussion will circle around how the results answer the research question. Concentrating on discussing the results, on the other hand, can generate a mental check list that the author addresses one by one. This could fragment the discussion and leave it up to the reader to assemble the pieces, which is contrary to the principle of conveying a clear message.

Organising the discussion

Inexperienced authors can be faced with the dilemma of where to start the discussion and how to proceed. Perneger

and Hudelson propose a framework for writing the discussion [5]. They suggest starting out by stating the main findings and discussing them in the context of published data, discussing the implications of the results, and ending with their strengths and limitations and finally possibilities for future work. However, one should not restate all the results or refer to figures or tables, unless it is a figure proposing or modifying a hypothesis. Following such a ‘template’ should yield a discussion that is, at least in principle, well structured. Some authors preface this ‘template’ with a brief statement on the current state of knowledge, such as

“Development of polarity in epithelial cells requires specialized localization of proteins to distinct PM domains. Increasing evidence has been gathered concerning the important role of adhesion system and cytoskeletal components in the various processes leading to this organization (41)” [6].

This is acceptable, providing that it is kept brief, as in this example.

Combining results with discussion

Many journals allow presentation and discussion of results in one section. If this is an option, the author should carefully consider both possibilities, because the data might be more easily dealt in one of the two formats. When results and discussion are combined, the results are organised into a coherent story, and the discussion accompanies the narrative as it unfolds.

Write in a simple, clear style

Many scientists seem to have an aversion to writing in a simple style that is clear and easy to read. They do not seem to heed the request of science journals that authors should “present their findings and conclusions in simply constructed sentences” [2]. It might be argued that the complexity of scientific prose arises from the complexity of the science. I propose that it is the complexity of scientific prose that frequently makes science difficult to read. For example, there is no scientific value in adherence to the passive voice, long parenthetical clauses and a pompous writing style.

Paragraphs: one topic each

Text is divided into paragraphs for a good reason: Each paragraph should address one central topic. We are always aware that a new paragraph signifies a change in topic. If a paragraph contains more than one topic, the reader misses that signal. Though a long paragraph is not in itself a problem, authors should be particularly wary of any long paragraph because it could mean that it deals with two or more topics. Though one cannot judge a paragraph as too long when it surpasses a certain number of words, any paragraph that goes beyond about one page should be scrutinised for multiplicity of topics.

Sentences: one idea each

While a paragraph should be devoted to only one topic, a sentence should be limited to stating only one fact, observation, instruction, idea, concept or argument. Sentences in English are generally structured to provide introductory or linking material at the beginning and new information

Writing the results and discussion of a research paper

at the end, which is known as the ‘stress position.’ Readers tend to pay greater attention to material in the ‘stress position’ [7]. If a sentence addresses more than one idea, this pattern is lost.

Avoid long sentences

Long sentences that are well written are not difficult to read, but it is difficult to write long sentences that maintain fluidity and clarity. Moreover, long sentences are at a greater risk of having grammatical faults. Long sentences can be shortened by deleting unnecessary words or phrases, and if this is insufficient, by splitting them. In the following example, the sentence is about a regulatory loop, but it mentions five successive steps:

“A feedback regulatory loop in which MYC directly binds and activates the transcription of the cluster *miR-17-92* that consequently negatively regulates E2F1 by direct interaction, while *c-Myc* is directly inducing expression of the E2F1 that in turn induces *c-Myc*, was recently described (37)” [8].

In such instances, splitting the sentence will facilitate assimilation of the information.

Avoid abuse of the passive voice

The passive voice used to be considered an essential part of the scientific writing style because it gives an air of objectivity. But journals have been encouraging the use of the active voice, and it seems that authors have been responding. The passive voice is a more awkward construction than the active voice. This is particularly true for long sentences because the main verb comes at the end. For example, the sentence in the previous section For example, the sentence in the previous section (reference 8) can be improved by converting to the active voice: “O’Donnell et al. (37) recently described a feedback regulatory loop in which...”

Avoid long parenthetical clauses

Parentheses are useful, but they work well only if the parenthetical material is brief. Multiple insertions of lengthy parenthetical material can make the sentence unreadable. One of the best examples of this is the following:

“We adopt this broad-scale approach to determine that relationships occur both at the level of the population (and hence not confounded by [1] potential environmental variation and/or [2] statistical nonindependence of individuals) and also across individuals (because [1] relatively recent colonization of the UK by rabbits [15], and [2] previous work [18] demonstrating extremely fine-scale genetic structuring in UK rabbits over short spatial scales both make it difficult to define what constitutes a ‘population’ for analysis)” [9].

Long and repeated interruptions of a sentence can oblige the reader to restart reading the sentence, and that is annoying. Long parenthetical material is better split off as a separate sentence, or perhaps even deleted if it is not important.

Avoid writing in a style that seeks to impress

Trying to sound scholarly by adopting an inflated language style is not a good idea for two reasons. First, an officious style can put off readers. Second, such a style is usually

convoluted and requires more words. Let us look at the following sentence:

“The answer to this question is still unclear, probably due to the limits of the techniques used to resolve temporally events that are almost coincident” [10].

What the author means is

“This question has not been answered probably because the techniques cannot resolve events that almost coincide.”

Vocabulary: Keep it simple

Finally, the choice of vocabulary is important. Scientists have many pet words and phrases. They are perfectly good parts of the language, but they usually have shorter or simpler alternatives. The CBE Style Manual advises authors to “Review the text of the manuscript to eliminate phrases and words that are not needed” [11]. Moreover, good writing requires variety, and insistence on the use of a particular set of vocabulary can cause the prose to be dull. For example, ‘due to the fact that’ can be phrased more simply as ‘because,’ ‘the number of cells was determined’ should be changed to ‘the cells were counted,’ and there is no justification for the omnipresent preference for ‘prior to’ over ‘before.’

Final words

The main purpose of writing a paper is to convey a message. To help achieve that effectively, it is useful to adopt the following guidelines.

1. Organise the results into a meaningful coherent story.
2. Reserve the results section only for presentation of the results.
3. When writing the discussion, follow the guidelines of Perneger and Hudelson [5].
4. Write in a direct, simple and clear style.

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Writing in science and marketing—Are they really separate worlds?

by Stefan Lang and Marc Esser



Emotional advertising versus rational science—is there any greater contradiction? Thus, we were understandably surprised when a seminar sponsor asked us to prepare a single workshop to cover both scientific writing *and* health care copywriting in German. We wondered whether a one-day seminar could do justice to the two topics, who the participants would be, and from which professions they would come. At the outset, we learned that most participants had one thing in common: an academic background in science, which—at least in Germany—frequently results in a cumbersome writing style.

The sponsor added that attendees would primarily come from three professional groups:

- Scientists in academia and industry who have to write both classic research papers and press releases about recent developments
- Product managers who are concerned with medical writing issues and, at the same time, need to evaluate the work of marketing agencies
- Communication agencies expanding into the medical-health market

Mainly, these participants have the same professional background: science or medicine. That means that they are doubtlessly well trained in their fields but—especially those educated at German universities—relatively inexperienced in writing. Because neither communication nor technical writing is a curriculum component at most German universities, students often get in the habit of adopting the tedious and sometimes incomprehensible style of German textbooks and scripts. Consequently, their texts—no matter whether they write scientific papers, sales brochures, or product manuals—suffer from the same communicative weaknesses.

Obviously, the main objective of writing is to communicate effectively, making comprehensibility imperative. When planning our workshop, we therefore asked ourselves whether a concept of comprehensibility exists that could be applied to both scientific writing and copywriting in health care. Research revealed that in the 1970s, the ‘Hamburg School’ of linguistics promulgated a theory of comprehensibility whose framework assumes four

The ‘Hamburg School’ of linguistics theory of comprehensibility assumes four dimensions: simplicity, structure, brevity, and stimulation

dimensions: simplicity, structure, brevity, and stimulation [1]. This seemed to fit our needs for teaching comprehensibility perfectly.

Four dimensions of comprehensibility

Simplicity

Students who grow up with traditional German college textbooks might come to think that complicated subjects demand complicated language, yet the opposite is generally true. Simplicity does not imply losing information or skipping over complex concepts. Neither does it mean that one should avoid technical terms that are obviously required because they are precise. But if the content is complicated and unfamiliar to readers, increased complexity hampers comprehensibility of both scientific and non-scientific works. This increased complexity frequently arises from the overuse of abstract or foreign words. ‘Higher symptomatology’, for example, leaves the reader unsure whether number, prevalence or severity of symptoms is meant. Orwell’s comment about Latin words, which he says, “fall upon the facts like soft snow, blurring the outline and covering up all the details” [2], is certainly apt in this context and can be extended to include meaningless phrases, unexplained terminology and abbreviations, or obscure, steadily changing synonyms.

Structure

While many authors spend hours and days fine-tuning their wording and syntax, they may neglect both overall text organisation and the structuring of paragraphs. Overall text organisation frequently reflects only the associative writer’s path of discovery, and paragraphs are viewed as nothing more than unsorted collections of information. Although an excellent scientist is likely to be a creative genius as well, the same individual needs to arrange his thoughts ‘logically’ in order to provide understandable texts for those who are not familiar with the subject. Both an introduction of a research paper that does not logically culminate in a hypothesis and a fancy website with unconnected facts scattered all over the place leave the reader helpless and disappointed.

Comprehensibility is improved by a text organisation that aids the reader. This includes a clear overall text structure that pulls the reader along the current of ideas and an argumentative paragraph structure. Basically, the contents of a paragraph are the introductory topic sentence, explanatory body sentences, and a concluding observation. Importantly, a well-structured text originates in the steps of the

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writing process itself. To crystallise the topic, an organisational concept needs to be developed that can be translated into the organisation of chapters and paragraphs. A rough draft is then written and revised in a separate step. This procedural approach results in scientific texts that are easily understood and marketing texts that make a longer-lasting impression.

Brevity

Although most guidelines for scientific, commercial, or literary writing consistently stress the importance of brevity, long and complicated sentences still characterise many Germans' writing, both in their native language and in English. Experience shows that only a few rambling sentences can make research papers or brochures almost incomprehensible. A good press release, for example, states the who, what, where, when, why, and how facts in the first paragraph. However, answering these W questions within the first sentence would simply overwhelm the reader. And while readers of scientific texts may go over a sentence twice to grasp the message, recipients of non-scientific texts are frequently not as patient. A complicated sentence may be enough for them to stop reading immediately.

Only a few rambling sentences can make research papers almost incomprehensible

Stimulation

Stimulation, a less tangible element of comprehensibility, seems to distinguish scientific from non-scientific documents. Advertising texts may stimulate readers' attention through emotion, imagery or humour. Consequently, advertising language also has to be entertaining and enjoyable in order to find an audience. In contrast, most peer-reviewed scientific journals usually reject emotional interjections and humour, but there are many examples of imagery in scientific texts: antibodies 'attack', proteins are 'tailored', and DNA has a phosphate-sugar 'backbone'. These stimulations demand greater awareness from the recipients and should, therefore, foster comprehensibility. But this kind of stimulation should be handled with care because any unexpected idea, message, or word that does not speak to an area of relevance may distract rather than stimulate readers' attention. However, in both scientific and non-scientific texts, patterns with strong linkages—such as problem-solution, comparisons, contrasts, or chronological orders—always stimulate readers' attention, thereby bolstering comprehension.

Strong linkages stimulate readers

Writing in science and marketing—the same principles apply

In conclusion, although scientific and copywriting languages differ significantly, the same principles of comprehensibility—simplicity, structure, brevity, and stimulation—apply. During our workshop 'Writing in Science

and Marketing'* we cover them comprehensively using illustrations taken from real-world scientific and marketing publications. We are confident that participants from various professions will benefit from the combined discourse on scientific writing and copywriting. Experience has shown that authors of both scientific and marketing texts better recognise the principles of comprehensibility when they engage with each other's texts. Moreover, thinking outside the box fosters creativity and, thereby, improves writing skills.

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*The workshop 'Writing in Science and Marketing' is offered as one day in-house seminar. It includes talks, exercises, and discussion.

Comical gene names

I search words in the Internet if I am not sure if they are proper/trade names, which should start with a capital letter. Recently I encountered Toll receptors. I thought that like Schiff bases or Amador products there could have been a scientist called Toll who discovered them and gave his name to them. Alternatively it could be that they acted like a toll, in which case the 'T' would be small. The Toll gene it turns out was discovered by the German Nobel Prize winner Christiane Nüsslein-Volhard. When she first saw a *Drosophila* with the mutated gene under the microscope, she shouted "Das ist ja toll!" (she probably would have said "That's amazing" if she had been English). The Dickkopf (thick head) gene was another German discovery; overexpression of this gene results in expansion of the prechordal plate. The hedgehog gene was not discovered by a Dr Hedgehog (or a hedgehog for that matter) either but gets its name because the mutant embryos are covered with denticles making them look like hedgehogs. Then there's the *sonic hedgehog* named after Sega's video game character Sonic the Hedgehog, not to mention *tiggywinkle hedgehog* named after the Beatrix Potter children's book character Mrs Tiggy-Winkle.

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Sources:

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Tools, tips and techniques for improving manuscript writing in large multifunctional teams

by Andrew Walker

Introduction

Modern electronic communications have made it very easy for teams to distribute documents and other materials. As a result, the numbers of contributors, reviewers and stakeholders for a given manuscript have increased dramatically in recent years. Authoring a manuscript in such large, diverse teams presents several challenges that can affect document quality, delivery timelines, or both. Faced with these challenges, the medical writer should work closely with the project leader to ensure that the team remains focused on the purpose of the document, that there is a plan to resolve differences of opinion quickly, and that there is clear guidance around the processes, timelines and team behaviours. These issues will be familiar to anyone working on pre-registration documents, such as study reports and submission documents, as they have always required input and buy-in from a wide range of disciplines and departments.

In this article, I describe some tools and techniques that can improve both the speed of delivery and the quality of the manuscript. Although these tools and techniques have been derived from working with regulatory documents, they are based on sound principles and therefore applicable to the preparation of manuscripts. There are however a number of caveats. Project leaders (i.e., publications managers, project managers or senior medical writers) within the sponsor company are best placed to improve team behaviours and drive changes in established ways of working. Contract medical writers (CRO or freelance) will have little opportunity to influence processes or behaviours directly. However, there is nothing to stop external contract writers raising ideas for improving speed and quality with the sponsor's project leader. As with any improvement project, there is no quick-fix, and medical writers and project leaders are advised to apply these tips, tools and techniques with subtlety and flexibility, according to the particular demands of the team.

Common issues

Each year, as part of the EMWA workshop, "Getting the Best from your Cross-Functional Teams", I ask the

delegates to provide examples of issues that arise when working on large projects. Almost all of the examples fall into one of five broad classes:

- **Poor project management:** inadequate timelines, tight deadlines, documents developed in parallel, lack of understanding around submission processes
- **Strategy issues:** lack of brief, changing brief, document context unclear, senior stakeholders not involved at early stage
- **Behaviours:** over-communication, new personnel bringing instability, requests for last-minute changes, contributors and reviewers not meeting deadlines or following agreed processes
- **Poor review:** inspectional rather than strategic review, document not reviewed before comments resolution meeting (CRM), comments that add no value
- **Conflict resolution:** differences of opinion, conflicting comments.

It is immediately evident that any one of these five challenges has the potential to reduce the quality of the document and delay its delivery. Influencing these factors is a difficult task, and success will depend on the role of the medical writer within the team.

Many medical writers will be familiar with the linear model of document production, whereby vital steps such as the

The kick-off meeting is an opportunity for the project leader to explain to the team how the manuscript will be produced

position of the manuscript within the wider project hierarchy, its conception, key messages, design and production all occur as separate steps performed by people working in different functions. In the worst case, the

writer is provided with a simple brief and a data set or publications list and will have little opportunity to influence the factors that affect quality on time. In the ideal situation, the manuscript is produced by an integrated matrix organisation with the medical writer and project leader (i.e., the sponsor's publications manager, project manager or senior medical writer) occupying key roles. In this way the medical writer and project leader can influence both the design elements of the document and the factors and processes that impact on quality.

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Touch-points for success

Assuming a best-case scenario in which the medical writer and project leader are part of an integrated team, there are several opportunities for them to engage and influence the wider team (Table 1).

Table 1 Touch-points for optimising document quality and delivery

Touch-point	Key activities
Kick-off meeting	Identify the authors (including the principal author), medical writers, reviewers and stakeholders. Agree on roles, responsibilities and behaviours. Define lines of communication between the authors, writers and senior stakeholders. Agree on the timelines, including the number and type of reviews.
Communication strategy meeting	Agree on the design elements of the manuscript: context, purpose, audience, required messages, structure and format. Capture the strategy in a detailed outline or prototype, and use the agreed lines of communication to obtain buy-in from the relevant stakeholders.
Data interpretation meeting	Once the strategy is agreed on, collect and interpret the data as a team and determine whether or not it supports the required messages. Agree on strategies, actions and timelines for any unresolved issues (e.g., further analyses, literature searches). Communicate with the key stakeholders so they are aware of any significant changes from the original brief or unexpected findings. Re-evaluate timelines.
Promote review best practice	Provide clear guidance and training for review teams so that their review adds value. Develop a prioritisation scheme. Consider a point-contact review system. Request comments in a standardised format.
Comments resolution meeting	Identify the functional arbiter or hierarchy for decision making before the meeting (e.g., statistician for efficacy, medic for safety, principal author to resolve conflicting opinions). Identify and group the key issues. Limit the discussion to these. Take ownership of the medical writing issues. Agree on strategies, actions and timelines for any unresolved issues (e.g., further analyses, literature searches). Communicate with the key stakeholders so they are aware of any significant changes from the original brief or unexpected findings. Re-evaluate timelines.

Kick-off meetings

A kick-off meeting is essential. The project leader should chair this meeting and act as overall sponsor for the manuscript. External medical writers should work closely with the project leader to ensure a common understanding of the aims of the kick-off meeting and the process for producing the manuscript.

The meeting should include the medical writer, lead authors, reviewers and stakeholders. The length of the meeting should be tailored to the size and complexity of the manuscript. This meeting should identify everyone who has contributed to the work presented in the manuscript and establish their credentials for inclusion as an author.

The kick-off meeting is an opportunity for the project leader to explain to the team exactly how the manuscript will be produced, including the timelines, number of review cycles, expectations during the review, and what the lines of communication will be between the medical writer, authors, reviewers and stakeholders. The agenda may also include a discussion of the impact of poor review, late comments and missed deadlines on quality and overall delivery. This is also an opportunity for the project leader to explain and gain an understanding of any new or radical tools or processes that will be introduced. The project leader should provide suitable meeting minutes

Reducing the impact of issues around the review requires techniques and specific ways of working

(or other output), describing the agreements, roles and responsibilities of the team, and timings, and ensure that they are distributed to the wider team including those who could not attend.

Communication strategy meeting

The communication strategy meeting should comprise the key authors, the project leader, the medical writer and any specialists who will contribute to the manuscript (e.g., statisticians, health economics specialists). The meeting objective is to reach a common understanding around the context, purpose, audience, messages, structure and format of the document. The medical writer should prepare the output, which can take the form of a detailed outline or a more structured prototype, depending on the complexity of the proposed manuscript. In either case, it should be reviewed and agreed on by the wider team before drafting commences. In the case of small, simple projects, the communication strategy meeting

A proforma allows the medical writer to easily combine all the comments

can be held as part of the kick-off meeting but it is important that the operational and strategic components are kept separate.

Data interpretation meeting

The need for a data interpretation meeting will depend on the nature of the manuscript. For projects that include new data or analyses, for example primary publications or reviews using meta-analyses, such a meeting is essential to establish a common understanding of the data and how they align with the agreements made at the strategy meeting. For other manuscript types, the need for a data interpretation meeting is less obvious, but in principle, it is important for the team to agree on how the material to be included in the manuscript supports the project objectives.

The review process

The review is one of the most important touch-points in the whole process: it's where the team assesses the medical writer's work! Accordingly, this raises the greatest number of issues for the writer, and these can be exacerbated by >

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> two other factors. Firstly, with few exceptions, the review team will have had little or no training or guidance on what constitutes a good review. Secondly, the ease of access provided by modern communications means that the number of people reviewing the manuscript can reach epic proportions (upwards of 40 is not unknown for large submission documents). The combination of these factors means that the medical writer may receive several hundred comments. Many of these will make no material difference to the quality of the document but they will still need to be resolved. Such a task can adversely affect the timelines for the manuscript and may even impact its quality. Reducing the impact of these issues requires techniques and ways of working that may be very new to many authors and review teams. Consequently, the project leader is best placed to introduce these concepts and new ways of working to the wider team. Contract writers should work closely with the project leader to develop these techniques within the project.

The project leader should strive to keep the discussion at the highest level

Train or coach the team in how to provide quality comments. This can be done at the kick-off meeting or as a separate training activity. Provide guidance so that the reviewers understand the difference between inspectional comments (typographic and grammatical errors, format issues, grammatical preferences, etc) and value-adding comments (technical accuracy, logic flow, support for messages, well-structured arguments, clarity of figures and

tables). Ideally, the review team should provide their expert input and leave the inspectional issues to the medical writer and the proof reader or quality control staff. Training materials can include hands-on working examples and one-page guidance sheets.

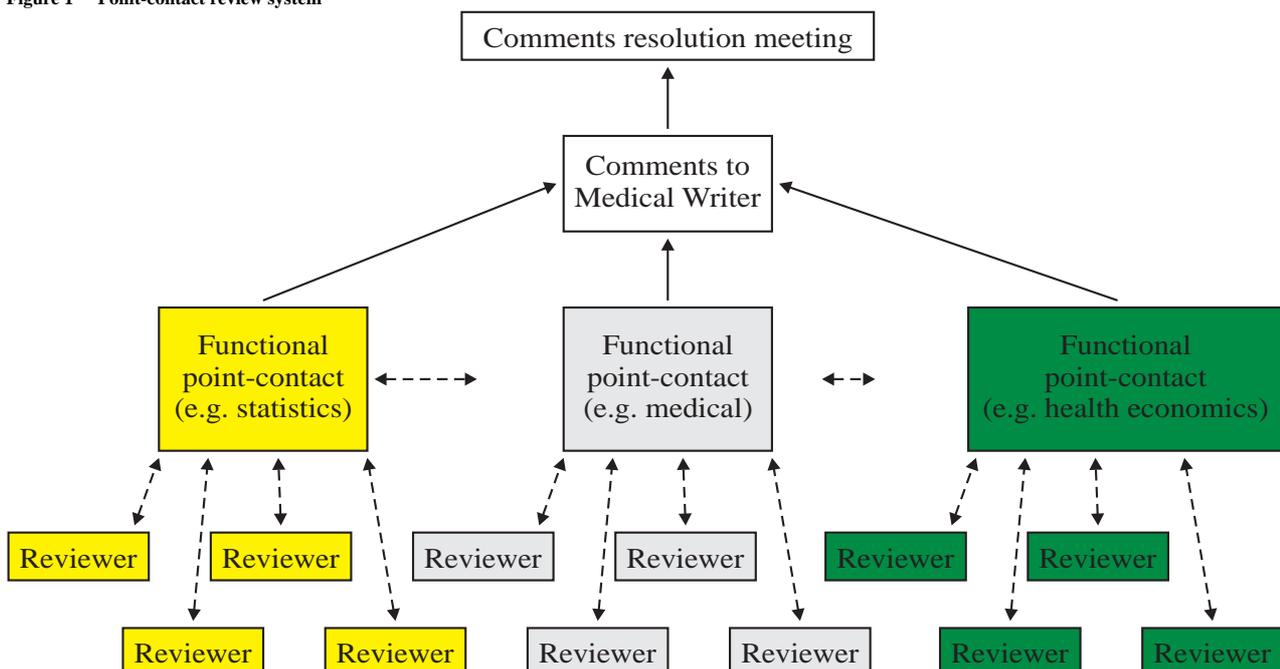
Train the team to use a prioritisation system. The ability to resolve comments at the CRM will be enhanced if they are sorted according to priority. The project leader and medical writer should work with the authors and reviewers to develop a scheme that they understand and are happy to apply. The key to success here lies in getting the authors and reviewers to understand how a properly applied scheme will allow efficient comment resolution and therefore save time for both the writer and the team. One such scheme is presented in Table 2.

Table 2 Prioritisation scheme for review comments

Priority	Definition
1	An important comment that requires discussion at the CRM. The reviewer will lead the discussion around his or her priority 1 comment.
2	An important comment that should be incorporated but does not require discussion at the CRM.
3	Typographic and grammatical errors, format issues, grammatical preferences. These will not be discussed at the CRM and will be dealt with by the medical writer and the quality control team.

Point-contact review. In very large teams, a point-contact review system will reduce the number of comments, encourage functional consensus, encourage timely comments, reduce priority 3 comments (see Table 2) and reduce duplication of comments. The principle of the point-contact system is shown in Figure 1. The point-contact system

Figure 1 Point-contact review system



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places reviewers in groups according to their skill set, that is, medics in one group, statisticians in another and so on. Each group has a point-contact who then manages the review of the document within the function. Each reviewer within a functional group provides his or her comments to the point-contact who then either holds a review meeting to gain functional agreement or is empowered to triage the comments. The agreed comments from each function are then provided to the medical writer.

The success of this system depends on the qualities of the point-contact and their relationship with the medical writer. Ideally, the point-contact will understand the principles of the point-contact process, have a good standing within the function, and understand the prioritisation scheme. The functional groups can be tailored to suit most situations to include, for example, a team within a given country, or all the reviewers at a particular research site.

The benefits of the point-contact system include clearer definitions of decision ownership, less influence of maverick personalities, better compliance with agreed processes and timelines and fewer people needed for comment resolution.

Standardise comment format. Automated review tools are becoming more common and provide the medical writer with comments in a standardised format. However, where such a tool is not available to all members of the team, or simply not available, the medical writer should ask reviewers to provide comments on a pro-forma (see Table 3). This allows the medical writer to easily combine all the comments and order them according to priority, reviewer's name, or page order as required for the CRM. This is always preferable and more efficient than receiving comments in different formats (i.e., track-changes, or marked-up copy, or bulleted lists in e-mails or word documents).

Table 3 Example of a pro-forma for collecting standardised comments

No	Page	Section	Initials	Priority	Comment	Action (medical writer)
1	1	Intro	AN	1	Need to include recent report of study published in JCO (A.N. Other: JCO, 2010.)	
2	1	Intro, para 1, line 3	AN	3	Please use b.i.d instead of twice per day.	
Etc	

Comment resolution meeting

The CRM is another important touch-point between the medical writer and the wider team. If a strategic review has been performed with correct prioritisation, standardised comments and a point-contact system, then comments resolution should be a simple discussion of the key issues. The project leader, working closely with the medical

writer, should group comments into common themes, should strive to keep the discussion at the highest level and avoid being drawn into discussion around the grammar and format issues that belong rightly to the medical writer. From experience, key opinion leaders and other senior stakeholders do not consider sifting through hundreds of priority 3 comments as best use of their time.

The medical writer should lead this meeting, identifying beforehand the people who own the decisions for any contentious point and the hierarchy for final arbitration. The project leader should document any deviation from the agreed strategy for the manuscript as well as any actions and timings for further work identified during the resolution process (e.g., additional analyses or literature searches). Finally, it is important that any issues are communicated to the wider team, including those not able to attend the meeting in person. The point-contacts can be used to obtain agreement on any contentious issues from the key personnel in their function.

Summary

This article describes some tools and techniques for optimising the development of manuscripts and other documents in large teams. These techniques have been used successfully in many teams, but it should be pointed out that not all of them have been immediately welcomed or have been successfully implemented in all teams. The benefits to the writing team (the medical writer and project leader) are significant and it is therefore worthwhile to make the effort to implement them. This requires continual training and coaching of the authors, reviewers and stakeholders, including lessons learnt analyses and continual refinement of the tools and techniques. However, from experience, those teams that have adopted these ways of working have, without exception, benefitted from both reduced delivery times and improved quality of output.

Acknowledgement

I would like to thank Jonathan Edwards and Dan Portess, AstraZeneca UK, for their help in the development and co-presentation of the EMWA workshop* on which this article is based.

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*The points raised in this article are discussed in more detail, along with practical exercises, in the EMWA workshop "Getting the best from your cross functional teams".



About cover letters for manuscripts submitted to biomedical journals

Elise Langdon-Neuner

I have often heard experts on manuscript-writing pronounce that manuscript submissions to biomedical journals must be accompanied by a well-written cover letter. In a quest to find evidence for this pronouncement, I asked eighteen European and American editors “How much importance is attached to the cover letter and what are you looking for that might not be in the abstract?” I also checked journals’ instructions to authors for mention of a cover letter and reviewed the literature on cover letters, which did not take long because there isn’t much. An editorial in *Medical Education* noted that, while it had previously been hard to imagine sending a parcel to an editorial office without a cover letter, in the first three weeks of 2005, when the journal moved to electronic submissions, 68% of papers were submitted without comments to the editor. As a result the editors thought the cover letter was becoming an endangered species [1].

Editors’ views ran from “I ignore cover letters” to “any author who fails to make use of them is an idiot”

Most cover letters go unread by the *NEJM*, according to information I received from the journal’s media manager. Their instructions to authors state that authors do not need to send a separate cover letter with their online submission because they offer a text box in which the authors can type information for the editor—but this can also be left blank [2].

By contrast, *The Lancet* stipulates that authors should use the cover letter to explain why the paper should be published in “a leading international general medical journal, rather than elsewhere (e.g. a speciality journal)” [3]. They also state that it is helpful to indicate what could be shortened in the paper because the whole paper can be reviewed and published on their website and a shortened version published in the printed journal.

The topic of cover letters was raised at one of the Committee of Publication Ethics’ annual seminars that I attended in London. Most editors said that they looked at cover letters, but disparate views were expressed as to their importance. Among editors representing a certain big journal at the meeting, those who read cover letters were in a minority, although one editor at the same journal stated that he always read the letters.

The views that I received from my questioning of editors ran the entire gambit from “I ignore cover letters because the manuscript should speak for itself” and “editors do not

rely on cover letters to explain the message” to “cover letters are a golden marketing opportunity” and “cover letters are a key part of the editor’s appraisal of a paper and I consider any author who fails to make use of them an idiot”.

As in the absence of specific requirements like those made by *The Lancet*, the author (or medical writer) will usually not know if an editor is of the ‘ignore’ or ‘always read’ ilk, it seems wise to take the time to write a cover letter—even though it might never be read. The comfort for the author then is that writing a cover letter can help to refocus the author’s mind on how the paper has been written. If the letter explains the message in a better way than the paper, the paper should be revised. In this sense, as one editor said, it is a last check before submission. And again, to quote an editor “A good cover letter will never make up for a poorly written abstract or poorly performed study, but it will help [those editors who read it] to decide whether it is worth getting the paper reviewed, who would be the best reviewers and if there is anything salvageable about the paper if the reviews are bad”.

What should I write in the cover letter?

In this article the term ‘cover letter’ is used for a letter accompanying the initial submission of a manuscript. Letters that accompany a revised manuscript, where it is important to detail the revisions that have been made, are not discussed, as these have a clearer raison d’être.

Disappointingly authors explain the topicality and importance of their work better in letters than in the abstract

The advent of online manuscript submission has obviated the need for letters that merely state that a manuscript is enclosed and make some non-specific general pleasantries. The modern cover letter provides whatever information the instructions to authors specify should be included in a cover letter and is a medium of persuasion.

Many journals reject a manuscript without passing it through an external review process. The trend of rejection without external review arose from increasing numbers of submissions and demands from authors for ever more rapid decisions, and it has risen in recent years with the great increase in research activity in some countries, such as China, where the use of English as a medium of scientific communication is not yet well established. Rapid rejection on the basis of internal review means that editors

Cover letters for manuscripts submitted to biomedical journals

often only read the manuscript abstract or the abstract and the cover letter. External reviewers are not usually given access to the cover letter in the electronic manuscript system, although the editor may send information to the reviewers from the letter.

One editor, who relies on the abstract only to give an initial sense of whether the paper is within the journal's scope and of good quality, explained that as the abstract should contain key information about the study "there would not be much to be gained from the author's point of view to include a cover letter". However, among the editors who considered letters to be important, albeit not essential, one wrote that she did read them because (disappointingly) authors explain the topicality and importance of their work better in the letters than in the abstract. But I also received comments that well-written manuscripts are often accompanied by badly structured and ill-prepared letters, indicating that the authors had help with the manuscript but not with the letter.

Information the journal might require in a cover letter

Even journals with online submission systems sometimes ask in their instructions to authors for information to be included in cover letters. The following is a list of the type of items which might be requested:

1. Confirmation that the data in the manuscript is original and the manuscript is not under consideration elsewhere.
2. Confirmation that none of the manuscript's contents have been previously published. Some journals request that copies of related papers be submitted as supplementary data so that the editor can check for possible duplicate, salami or prior publication. Prior publication does not include conference abstracts/posters. You would be wise, however, to mention such previous publication.
3. Confirmation that all authors have read and approved the manuscript and its submission to the journal.
4. Confirmation that all authors have agreed to be authors and accept responsibility for the study or that the corresponding author takes full responsibility for the contents of the paper.
5. A few journals (e.g. *The Lancet*) request that copies of previous reviews of the submitted manuscript be included as supplementary data, in which case you should explain in the cover letter what you have done to deal with the reviewers' comments.
6. Financial disclosure including funding, employment by a sponsor, consultancies, share ownership, equity interests or patent-licensing arrangements. If no potential conflict exists, this should also be stated.
7. Whether any of the material could be published as data supplements rather than in the print version of the article.

8. Full contact details of the authors' postal/e-mail addresses, telephone and fax numbers (in addition to inclusion of this information on the title page of the manuscript).
9. Agreement to pay for colour figures or for online fees if the submission contains supplementary files.

Information that might be included to increase the manuscript's chances of external review

Where the online submission system is silent on cover letters but asks the authors to include information directly in the submission system, a letter can be used to expand on the information provided. Otherwise the task of the cover letter is to persuade the editor that the manuscript is of sufficient interest to warrant sending it out for external review. The following is a summary of the type of things editors said they wanted to read about in the cover letter as well as suggestions gathered from the 'cover letter' literature.

The cover letter's task is to persuade editors the manuscript is of sufficient interest for external review

1. Why you conducted the study and contextual details of the research project.
2. A description in everyday terms of what the paper is about and its major implications. Do not reiterate the abstract and avoid too many technical details.
3. What is unique about the study, and how it differs from other studies. The significance of the study results should be neither under nor overplayed. As John Swales emphasises, dropping hints that you consider your paper to be eminently publishable at best is only likely to raise some quizzical editorial eyebrows [4]. The cover letter must be consistent with the manuscript. One editor said she was irritated when the cover letter enthused about promising results which were not to be found in the manuscript submitted.
4. A statement that the study is the first of its kind. This is particularly important if the journal does not allow claims of priority in the manuscript, as the significance and novelty of the work can always be explained in the cover letter.
5. Why the journals' readers would be interested in the work. If an article relevant to your study has recently been published in the same journal, refer to the article to show that you read and are familiar with the journal.
6. What the paper will add to the literature. Emphasise any unanticipated or surprising results.
7. Information about controversies in the field and how the paper is positioned within a debate.
8. If you have not published in the area before, give the basis of your expertise and years of experience in the field. One editor impressed me by saying that when authors told her "this is my first paper and I'd welcome any feedback and assistance you can give" she was happy to keep working on it. The difference that

Cover letters for manuscripts submitted to biomedical journals

- > this can make, she explained, is that the editor is more likely to ask the author to revise the manuscript than to reject it on round one.
9. If no opportunity for suggesting reviewers is provided in the online submission a cover letter is a valuable opportunity. One editor commented that the convenience of receiving names of reviewers and their e-mail addresses can make the difference between sending out for external reviewer and making a decision to reject. Collaborators or co-authors of previous papers should not be suggested. Editors sometimes check PubMed or other databases before sending papers out to review. The names of people who should not be chosen as reviewers can also be mentioned. Joshua Finkelstein from *Nature* considers this information useful, acknowledging that competition and bias exist [5]. The reason for excluding a potential reviewer should be given; one editor stated that without an explanation she did not feel obliged to consider such requests.
 10. Joshua Finkelstein recommends that if you've talked with an editor about the work (at a meeting, for example), you should mention this in the cover letter. The manuscript might be assigned to another person in the editorial team who will then ensure that their colleague sees the paper before any editorial decision is made [5].
 11. A statement that the manuscript is based on a conference presentation (if it was!)—even when this has been mentioned in the manuscript.
 12. A description of any other submission or previous publication that might be considered redundant or may duplicate part of the manuscript.
 13. Information that you have already published on the topic or have a similar paper published elsewhere.
 14. If necessary: a persuasive explanation of why the manuscript does not comply with the instructions to authors, for instance, if the word count exceeds the word limit stipulated in the instructions, or the format is unconventional.
 15. If the journal requires people whose names appear in the Acknowledgements to give permission to be named, the cover letter should include confirmation that permission has been granted and the permission letters/e-mails can be uploaded as supplementary data.
 16. Finally, Steven Gump in his article on cover letters suggests that closing the letter with a congenial note places trust in the editor and reminds him that you are eager to receive his decision [6]. John Swales advises refraining from exerting pressure with terms like “as soon as possible”. He also considers there is nothing to be gained by such endearments as offering to revise [4].

Sample letter covering the points an editor wanted to read in a cover letter*

Dear Dr Besteditor

We are pleased to submit our manuscript for consideration for publication in the Journal of Excellent Research.

In Wonderland, more than 60% of the population lives in urban areas and most of them have never or only once seen a tree. Urban men are in particular affected by this. To date, no scientific attention has been given to the determinants of tree-spotting among this afflicted population. This article describes a theory-based analysis of the primary psychological determinants of tree-spotting behaviour among these men. Results of this study are important for the development of focused intervention programmes targeting rural men in particular.

We believe that our article is of interest to the Journal of Excellent Research as it falls within the scope of the journal on publishing psychological studies of vulnerable populations. In addition its open access would ensure a wide distribution of our results.

The manuscript reports original research and is not under review with another journal. The authors have no conflicts of interest and have all read and approved the manuscript.

We are looking forward to your response.

Yours sincerely
Hopeful Author PhD

* The names in the letter have been changed.

Length and format of the cover letter

Ideally, the cover letter should not exceed one page—as one editor commented, there's nothing worse than a rambling letter. If you are wondering how you can include all the above information, see the example in the Box. It covers points 1-6 and 16. The rest of the suggestions were not applicable for this manuscript. The final paragraph of the letter provides details that the instructions to authors required to be in the cover letter.

Ideally, cover letters should not exceed one page

The cover letter gives a first impression of the authors and establishes their credibility. Attaching a letter on headed paper from your academic institution, company or organisation as a pdf/scan in an electronic submission tells the editor where you come from. If, for example, the academic department lists its professors on its headed paper, the editor might recognise the names. You should also use your job title and academic degrees.

Your credibility will suffer a nasty blow if you don't get the name of the editor and journal right! More than one editor told me that it was amazing how many letters arrive

Cover letters for manuscripts submitted to biomedical journals

addressed to the former editor of the journal, or editor of another journal that has just rejected it—to quote an editor “interesting information for the editor but not always in the interest of the authors”. Writing the former editor’s name shows you know little about the journal and maybe also the literature. An incorrect journal name raises suspicions of duplicate submission or doubts about whether you had intended to submit to that journal.

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Do something worthwhile in your coffee break

Rather than your computer sitting idle while you have a coffee break or make a phone call, why not use the slumbering computing power to help work on medical problems like AIDS, cancer, malaria and tuberculosis? World Community Grid uses unused computer resources to form a huge computing grid that can analyse vast amounts of data in a few months, that would previously have taken years. The grid also works on other research projects; recent ones were nutritious rice and clean energy.

You have to register, download a free software program, and that’s it. (If it’s not your own private computer system, you have to get the permission of the system’s owner.) Have a look at www.worldcommunitygrid.org and “become part of a community that is helping to change the world”.

Pamela Waltl
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How to stop worrying and learn to love the peer-review process

by Dorothy Pennachio and Phil Leventhal



Research journal editors are often asked by groups like EMWA, American Medical Writers' Association, Counsel of Science Writers, and so on, to make presentations about how to get papers published. Medical writers want to know how to make their work acceptable. Should I send a pre-submission inquiry? What is the best format for the paper? What about graphics? What should be included in an attention-getting, professional-sounding cover letter? Should I call the editorial office with my questions, or would that be bothering them?

These questions are all important, but it is the peer-review process that strikes the most fear into medical writers' hearts. How do I deal appropriately with those difficult reviewers' comments and criticisms? What if the co-authors don't agree on how to respond? Do we have to respond to every comment? What if we don't agree with the referee?

The emotional upset caused by a review can be difficult to handle. Anger is often the first response to a negative review. Who does that referee think he is? How could he be so unaware of this topic to not understand? Did he not read the paper? Why is the reviewer such a jerk? Does he have a personal grudge against one of the authors?

Also, a rejection or even being asked for a revision can leave a writer, particularly an inexperienced one, feeling inadequate. A negative review can invite criticism or doubt from a client, boss or co-worker. Silly, perhaps, but these stressful and counterproductive emotions often raise their annoying little heads. And these emotions lead to fear. One writer put it this way: "Sometimes, after reading a review, I just want to curl up into a little ball, become invisible and forget about ever needing to publish that paper after all." Another young writer explained, "I was traumatised by the peer review and never want to write another manuscript."

So, how do you stop worrying and learn to love the peer-review process? Educate yourself about how to effectively satisfy reviewers and editors and keep in mind that you can use the process as a chance to improve the paper and to become a better writer. Keeping these things in mind should help you tackle the peer-review process with confidence.

How the review process works

When the editorial office receives a manuscript, generally an editor will first determine whether the paper is of sufficient interest for that journal and its readership. In some cases, the editor will decide that the article is not novel enough or is not appropriate for their readership and will

reject it without further review. If the editor decides that it is of sufficient interest, the manuscript will be sent, typically, to two or three experts for a review.

Once the editorial office has received reviews from the referees it has invited, one of a couple of things can happen. Most journals blind the reviews and send them out 'raw' to the authors, letting the chips fall where they may. Some comments from the editors and production team may be added to the report, such as "Please improve the resolution of your figure; it should be at least 300 dpi." This works well for some. The argument in favour of this method is that the authors see exactly what the referees are saying without editors mucking about. Other journals read through the referees' reports and create a new document that amalgamates the blinded comments. Through that process, any nastiness or counterproductive phrases are eliminated, leaving just constructive, helpful items. Again, some comments from the editors and production team may be added.

The editor makes a decision about whether the manuscript is acceptable for publication using the reviews for guidance. In most cases, the manuscript will be either conditionally accepted with a request that reviewers' comments are addressed or it will be rejected but with an invitation to resubmit following major changes. These decisions may also be referred to as 'accept with minor revisions' and 'accept with major revisions', respectively. The manuscript may also be rejected because the reviewers agree that it lacks merit. It is almost unheard of for the manuscript to be acceptable as is, so you should expect to have to do some amount of additional work to get your manuscript published.

What to expect from the editorial office

Most journals, except those promising rapid publication, will give a decision within 2-3 months after receiving the manuscript. If it has been longer than 3 months and you still have not heard, it's probably best to call the editorial office to check on its status. These days, many journals have online manuscript submission and tracking systems, which you can use to follow the status of your manuscript; however, if its status has been 'under review' for too long, you should contact the editorial office to see why it is being held up.

You will receive a letter with the editor's decision along with a peer-review report. Here are some examples of letters that you might receive from the editorial office once it has received the referees' comments:

How to stop worrying and learn to love the peer-review process

Dear Dr. Smith,

Based on the comments from our editors and reviewers in the attached document, the journal has determined that your manuscript requires revision before it can be considered further for publication in this journal.

We would be pleased to reconsider a revised manuscript for publication and encourage you to address those comments.

Best regards,
Eddie Editor

Dear Dr. Smith,

Thank you for submitting your manuscript to the *Central European Journal of Foot Science*. Peer review of your manuscript has been completed. Unfortunately, the reviewers identified a number of shortcomings and did not recommend the manuscript for publication.

On the basis of the reviewers' comments, the manuscript cannot be considered further for publication in the journal. Reviewer comments are attached below for your information.

I regret having to send you this negative decision about your manuscript and hope that you and your colleagues will consider submitting other manuscripts to the journal in the future.

Sincerely,
Edward Editor

Dealing with rejection

The usual responses to an outright rejection are shock and anger. You might ask yourself, "How could they be so heartless?" or "How could they have not understood?" Take a deep breath. Put the review down for a day or two and come back to it when you have a chance to cool off. Read it a second time, this time trying to come from the reviewers' or editor's point of view.

Rejection without review

Generally, a rejection without review means that you did not target the right journal. In other words, the editor felt that the target audience or subject matter was not appropriate or novel enough for the journal's readership. Perhaps the authors were aiming too high and had unreasonable expectations. For example, you might have sent the article to the *New England Journal of Medicine*, a very high-impact journal, when it was in reality more appropriate for the *Central European Journal of Medicine*. The work was not ground-breaking but it may still be worth publishing.

Rejection following review

If the paper has been rejected following a review, it often means that, on the basis of the review, the editor feels that manuscript is not of high enough quality to publish in their journal. There could be flaws in the design, execution or analysis of the study. This will not usually be your responsibility as medical writer, especially if the article has already made it through an internal review. In that case, read

through the review document from the point of view of the reviewers. Then use what you learn to help the authors see where the flaws are and how they might be remedied.

The editor may also reject the manuscript because there is not enough space to publish it in the journal. Of course, this is generally not a problem for on-line journals. This means that the other manuscripts with higher priority crowded out yours, which is another way of saying that other manuscripts are more novel or of greater general interest than yours. Finally, the manuscript could also be rejected because, on the basis of the reviews, the editor feels that the material is not novel enough for their journal.

Don't despair

Regardless of the reason for rejection, don't despair. There are other journals out there. Just make sure you pay close attention to editors or reviewers' comments and criticisms before sending it to the next journal.

Conditional acceptance or an invitation to resubmit with major changes: Dealing with reviewers' comments

Receiving a conditional acceptance or an invitation to resubmit with major changes may leave you with mixed emotions. After reading the review, you might have some of the same feelings as after an outright rejection. At the same time, there is hope for getting your article published, but it might require a lot of additional work.

As with a rejection, take a break before beginning to respond. When you've cooled down, go back and read the review document from the point of view of the referees. Remember, they are human and might not have understood your paper. Also remember that if the reviewers, who are experts in this area, don't understand, the readers will probably not understand either. So, responding to the reviewers' comments and criticisms is a chance for you to improve the manuscript...and become a better writer.

The review report may contain a long and daunting list of comments and criticisms to address. It may even come to several pages and dozens of individual comments. Each point may be micro-specific. That's okay. This can help you effectively address each objection or suggestion separately. 'Trees' and 'leaves' don't get lost in the 'forest' using this tried and true technique.

Dealing with such a review can be like eating a whale. Don't focus on the enormity of the whole task. Instead, attack the job a little at a time. Also, remember that you do not have to make all of the changes requested, but you do need to address each point. If you do not want to make a change they suggested, you need to convince the editor why not.

The work you do in responding to the review is every bit as crucial as the work you did on your original submission. When responding to the report, expend the same level of effort as when you created your paper. It is this version, once mulled over, evaluated and possibly accepted, that goes to press. >

How to stop worrying and learn to love the peer-review process

> **Writing the response document**

To respond to the reviews you will need to prepare a high-quality response document. This consists of a letter to the editor briefly explaining that you have responded to all of the comments and criticisms, followed by point-by-point responses to each comment. Generally, it helps to format the point-by-point response so that it is easy for the editor (and possibly reviewers) to find each comment, your response, what changes have been made to the text, and where they can be found. Unless the editorial office has already done it for you, it might help to number the individual comments and criticisms. An example of a well-formatted response document is shown in Figure 1.

Some tips in writing the response document:

- **Respond completely and comprehensively to each of the referees' points.**
- **Make it easy for the editor and reviewers to identify revisions.** Some journals may instruct you to send a version using tracked changes or a version where changes have been highlighted. In addition, when describing a change in your response document, indicate the line and page number of where it can be found. You can either do this in continuous text as shown in Figure 1 or in tabular format.
- **Use a professional tone.** Ensure that your responses are polite and nonabrasive. Don't be obsequious or excessively polite. Thanking a referee for a comment

Figure 1. A well-formatted response document.

Dear Editor,

Thank you for your and the reviewers' comments regarding our manuscript "Safety and efficacy of drug X in the treatment of *Tinea pedis*" (MS #1111). We have made changes to the manuscript as outlined in the point-by-point response below. There was some disagreement between the two reviewers with respect to the level of statistical detail to include in the manuscript, which we resolved by moving some of the information from the results to the methods and footnotes. We hope that these changes make the manuscript acceptable for publication in *The Kentucky Journal of Medical Science*.

Sincerely,
John Smith

Response to reviewers' comments

Reviewer: 1 ← Each reviewer indicated

(1) The results section now spends more time explaining the statistical analysis used and why they were used, then what the outcome of each analysis really means in reference to the data. On Line 222 - Please don't repeat what test was done, give the results and the significance or lack thereof for those results. ← Each comment numbered and formatted to differentiate it from the response

Response
We have simplified the text to make it easier to read and understand. For example, we have moved details about the statistical tests and the degrees of freedom, etc. to footnotes. The paragraph now reads as follows:

"Statistical analysis showed a significant time × drug interaction ($P=0.025^a$), which means that the two drugs had significantly different effects over the course of the study. The results were not affected by dosing regimen (once vs. twice daily), time of dosing, country, sex, or age of the patients (data not shown)." (Page 18, line 27) ← Changes to the text specifically indicated

(2) In Fig. 2, it would be more meaningful to the reader to overlay the 95% confidence interval over the fit line. So please add them to the figure. ← Page and line number of modified text indicated

Response
Because the slopes are calculated by repeated measures analysis, we must include the 95% confidence intervals as lines. We have included this information in the revised Figure 2.

How to stop worrying and learn to love the peer-review process

that improved the paper is okay, but you don't need to thank the referee for each comment. Also, don't be pedantic, which could be perceived as insulting. Finally, it's perfectly reasonable to disagree with a reviewer's comment; just state your reasons. Referees have been known to misunderstand a premise. Again, state why you disagree and explain how you resolved it.

Dealing with difficult comments or reviews

Remember that peer review is not an adversarial process. Everyone involved in the process—journal editors, authors, referees—are doing this work so as to ensure common goals of excellence, transparency, authenticity, scientific integrity and defensibility. However, referees are human and their comments may sometimes seem aggravating or abrasive.

- **Requests for extensive additional data, analysis or work.** Do the additional work if you can and if you agree that it adds to the paper. If you disagree that additional work is needed, feel it's outside the scope of the article, or is impossible, explain in your response.
- **Conflicting requests by different referees.** Do your best to satisfy all reviewers. If that is not possible, you should explain why. If necessary, contact the editorial office for guidance on what to do if there is no obvious way to satisfy everyone.
- **Comments that seem abrasive, aggressive or insulting.** Ignore and do not respond to the negative tone of the comment. Keep in mind that you may not be reading the comment with the same tone as the referee that wrote it. Address the underlying issue in the comment only. Remain professional. If you truly think that the reviewer has a grudge against you or one of your co-authors or is being unprofessional, contact the editorial office, but remain professional when you do.

What happens after you send in your response document and revised manuscript

Editors differ as to how they handle revisions. Some send them back to the original referees, or at least to the most critical referee, and rely upon them to determine whether the issues have been adequately addressed. Other editors evaluate revisions themselves, especially if the changes are minor. It is not uncommon to go through additional rounds of comments, responses and changes to the manuscript. This might seem annoying, but it is all in the interest of getting a high-quality manuscript published.

Conclusion

Stay cool, maintain a professional tone and prepare a response document that is easy to follow and fully addresses all comments. Although you might not learn to love the peer-review process, fear of it can be alleviated by keeping in mind that it provides a chance to improve the quality of your manuscript and improve as a writer.

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Limericks

Limericks are humorous, nonsensical, or bawdy verse of five anapestic lines usually with the rhyme scheme *aabba*. (<http://www.thefreedictionary.com/Limerick>)

According to Wikipedia the origin of limericks and why they are so named is unknown but the name is generally thought to be associated with the county in Ireland of that name. They may have originally been parlour games devised by Maigue poets with a refrain "Will [or won't] you come (up) to Limerick?". Their usage was first documented in England in 1898 but before this date Edward Lear had already written 212 limericks in his books of nonsense, although he did not call them limericks.

Limericks are traditionally both humorous and obscene. The following limerick of unknown origin makes the point.

The limerick packs laughs anatomical
In space that is quite economical,
But the good ones I've seen
So seldom are clean,
And the clean ones so seldom are comical.

Here is a comical one from the Phallological Museum in Husavik, Iceland:

A lady while dining at Crewe
Found an elephant's wang in her stew
Said the waiter, "Don't shout,
Or wave it about,
Or the others will all want one too."

Sources:

[http://en.wikipedia.org/wiki/Limerick_\(poetry\)](http://en.wikipedia.org/wiki/Limerick_(poetry))
<http://www.phallus.is>

Kari Skinningrud wrote 2 limericks for EMWA, see *TWS* 2006; 15(2):67.



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STRICTLY NO AGENCIES.



Peer-reviewed publications in a communication strategy

by John Carpenter

Memo to all company employees

Great news – our scientists have discovered a wonderful new drug that they believe will revolutionise the treatment of emwatitis. We will shortly start trials to confirm the early promise that Supadrug has shown in in-vitro tests.

Dick Marrvel
CEO
Wundapharma Inc.

News item

Wundapharma shares have risen sharply on the London, New York and Tokyo Stock Exchanges in response to the announcement by CEO Dick Marrvel that the company has discovered a new drug, Supadrug, for the treatment of emwatitis

Announcements such as this signal that a pharmaceutical company has completed the early stages in the development of a new product. It also signals that the company's financial wizards have worked out that it will be worth putting the experimental compound into the next (and most costly) phases of development—Phases II and III. In other words, they believe that the projected sales of the drug will cover (and, they hope, exceed) its anticipated development and marketing costs.

Phases II and III burn both money and time. And time is at a premium because the patent-protection clock starts ticking as soon as the patent is granted—usually during or even before Phase I. Currently, it takes about 10–12 years to bring a new product to the market, by which time only about 7 years of patent protection remain in which the company can recoup the product's enormous development costs—typically in excess of €600 million. Sales of the new product must therefore be as high as possible as soon as possible after marketing authority is granted if the company is to recover the product's development costs (and thus be able to invest in the development of new products) before other companies start selling their own brands of the drug. Telling potential prescribers, healthcare funders, patients, carers and the general public about the new product, therefore, is far too important to be left to chance. This is where communications strategies and communications plans come in as parts of an overall marketing strategy.

Let's define a few terms here. A **communications strategy** is the overall approach the company intends to use to tell

the world about its new product. It usually forms part of the company's marketing strategy for the product. The communications strategy summarises what will be done. The **communications plan**, on the other hand, is the method by which the communications strategy will be delivered—how, where, when and to whom. The communications plan itself will have many parts (and different companies use different terms) but the main elements usually centre on a publications schedule and a publications tracking system. A **publication** is any item of communication that is made available as part of the communications strategy (see Box for some examples). In this article, I describe my own views about some aspects of peer-reviewed publications in communications strategies and plans. I don't intend to discuss tracking systems as Ruth Whittington has dealt with this in a previous issue of TWS [1].

Communications plans

When I was learning to fly a glider, I was told a little story: 'A pilot who survived after parachuting from a stricken aircraft was asked by a reporter when he decided to bail out. "Twenty five years ago", he replied.' This anecdote illustrates the importance of planning. What the pilot meant was that many years ago he had made a series of plans covering all eventualities. When the emergency cropped up, he knew exactly what to do because he had planned for it. This attitude is also encapsulated by the adage: "If you enjoy crisis management, you don't need to plan."

There are many reasons, then, for developing a communications plan. Perhaps the most important is to plan (and therefore control) the flow of information. There will be times when masses of information become available to the company and other times when new information is scarce. Communication planning helps identify these times of glut and famine so that the flow of publications communicating this information can be tailored to cover these periods of scarcity as effectively as possible. Planning also makes it easier for the company to manage internal and external (agency) resources and budgets.

The dossier submitted to the regulatory authority will usually contain a variety of reports written over a number of years. These will typically include preclinical studies investigating such aspects as the drug's pharmacology, mode of action and pharmacokinetics, in-vitro and animal

A communications plan makes it easier to control resources and budgets

A communications plan should be made as early as possible

Peer-reviewed publications in a communication strategy

> toxicity studies, as well as studies in humans, e.g. low-dose volunteer studies, small open-label and dose-finding studies in patients, and several large, double-blind, controlled clinical trials. Such studies are conducted over a long period—the time from discovery of the active compound to marketing authorisation is at least 10 years for most drugs—and a large-scale clinical trial can take years to design and conduct. What's more, when all the results are in and analysed, it takes time to produce the clinical study report, even for a team of EMWA-trained medical writers.

When, then, should the communications plan be made? The facile answer to this is: "As early as possible". In practical terms, it's a good idea to have some form of plan in place well before the company makes the final decision to move from preclinical testing to the clinical phases of development. In fact it is probably worth starting to develop a communications plan as soon as there are data

Peer-reviewed publications...are highly regarded by doctors and have a greater influence on prescribers

suitable for publication in a peer-reviewed journal. Typically, such data will come from early pre-clinical experiments. Unfortunately, preliminary, preclinical research can be difficult to incorporate into a proactive plan. This is in part because those who carry out the research are usually very distant from those who will publicise and sell the product, and in part because it is difficult to predict what early research will find. Nevertheless, research scientists at most pharmaceutical companies want to see their research published. And in the most 'prestigious' (whatever that means) journals.

Why peer-reviewed publications?

From an ethical point of view, I believe that all studies into the product's properties should be submitted to peer-reviewed journals—there is no place for cherry picking by only submitting favourable studies or results. This is both deceitful, as it conceals unfavourable information from prescribers and patients, and unscientific, as it distorts systematic reviews and meta-analyses. Clearly there is a problem with studies that produce 'negative' results. In the past there was a belief (probably unjustified) that journals would not accept negative studies. Many of the most respected journals have undertaken to publish reports of well-designed studies, whether negative or positive. There are now legal requirements for pharmaceutical companies to make the designs and results (and possibly in future the raw data) of clinical studies available, although there are as yet no requirements for such studies to be submitted to peer-reviewed journals. I see no reason why all clinical studies on new products or products in development should not be written up for submission to peer-reviewed journals. I suspect, however, that things will be rather

different in 10 or 20 years' time, when open-access electronic publishing may well be the norm, and the process of 'peer review' could be very different from what it is today.

A major headache for authors of papers based on clinical studies is deciding what to leave out. Most clinical study reports contain far too much data for a single paper. The skill is to report only the key findings of the study without unnecessary detail and without distortion. Most importantly, the writer must ensure that adverse effects are reported properly. Marketing departments in pharmaceutical companies seem to have an in-built aversion to reporting adverse effects of their new wonder drugs. This is misplaced. If you tell people honestly what adverse effects to expect, patients and prescribers will be less upset when these adverse effects occur than if they come as a surprise.

One key reason for using peer-reviewed publications to support marketing strategies for new products is that doctors are becoming increasingly suspicious of pharmaceutical companies' direct sales activities [2]. Many doctors no longer agree to speak to sales representatives, for example. Peer-reviewed publications, on the other hand, are highly regarded by doctors and have a greater influence on prescribers than other activities of pharmaceutical companies [2]. In addition, government agencies that assess whether national healthcare systems should pay for new products, such as the National Institute for Health and Clinical Excellence (NICE) in the UK and Germany's Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG—Institute for Quality and Efficiency in Healthcare) make recommendations based largely on studies published in

The communications plan is a vital database

peer-reviewed journals. The preparation of all such publications must therefore be planned carefully.

What does fitting a peer-reviewed publication into a communications plan or strategy involve? A key consideration is timing. Working backwards from when the company wants the paper to be published, the plan should take into account the time it will take to produce the version of the paper that will be submitted to the journal, bearing in mind that several rounds of review and approval will be needed. These should be specified in the communications plan, as should details of who is to write, review and revise the manuscript. The time from submission to publication is rarely less than 6 months, even though the time to acceptance is typically 4 months. Most journals usually promise to return referees'/editors' comments to the corresponding author within 6 weeks. As few papers are accepted without changes, planners also need to add the time for two rounds of refereeing (perhaps 3 months). Then you need to add the time it takes authors to revise the manuscript, plus the time it takes to resolve the desk editor's queries and correct the proofs.

Peer-reviewed publications in a communication strategy

What about choice of journal? All authors want their papers published in highly prestigious journals. The problem is that there is no good, unbiased, objective measure of prestige. 'Impact factor' is often cited as a useful measure of a journal's standing, but this is a flawed tool, discussion of which is beyond the scope of this article. The communications planner should ask her/himself two questions: "Which journal will deliver this information to the highest number of our intended audience?" and "What is

the rejection rate of our target journal?" The cynic might even say that the average prescriber has no idea of what an impact factor is or what a particular journal's impact factor is. As a rough rule of thumb, the higher the impact factor, the higher the rejection rate (see box in the first column on this page), and rejection by your first-choice journal delays publication, even if the rewritten paper is accepted immediately by your second choice journal.

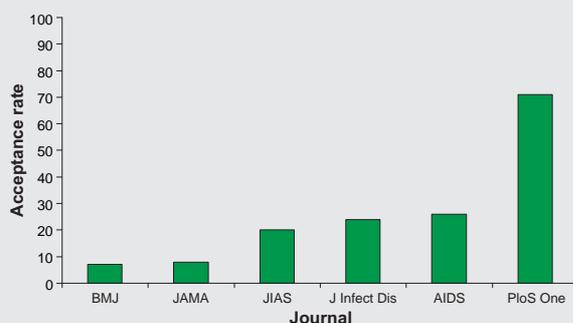
The communications plan is also a vital database of those publications that contain evidence supporting key messages and claims about the product. It should be borne in mind that most regulatory authorities and codes of practice require that all data the company uses in its marketing campaign, including preliminary pharmacology, must be published in peer-reviewed journals. Even if local regulations allow claims to be supported by non-peer-reviewed publications, my view is that this is both unnecessary and unethical. It is therefore vital that all peer-reviewed publications are planned and appear in the communications plan.

Conclusions

In conclusion, planning the flow of reliable information about new medicines is vital to their timely uptake and introduction into mainstream medical practice. Peer-reviewed publication is the most ethical and trustworthy route for the dissemination of information about such new medicines.

Factors affecting rates of acceptance of articles for publication

Acceptance rates of selected journals (2009)



Acceptance rates of high impact journals (e.g. *BMJ* and *JAMA*) are often below 10% as shown by this graph compiled by *The Journal of the International AIDS Society (JIAS)* published with permission from the journal and with thanks to Mirjam Eckert. Acceptance rates are shown as a percent, *BMJ*, 7% (Wikipedia); *JAMA*, 9% (*JAMA* website); *AIDS*, 26% (personal communication); *J Infect Dis*, 24% (personal communication); *PloS One*, between 60 and 80% (from a *PloS One* blog in 2007); *JIAS*, 20%. *PloS One* and *JIAS* are online only journals which grant immediate open access to all accepted articles published. As noted by Iain Hrynaskiewicz in his article on page 201 of this issue of *TWS*, online publishing allows a journal to accept and publish more articles but acceptance rates also differ according to editorial policies of journals and *PloS One* has different policies even from other *PloS* journals. Some journals, e.g. *Nature* and *Science* receive a lot of pre-submission enquiries so may never receive manuscripts which they might otherwise reject as being of no interest to the journal. There are therefore a number of reasons as to why acceptance rates differ and data is not always easily available, although information can often be obtained through a direct approach to a journal's editorial office.

Examples of publications commonly used in communications strategies

- Abstracts of posters and oral presentations at conferences
- Product monographs
- Papers in peer-reviewed journals (including reviews)
- Letters to the editor
- Educational materials for healthcare professionals, patients and their families
- Newsletters (both for circulation within the company and to healthcare professionals)
- Conference reports
- Training materials for sales representatives
- Sponsored symposia at conferences

Note: This list is by no means complete!

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■ Research article

Adherence to the CONSORT guideline in papers written by professional medical writers

by Adam Jacobs

Abstract

Background

Many papers in the biomedical literature are drafted not by those who did the research, but by professional medical writers. CONSORT guidelines give specific recommendations for items that should be included in publications of randomised controlled trials. This study investigated whether papers written by professional medical writers were more compliant with the CONSORT guidelines than other papers.

Findings

All randomised clinical trials published in the journal *Current Medical Research and Opinion* between October 2004 and August 2009 were included in this study. Data were abstracted by two researchers, both of whom were blind to the objectives of the study; one recorded whether each CONSORT item was absent, present but incompletely described, or completely described and the other checked each paper for whether a medical writer had been acknowledged and whether the paper had industry sponsorship. The mean number of completely described guidelines was compared between papers written by a medical writer and those written by others. The secondary analysis was to compare industry-sponsored papers with those that did not declare industry sponsorship. 241 papers were included, 93% of which were industry sponsored; 63% acknowledged assistance from a medical writer. Papers that acknowledged medical writers complied with more CONSORT items (17 of 22) than those that did not (16 of 22; difference between groups 0.75 items completed, 95% CI 0.07 to 1.43, $P = 0.03$). Too few non-industry-sponsored papers were found to allow a meaningful comparison of industry and non-industry-sponsored papers.

Conclusions

Papers that acknowledged assistance from professional medical writers were more likely to comply with the CONSORT guidelines than papers that did not. However, the difference was small, and the practical importance of the difference is unknown.

Introduction

Many papers in the biomedical literature are drafted not by those who did the research, but by professional medical writers. Many professional medical writers receive training in how to write papers, and write papers and other medical documents as a full-time job. It might therefore be

hypothesised that they are better qualified to write papers than most researchers, for whom writing the paper is often simply an unfortunate extra chore that needs to be done at the end of a piece of research.

However, despite the theoretical benefits of assistance from professional medical writers, there are almost no data to show whether those benefits are realised in practice. In a systematic review in 2003, Lagnado only found anecdotal evidence that professional medical writers improve the quality and readability of papers, and concluded “I did not find firm evidence to support these reported benefits.” [1]

Measuring the writing quality in published papers is hard to do, as many aspects of writing quality are subjective. However, the CONSORT guidelines give specific recommendations for items that should be included in publications of randomised controlled trials, with a 22-item checklist [2]. The extent to which papers of randomised trials comply with the CONSORT guidelines could be considered a measure of the completeness with which the research is documented, which is one measure of writing quality, albeit a measure of only one dimension of a complex multi-dimensional concept. The aim of this study was to determine whether papers written by professional medical writers were more compliant with the CONSORT guidelines than other papers. An updated version of the CONSORT guidelines has recently been published [3]; however, this research pre-dates the publication of those guidelines and therefore used the 2001 version.

Methods

The primary objective of this study was to determine whether papers written by professional medical writers are more likely to comply with the recommendations of the CONSORT guideline than papers that were not written by professional medical writers. A secondary objective was to determine whether industry sponsorship of papers was associated with compliance with the CONSORT guideline. Involvement of professional medical writers and industry sponsorship are often considered as a single issue, although in reality they are two quite distinct concepts.

All randomised clinical trials published in the journal *Current Medical Research and Opinion* between October 2004 and August 2009 were included in this study. That journal was selected because it has a high proportion of papers written by professional medical writers and was therefore expected to yield a sufficient number of such papers for

Adherence to the CONSORT guideline in papers written by professional medical writers

analysis. A previous pilot study (unpublished) in a wider range of journals failed to yield useful results because the number of papers acknowledging professional medical writers was too small to allow meaningful comparisons. The date range was chosen for pragmatic reasons, as we had had a subscription to the journal since October 2004 and therefore had full text articles available since that date. The instructions to authors of *Current Medical Research and Opinion* had recommended that manuscripts of randomised controlled trials comply with the CONSORT guideline since April 2005.

Data were abstracted by two interns, both of whom were blind to the objectives of the study to avoid any bias in collecting the data. Both interns were science graduates and received brief training in the methods of the study. One intern (VM), who was not aware that the study was designed to compare papers written by professional medical writers with those that were not, compared each paper with each item in the CONSORT checklist, and recorded whether the item was absent, present but incompletely described, or completely described. The other intern (AM), who was not aware that the study was designed to assess compliance with the CONSORT checklist (or indeed any other measure of quality), checked each paper for whether a professional medical writer had been acknowledged (rated as yes, no, or unclear), and whether the paper had industry sponsorship. Although it was not always easy to infer the nature of any writing assistance from often vague statements in acknowledgements, we attempted to define the involvement of a professional medical writer as someone who had had a role in drafting the manuscript, and if it was clear that only editing of an already complete manuscript was being acknowledged, we did not count that as writing assistance.

A total score was calculated for each paper as the sum of the items that were completely described (minimum = 0, maximum = 22). If an item was not completely applicable, a full point was awarded if the paper described the parts that were applicable and contained sufficient information to be sure other parts were not applicable. The primary analysis was a t-test of the difference in those scores between papers written by a professional medical writer and those that either were not or were unclear. A secondary analysis was done to compare industry-sponsored papers with those that did not declare industry sponsorship. As a sensitivity analysis, the total score was recalculated with the addition of half a point for each item that was present but incompletely described.

As a further sensitivity analysis, the odds of completion of CONSORT items were investigated by logistic regression. Because items within a specific paper would be expected to be correlated, a random effects logistic regression model was used in which the paper was included as a random effect, and acknowledgement of a professional med-

Table 1. Characteristics of the included papers

Source of funding	No medical writer acknowledged	Acknowledgement unclear	Medical writer acknowledged	Total
Industry	60 (27%)	17 (8%)	147 (66%)	224 (100%)
Other	9 (53%)	3 (18%)	5 (29%)	17 (100%)
Total	69 (29%)	20 (8.3%)	152 (63%)	241 (100%)

ical writer and the number of the CONSORT item were included as fixed effects.

Exploratory analyses were done to calculate the odds ratios and their confidence intervals for completion of each CONSORT item individually.

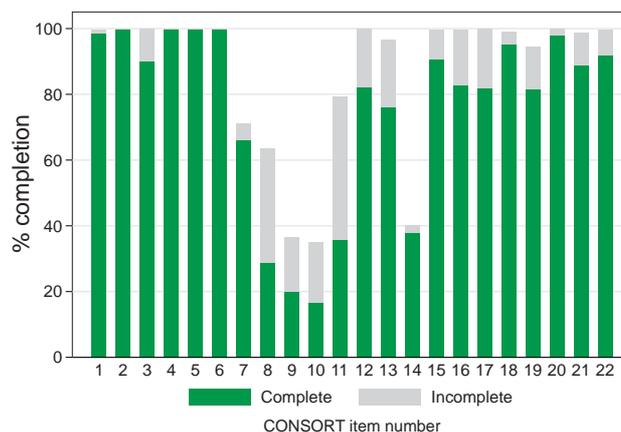
Results

241 papers were included in the study. Details of industry sponsorship and acknowledgement of professional medical writers are shown in Table 1. As expected for a journal that focuses on industry-sponsored research, the overwhelming majority of papers were industry sponsored, and a little over half clearly acknowledged assistance from a professional medical writer.

Most CONSORT items were at least partially described in almost all papers, although some were less well described (Figure 1). Items that were particularly poorly described by both groups of writers were items 9 (concealment of random allocation), 10 (implementation of randomisation), and 14 (dates of recruitment and follow up periods). The frequency of reporting of each CONSORT item by medical writers and other writers is given in Table 2.

Papers that acknowledged professional medical writers complied with more CONSORT items than those that did not (Table 3). The difference between groups was statistically significant for the primary measure of counting only complete CONSORT items (difference between groups 0.75 items completed, 95% CI 0.07 to 1.43, $P = 0.03$) but not for the secondary measure in which half points were counted if items were present but incompletely described (difference between groups 0.53 items completed, 95% CI -0.02 to 1.07, $P = 0.06$).

Figure 1. Overall compliance with CONSORT items



Adherence to the CONSORT guideline in papers written by professional medical writers

> **Figure 2. Odds ratios for completion of each CONSORT item**

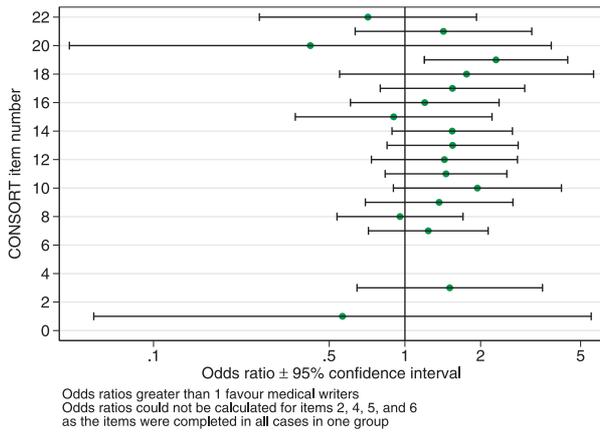


Table 3. Number of CONSORT items completed

	Papers probably written by medical writers (N= 152)		Other papers (N = 89)	
	Mean	SD	Mean	SD
Number of CONSORT items completed	16.9	2.5	16.1	2.7
Items completed with half marks for incomplete items	18.0	2.0	17.5	2.1

Table 2. Frequency of reporting of CONSORT items

CONSORT item	Paper section	Topic	Description	Frequency of reporting n (%)	
				Medical writer	Other writer
1	Title & abstract	Title and abstract	How participants were allocated to interventions	149 (98.03)	88 (98.88)
2	Introduction	Background	Scientific background and explanation of rationale	151 (99.34)	89 (100.00)
3	Methods	Participants	Eligibility criteria and the settings and locations where the data were collected	139 (91.45)	78 (87.64)
4		Interventions	Precise details of the interventions intended for each group; how and where they were administered	151 (99.34)	89 (100.00)
5		Objectives	Specific objectives and hypotheses	151 (99.34)	89 (100.00)
6		Outcomes	Clearly defined primary and secondary outcome measures; any methods used to enhance the quality of measurements	152 (100.00)	88 (98.88)
7		Sample size	How sample size was determined and explanation of any interim analyses and stopping rules	103 (67.76)	56 (62.92)
8		Randomisation, sequence generation	Method used to generate the random allocation sequence, including any restrictions	43 (28.29)	26 (29.21)
9		Randomisation, allocation concealment	Method used to implement the random allocation sequence, clarifying whether the sequence was concealed until interventions were assigned	33 (21.71)	15 (16.85)
10		Randomisation, implementation	Who generated the allocation sequence, enrolled participants, and assigned participants to their groups	30 (19.74)	10 (11.24)
11		Blinding	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated	59 (38.82)	27 (30.34)
12		Statistical methods	Statistical methods used to compare groups for primary outcome(s); methods for additional analyses	127 (84.11)	70 (78.65)
13	Results	Participant flow	Flow of participants through each stage. Describe protocol deviations from study as planned, together with reasons	120 (78.95)	63 (70.79)
14		Recruitment	Dates defining periods of recruitment and follow-up	63 (41.45)	28 (31.46)
15		Baseline data	Baseline demographic and clinical characteristics of each group	137 (90.13)	81 (91.01)
16		Numbers analysed	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat"	127 (83.55)	72 (80.90)
17		Outcomes and estimation	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision	128 (84.21)	69 (77.53)
18		Ancillary analyses	Address multiplicity by reporting any other analyses performed	146 (96.05)	83 (93.26)
19		Adverse events	All important adverse events or side effects in each intervention group	131 (86.18)	65 (73.03)
20	Discussion	Interpretation	Interpretation of the results	148 (97.37)	88 (98.88)
21		Generalisability	Generalisability (external validity) of the trial findings	137 (90.13)	77 (86.52)
22		Overall evidence	General interpretation of the results in the context of current evidence	138 (90.79)	83 (93.26)

Adherence to the CONSORT guideline in papers written by professional medical writers

The logistic regression analysis also showed that CONSORT items were significantly more likely to be completed in papers with a clear acknowledgement of a medical writer (odds ratio 1.44, 95% CI 1.04 to 2.00, $P = 0.03$).

In the exploratory analysis of the odds ratio for each individual CONSORT item, most 17 of 22 odds ratios were greater than 1, showing that the item was more likely to be completed in papers with a clear acknowledgment of a medical writer (Figure 2). However, the difference was statistically significant only for item 19 (reporting of adverse events) (odds ratio 2.30, 95% CI 1.19–4.44, $P = 0.01$).

No significant differences were noted between industry-sponsored and independent publications on any measure. The ability of this study to determine the effect of industry sponsorship was severely hampered by the small number of papers without industry sponsorship.

Discussion

There are very few existing data on whether professional medical writers improve the quality of publications. This study has shown that papers that acknowledged professional medical writers were more compliant with the CONSORT guideline than papers that did not. The difference was small but statistically significant and although this is only one proxy measure of article quality, the result is important as it provides evidence towards a much discussed but seldom answered question. Unfortunately, there were too few non-industry-sponsored publications to allow meaningful comparison with industry-sponsored publications, so this study was unable to meet its secondary objective.

It has been suggested that randomisation, avoidance of exclusions after trial entry, and blinding are the most important methodological components of controlled trials [4]. It has also been reported that trials that used inadequate allocation concealment compared with those that used adequate concealment had larger estimates of effect [4,5]. Therefore, it could be proposed that the most important CONSORT items to include as markers of study quality are items 9 (concealment of random allocation), 10 (implementation of randomisation), 11 (blinding), and 13 (participant flow); items 9 and 10 were poorly reported by both groups in this study. However, items 9, 10, 11, and 13 were all more frequently reported in papers that acknowledged professional medical writers than those that did not. It therefore appears that professional medical writers do better than other writers on items that make important contributions to the quality of reporting, although reporting of these items was far from perfect even in the articles that acknowledged medical writers.

Some limitations need to be borne in mind when considering the results of this study. The most important is that if a paper does not acknowledge a medical writer, that is not proof that no medical writer was involved, as it is possible that an unacknowledged medical writer (or

ghostwriter) assisted with the paper. A substantial proportion of papers written by medical writers do not contain an acknowledgement of the medical writer's contribution [6], although that proportion is decreasing, probably as a result of recent guidelines that have emphasised the importance of acknowledgement of medical writers. However, as 2 of those guidelines [7, 8] were published in *Current Medical Research and Opinion*, and that journal has been keen to engage constructively with professional medical writers, it seems likely that the proportion of unacknowledged contributions by medical writers would be lower than in biomedical publishing as a whole.

It is likely, therefore, that most of the papers that did not acknowledge medical writers were written by the researchers, but some misclassification bias could have affected this study. In this context, misclassification bias could result either from papers that were truly written by medical writers being classified as having been written without their assistance, or vice versa. The effects of such misclassification bias are hard to determine and could act in either direction. On the one hand, it is possible that such misclassification bias could have diluted the effect seen in this study, as a result of the involvement of medical writers in some of the papers classified as having been written without their assistance. If that were the dominant effect of misclassification bias, then the true benefit of professional medical writers would be greater than suggested by the results shown here.

However, it is also possible that medical writers who are not acknowledged simply lack the professionalism of their acknowledged colleagues and do not keep sufficiently well informed about current guidelines, which would make them less likely to insist on acknowledgement as well as less likely to adhere to the CONSORT guidelines. If that is the dominant effect, then it is possible that this study may over-estimate the benefit of medical writers.

This study was not a randomised trial and papers written by professional medical writers may differ from the others in other ways. However, as all papers were taken from the same journal, any differences between the papers should be reduced, but systematic differences between the groups of papers cannot be ruled out. Data were extracted by only one person, and it is therefore likely that there were some errors in data collection. However, any such errors would have the effect of adding random noise to the data, which would tend to obscure any difference between the two groups of papers, and therefore be likely to bias the results towards the null hypothesis. If such errors were common, then the true difference between the groups may be greater than reported here. Importantly, neither of the researchers extracting data was aware of the study hypothesis, so it is unlikely that any systematic bias could have affected the results.

Adherence to the CONSORT guideline in papers written by professional medical writers

> A further limitation is that this study was only able to examine the final published manuscripts. We do not know whether medical writers were responsible for including items in the CONSORT checklist. It is possible that a medical writer may have initially included some items which were subsequently deleted, or have initially omitted some items which were subsequently added, as many changes would be made to a medical writer's first draft both by the named authors and in response to requests from peer reviewers.

In conclusion, papers that acknowledged assistance from professional medical writers were more likely to comply with the CONSORT guidelines than papers that did not. However, the difference, although statistically significant, was small, and the practical importance of the difference is unknown.

Acknowledgements

I thank Val Mendes and Amal Mockbil for collecting the data for the study during internships at Dianthus Medical Limited. I thank Sara Hughes of Dianthus Medical Limited, who assisted with preparation of the manuscript in accordance with the European Medical Writers Association

guidelines. I am also grateful to Tom Lang for a thorough and constructive peer review of this paper after submission to *TWS*.

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Globalisation



Biomedical publishing in the Internet age

by Iain Hrynaszkiewicz

The Internet has revolutionised science publishing but it has also challenged traditional business models. The shift to online content has already ‘disrupted’ the newspapers and the same could be said for biomedicine [1]. However, publishers that are embracing the web and offering innovative online services are growing substantially.

The role of the (online) publisher

With the advent of online, open access publishing the role of the publisher is changing. Rather than being the steward and gatekeeper of content, an online publisher is a service provider—serving the scientific community by helping to maximise the pace of research and disseminate results quickly. Developments in online publishing workflows have, for example, enabled research articles to be published on a journal website as soon as they are editorially accepted, and to be indexed in PubMed (and numerous other permanent bibliographic archives) within hours. Traditional roles, such as contributing high quality, value-added content and preserving that content indefinitely, still apply; however, the wealth of information and formats now available online requires innovative tools to meet the needs of today’s researchers and clinicians. And successful publishers must be collaborators to fulfil these roles by working with clinicians [2], and of course all others involved in the process of information transfer, editors and librarians included.

Under traditional publishing models researchers, who may spend many collaborative years working on a research project, transfer the right to distribute that work to a publisher, which covers its costs by selling access to the content back to the scientific community. The publisher fulfils a variety of functions, such as administering peer review, typesetting, printing and copyediting. But out of the paradox of the results of publicly funded research being available only to those who can afford ever increasing subscription costs, the online, open access movement was born.

Open access publishing

Under the open access model every research article is immediately and freely available without any barriers or other requirements for access, other than being able to connect to the Internet. Broadly speaking there are two mechanisms for providing open access to research. Firstly, self-archiving by authors or via institutional repositories (often called ‘green’ open access) and secondly via journals that publish open access articles (‘gold’ open access;

for a more detailed overview see [3]). But for many publishers open access does not just mean content is free to read. Some open access content is also free to be re-used, redistributed, in whole or in part, with no permission from the authors or publisher required. And the authors—not the publishers—retain the copyright for their work. This is achieved by publishing under the Creative Commons attribution licence [4], and has been adopted by some open access publishers, such as BioMed Central, Public Library of Science (PLOS) and the *BMJ* (for research articles). To defray the costs of the publishing service a publication fee, or article processing charge, can be levied for each accepted article.

Established in 2000, BioMed Central was the first commercial open access publisher, although the market has grown substantially over the past decade with the appearance of other, start-up open access publishers. However, growth in the open access market has been driven substantially by traditional publishers experimenting with the model, and offering their authors an open access option.

Ten years on and nearly 10% of all scientific, technical and medical (STM) journals are published under the open access model, and open access journals are now growing at a faster rate than STM titles overall [5]. The Directory of Open Access journals now includes over 800 medical journals and more than 5000 journals in total [6]. The commitment of research funding agencies and universities to open access has been an important driver of growth, and many now mandate open access and some also provide specific funds to cover the costs of publication [7].

The impact of open access

The immediate benefit for authors who publish in online open access journals is visibility of their work. Removal of subscription barriers leading to increased readership is self-evident (although it has been demonstrated [8]); and the fact that all the pages of online open access journals are often fully index-able and crawl-able by Internet search engines increases online visibility further. The pages of BioMed Central’s 207 journals and its related websites are, for example, accessed more than 27 million times per month. And a growing body of evidence suggesting that open access articles are more frequently cited than those that are behind subscription barriers is also emerging [9, 10].

Biomedical Publishing in the Internet age

> **Increasing quality and quantity**

Space has traditionally come at a premium in journals but when publishing online space becomes virtually limitless. Word, reference, table and figure limitations can be a source of author dissatisfaction—not least because they can often seem arbitrary—and removing them has immediate benefits of reducing demands on invariably busy authors' time. But the less obvious, longer-term benefits of publishing science on the unrestricted web are not to be underestimated.

Publication bias favouring positive results—those that favour the medical intervention or drug being investigated—is a widespread problem in medical research [11] with serious consequences for evidence-based medicine and, as a result, for patient care. The availability of unlimited space and increasing numbers of journals on the Internet should help, at least partly, to combat this problem, as all sound scientific research should find a venue for publication. Online publishing facilitates not only the publication of more articles but of more substantial articles. Numerous deficiencies in the reporting of medical research have been—and continue to be—documented, particularly in the field of clinical trials [12]. There is a need to increase the quality as well as the quantity of research reports, and improvements in the reporting of health research are, albeit slowly, being made, driven by initiatives such as the CONSORT checklist [13] for clinical trials and, more broadly, the EQUATOR Network (<http://www.equator-network.org/>)—a library of reporting guidelines for health research. Policies and legislation calling for greater transparency in clinical research have led to the growth of prospective clinical trial registration [14] and, in 2007, the mandatory reporting of trial results supporting FDA drug applications. The removal of limitations on the number and length of publications enables all relevant information about clinical trials to be made available including study protocols and all results—regardless of the outcome or any perceived level of interest [15].

Information overload?

Online publishing has facilitated rapid and sustained growth in the volume of medical literature. The rate of growth has doubled every 20 years and by 2012 the annual accession rate of medical articles is predicted to exceed 1 million [16]. The implications of an 'information overload' for researchers, policy makers and peer reviewers are numerous, but some innovative solutions have been found.

A number of publishers, including BioMed Central, Nature and PLoS, use a peer-review cascade system, where their more selective journals that reject a high proportion of articles offer publication in a less selective title with peer review expedited. With the consent of authors and peer reviewers, reports and recommendations can be shared and articles can move both up and down the cascade if the editors feel an article may be better suited to a title with a different threshold of acceptance. This approach offers flexibility, reduces publication delays and makes the most effective use of a valuable but limited resource—peer reviewers' time. It also avoids saddling experts with the

repeated review of some studies as they 'do the rounds' at different journals before eventually being published. If research is sound it should be a question of *whether* to publish; if research is potentially of high interest authors can consider *where* to publish. Inter-publisher sharing of peer reviews and submissions is also happening via initiatives such as the Neuroscience Peer Review Consortium.

For readers, a number of online literature evaluation services have emerged. Mektosj's 'Papers' software and Mendeley's online reference management tool both describe themselves as being equivalent to Apple's music management software iTunes, but for papers. These services enable researchers to create a personal digital library of articles and share and evaluate them online, facilitating collaborative exchange of research trends. The Faculty of 1000 Medicine is a subscription service that produces short evaluations of published articles, written by commissioned experts (faculty members). Another subscription service, Science Watch's 'Hot Papers', aims to track articles by quantitative literature analysis, and alert researchers, policy makers and journalists to important research.

Measures of success in the Internet age

Impact Factors continue to be a source of much debate in scholarly publishing. With the rapid growth in online journals, many yet to receive an Impact Factor, alternative metrics have emerged. Scopus, a subscription product from Elsevier, analyses citation data from a wider number of journals than those included in Impact Factor calculations. The freely available SCImago Journal Rank (SJR)—which uses Scopus data—uses an algorithm similar to Google's PageRank to differentially weight the citations according to the impact of the journal in which the citation occurred, which can produce marked changes in journal rankings compared with the Impact Factor [17].

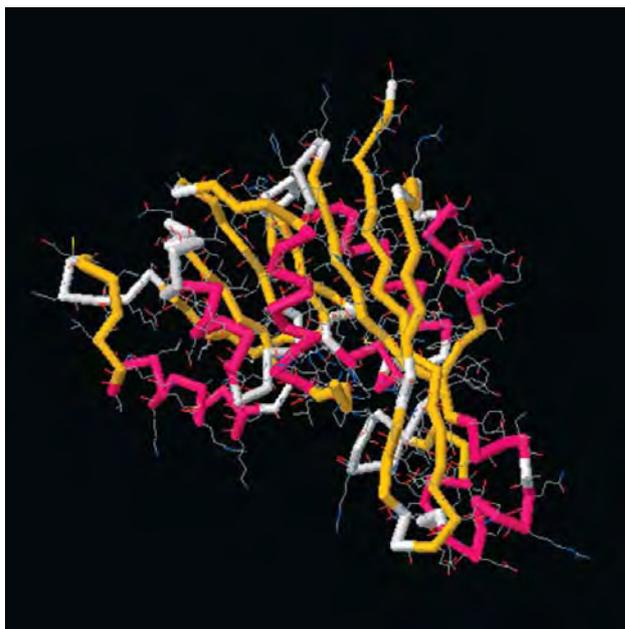
However, a 2005 survey of senior researchers found that, in the Internet age, many authors now believe article downloads—readership—to be a more credible measure of success than citations [18], which questions the validity of focussing the metrics of success on the journal. Moreover, impact can now be measured in a variety of ways at both article and author levels.

Web technology enables us to measure how many times individual articles have been downloaded and rated, and the comments of the community relating to the article, whether these are on the journal website or through other social media postings. So-called 'article-level metrics' are still in their infancy and, like Impact Factors, are not absolute quality measures but, as more data become available, they will likely become more purposeful—and more influential [19].

Author evaluation tools allow tracking of an individual's publications, citations, affiliations and co-authors. From publication and citation data over time we can derive an author's 'h-graph' or 'h-index', which was first developed by physicist J.E. Hirsch [20], and can be considered as part of research grant awards. It can also be calculated for groups of authors or articles.

Biomedical Publishing in the Internet age

Figure 1:



Legend: Example of 3-dimensional, fully rotatable, protein structure, published as an additional file with an open access research article. Screen-grab reproduced from [22].

Beyond the journal article

Myriad supplementary materials and data types can now be published online with journal articles. This includes embedded videos, mini-websites, embedded 3-dimensional structures [21] (Figure 1) and graphical abstracts. While the majority of published articles are effectively an online version of what was previously, or still is, available in print, in 2009 the journal *Cell* launched its ‘article of the future’ concept [22]. It envisages a hierarchical presentation that aims to allow readers to drill down to the desired

level of detail, and a tabbed browsing structure similar to those increasingly employed on websites and web-browsing software.

Increasing availability online of data and metadata (data about data) will in the future enable semantic enrichment of articles, which will further facilitate automated machine readability and processing of content. This could enhance articles by, for example, marking up of textual terms (to highlight key concepts; Figure 2); enabling interactivity with figures, and allowing readers to view cited articles in context. This concept has been demonstrated in principle, although further development of more automated process and standardized language are required to facilitate these enhancements on a large scale [23].

Data sharing and publication

Open access publishing is not just about research results but is, increasingly, also about open access to data behind those results—‘Open Data’. The concept of sharing the raw, unprocessed, research data underlying scientific articles is not a new idea but in medical research calls for greater availability of raw data have been increasing in recent years, from journals and research funding agencies—a number of which now mandate data sharing [24].

There are many benefits to sharing data including replication or validation of findings, additional hypothesis testing, teaching, enhancing the safety of medicines, and integration with new scientific studies [24]. Sharing data helps to maximise the value of data and promotes transparency, and the underlying data can often be published alongside journal articles as supplementary material.

Patients as well as scientists can find it useful to share data and experiences, which can create new potentially valuable sets of data—a concept demonstrated in services such as patientslikeme.com.

Figure 2

turn all highlighting off | date | disease | habitat | institution | organism | person | place | protein | taxon

Top | Abstract | Author Summary | Introduction | Methods | Results | Discussion | Supporting Information | Acknowledgements | References | Data Fusion Supplements

Introduction

At present, one billion of the world's population resides in **slum settlements** [1]. This number is expected to double in the next 25 years [1]. The growth of large urban populations which are marginalized from basic services has created a new set of global health challenges [2],[3]. As part of the Millennium Development Goals [4], a major priority has been to address the underlying poor sanitation and environmental degradation in slum communities which, in turn, are the cause of a spectrum of neglected diseases which affect these populations [2],[3],[5].

Leptospirosis is a paradigm for an urban health problem that has emerged due to recent growth of **slums** [6],[7]. The disease, caused by the **Leptospira spirochets**, produces life-threatening manifestations, such as **Well's disease** and severe **pulmonary hemorrhage syndrome** for which fatality is more than 10% and 50%, respectively [7]–[9]. **Leptospirosis** is transmitted during direct contact with animal reservoirs or water and soil contaminated with their urine [8],[9]. Changes in the urban environment due to expanding slum communities has produced conditions for rodent-borne transmission [6],[10]. Urban epidemics of **leptospirosis** now occur in **cities** throughout the developing world during seasonal heavy rainfall and flooding [6],[11]–[13]. There is scarce data on the burden of specific diseases that affect slum populations [2], however **leptospirosis** appears to have become a major infectious disease problem in this population. In **Brazil** alone, more than 10,000 cases of severe **leptospirosis** are reported each year due to outbreaks in **urban centers** [19], whereas roughly 3,000, 8,000 and 1,500 cases are reported annually for **meningococcal disease**, **visceral leishmaniasis** and **dengue hemorrhagic fever**, respectively, which are other infectious diseases associated with urban poverty [20]–[22]. Case fatality (10%) from **leptospirosis** [19] is comparable to that observed for **meningococcal disease**, **visceral leishmaniasis** and **dengue hemorrhagic fever** (20%, 8% and 10%, respectively) in this setting [20],[23],[24]. Furthermore, **leptospirosis** is associated with extreme weather events, as exemplified by the El Niño-associated outbreak in **Guayaquil** in 1998 [25]. **Leptospirosis** is therefore expected to become an increasingly important slum health problem as predicted global climate change [26],[27] and growth of the world's slum population [1] evolves.

Urban **leptospirosis** is a disease of poor environments since it disproportionately affects communities that lack adequate sewage systems and refuse collection services [6],[10],[11]. In this setting, outbreaks are often due to transmission of a single serovar, **L. interrogans serovar Copenhageni**, which is associated with the **Rattus norvegicus** reservoir [6], [28]–[30]. Elucidation of the specific determinants of poverty which have led to the emergence of urban **leptospirosis** is essential in guiding community-based interventions which, to date, have been uniformly unsuccessful. Herein, we report the findings of a large seroprevalence survey performed in a Brazilian slum community (*favela*). Geographical Information System (GIS) methods were used to identify sources for **Leptospira** transmission in the **slum environment**. Furthermore, we evaluated whether relative differences in socioeconomic status among slum residents contributed to the risk of **Leptospira infection**, in addition to the attributes of the environment in which they reside.

Legend: The first three paragraphs of the Introduction from a semantically enhanced research article, with instances of all the semantic classes highlighted, as described in Figure 3 in [23]. Figure reproduced from [23].

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> Some open access publishers are increasingly committed to data—sharing, publication, preservation and re-use. Some journals, such as *BMC Research Notes*, publish ‘data notes’ (or data papers, in journals such as *Ecological Archives*), which are short descriptions of publicly-available biomedical datasets or databases. Data sharing and publication is not without its challenges. In clinical research where data have inherently arisen from the confidential doctor-patient relationship then privacy must be protected, unless consent for publication of potentially identifying information has been obtained. Preservation of anonymity is especially important in an online, open access arena and this has led to the development of guidance and best practice for sharing clinical data, by editors of open access journals [25].

Other challenges of sharing data include issues of ownership, copyright and commercial sensitivity. However, many non-clinical research communities, such as evolutionary biology, ecology and genomics have already begun mandating raw data deposition as conditions of journal publication, analogous to how most medical journals now require prospective registration of clinical trials [26]. This has led to growing numbers of data repositories, such as Dryad and the Dataverse Network, and the role of online publishers needs to further evolve to include ensuring permanent links to research data are available in published articles.

The new scientific record?

Gillam and colleagues [16] have suggested that, facilitated by open, standardised medical research data and the semantic web, we may be approaching a ‘healthcare singularity’ by 2025—when translation of research discoveries into medical practice will be instantaneous (for comparison, the time from discovery to widespread use of penicillin in patients was around 20 years). The same collection of (open access) work, *The Fourth Paradigm*, also envisages that in the future data, and computational software tools to analyse that data, will be as integral to the scientific record as IMRaD articles are today [27]. This change in scholarly communication will not happen unaided, but the possibilities to enhance patient care with open data on the web are staggering. In years to come a doctor might use a clinical decision support tool on her smart-phone to analyse real-time data from integrated electronic health records, the patient’s genomic profile, evidence-based medicine databases and records of ongoing clinical trials [28], and localized drug resistance data [16]. The doctor could then recommend the most effective, rapidly available and personalized treatment or recommend enrollment into a randomized clinical trial if the evidence for a treatment in their patient may be uncertain. And all of these data could be shared instantly to help drive future research and knowledge discovery. This might, today, seem intangible but Gillam [16]—again—reminds us that secure technology to put patients in control of their electronic health information is already being developed by companies such as Microsoft and Google.

So if data and software rather than articles become the scientific record, what role will remain for writers and

publishers? The formats of biomedical communications in the Internet age are, without a doubt, evolving. Articles are becoming more interactive, more flexible, more data-driven and more independent of the status of the journal in which they are published. But driving these changes will continue to require innovative software and tools, developed by collaborations between scientists, medical information professionals and publishers. Although re-usable shared data have tremendous potential to drive new medical discoveries value-added content, contextualised and adapted for the intended audience—whether clinicians, academics or patients—will continue to be needed. Which means, that for the foreseeable future, we will always need writers.

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Acknowledgements

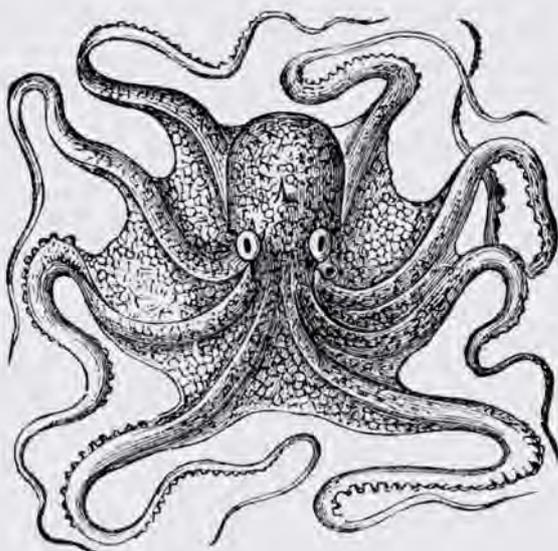
This article is based on a lecture given by IH at the EMWA meeting in Lisbon on 12 May 2010. The author would like to acknowledge Dr Melissa Norton and Ms Deborah Kahn at BioMed Central for contributing slides to the lecture and, as such, some concepts presented in this article.

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Octopus



A delight not to be missed—no this is not a foodie box it's about the plural of the word octopus. What would you say if you told a friend you had been swimming in the ocean and you saw a bunch of 8-legged cephalopods? For a full answer listen to an editor from *Merriam Webster's Colligate Dictionary* at <http://www.wimp.com/octopusplural/>

With thanks to **Adam Jacobs** for passing on this site.

Biomedical Publishing in the Internet age

Definitions box

Chirality or stereoisomerism

If a carbon atom in a molecule (drug or any other chemical) has four different substituents, that molecule can have one of two different three-dimensional structures. This is analogous to a pair of gloves—they have the same structure but are mirror-images of one another and cannot be superimposed on one another. These two mirror-image forms are known as *enantiomers*. A molecule can have more than one of these *chiral centres*, which means that more than two *stereoisomers* can exist, although they will not all be mirror images of one another. For example, if there are two chiral centres in a molecule, there can be four stereoisomers (provided that the molecule does not already have an internal plane of symmetry). There is a standard system for describing the configuration of groups around a chiral centre; the arrangement is described as either R (rectus—Latin for right) or S (sinister—Latin for left). Our molecule with two chiral centres can therefore be R-R or R-L or L-L or L-R. The R-R and L-L forms will be mirror images (enantiomers) as will R-L and L-R, but R-L and L-R will not be mirror images of either L-L or R-R.

When chemicals are synthesised using standard organic chemistry methods, the yield usually contains equal proportions of all the stereoisomers. This is known as a *racemic mixture* or a *racemate*. Although stereoisomers are essentially identical in terms of their chemical and physical properties, they may have very different pharmacological or toxicological properties. When only one of the stereoisomers has the desired pharmacological activity and the other stereoisomer(s) is/are either inert or have no detrimental properties, it is seldom necessary to develop a synthetic process to produce only the active stereoisomer. The racemic mixture will be pharmacologically active but will be less potent than the single stereoisomer because it is diluted by inactive molecules (if there are two stereoisomers and one is completely inactive, the racemate will have half the potency of the active stereoisomer as you will need to use twice as much to produce the same effect). However, when one of the stereoisomers has undesirable activity, the manufacturer may decide to develop a synthetic process that yields the desirable stereoisomer (i.e. the one with the desired pharmacology) but not the undesirable stereoisomer(s). This can be very expensive, and the decision has to be made early in drug development because all studies carried out on the drug for registration purposes will need to be made using the single stereoisomer.

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Coyness or necessary imprecision?

by Françoise Salager-Meyer

Today's scientists are urged to use a style of writing which projects both personal modesty and honesty. Argumental arrogance and exuberance are not well seen by the scientific community. By contrast, humility, coyness and cautiousness are. As Myers puts it, researchers have to present themselves as "the humble servants of the discipline" [1]. According to Blisset: "If a scientist is articulate, persuasive, if he goes to the heart of the matter, he is open to attack" [2]. Myers provides us with a nicely illustrated case study of two well-established biologists who struggled to get their papers published because their arguments were too arrogantly expressed [3]. As Myers observes, the authors had to rewrite their article four times, "so that the published versions are hardly recognisable as related to the first submission". As a consequence, everything must be toned down; speculation can obviously be made but it must be apologised for.

The linguistic technique used to express uncertainty in English has been called *hedging* since 1972 when the linguist George Lakoff defined it as words used "to make things more or less fuzzy" [4]. Examples of words sometimes used in different types of hedges include¹ *may, might, could; assume, seem, suggest; apparently, likely, possibly; about, tentatively; if, unless; although, but; instead, unexpected, and yet* [see 5].

Hedging has gained growing attention since its great frequency in the 1953 *Nature* article by Watson and Crick [6] that was widely reprinted because it made news coyly suggesting the structure of DNA, which was not defined in our dictionaries until more than a decade later. The article begins with a 'compound hedge': "*We wish to suggest*" a structure [...] and it ends: "It has not escaped our notice that the specific pairing we have *postulated* immediately *suggests a possible* copying mechanism for the genetic material. Full details of the structure, including conditions *assumed* in building it [...] will be published elsewhere".

This attitude of uncertainty continues. It leads scientists to publicise progress they are making even when it is not decisive; progress is noteworthy even when it is not conclusive. On February 25, 2009, newspapers cited a finding about prions but added the need for further study [7]. Yale University released to the journal *Nature* the news that

their researchers had "found that cellular proteins called prions activate the process by which amyloid-beta peptides impair brain function" of Alzheimer's patients. The senior author was Stephen Strittmatter, who is a professor of neurology and director of Cellular Neuroscience, Neurodegeneration and Repair at Yale School of Medicine. He was quoted adding: "The study does not *suggest* that these proteins convert to an infectious agent in Alzheimer's disease, but the findings do *suggest* that the role of these *normally* harmless proteins in common neurodegenerative diseases warrants further study."

I think that when we know that we actually do live in uncertainty, then we ought to admit it; it is of great value to realise that we do not know the answers to different questions. This attitude of mind—this attitude of uncertainty—is vital to the scientist, and it is this attitude of mind which students should first acquire. It becomes a habit of thought. Once acquired, one cannot retreat from it anymore.

Hedging may present the true state of the writers' understanding, namely, the strongest claim a careful researcher can make

Back to the concept of hedges itself. The literature on hedges provides us with two conflicting—although not mutually exclusive—standpoints on the *raison d'être* of hedges. The first (and most widely accepted) view associates hedges with unscientific imprecision and defines them as "linguistic cues of bias" [8], i.e. understatements used to convey (purposive) vagueness and tentativeness, and to make sentences more acceptable to the hearer/reader, thus increasing their chance of ratification and reducing the risk of negation. This necessity for ratification is caused by the inherent refutability of sentences. Indeed, Lakoff pointed out that natural language sentences are very often neither true nor false or nonsensical, but rather true to a certain extent and false to a certain extent, true in certain respects and false in others [4].

Along the same lines, Myers argued that claiming precision is not appropriate in all situations and that scientists do not always want to be precise [1]: "Sometimes we want to be vague," assert Kong et al. [9]. This concept of fuzziness and (necessary) imprecision was developed further by other researchers [10-17], including Brown and Levinson, who considered hedges as strategies for minimising the threat to face that lurks behind every act of communication [18]. They all, in one way or another, state that

¹ Words written in italics in the examples provided hereafter correspond to hedges.

Coyness or necessary imprecision?

hedges are used to signal distance, to “unobtrusively inject an author’s personal view into his communication” [17], to protect one’s own reputation as a scientist, to avoid absolute statements which might put the researchers (and the institution they work at) in an embarrassing situation, to express the extent to which the writers commit themselves to the truth value of their statements and to allow the researchers to be more open to other possibilities of interpretation. According to Swales, hedges are rhetorical devices used for “projecting honesty, modesty and proper caution in self-reports and for diplomatically creating space in areas heavily populated by other researchers” [19]. Quite originally (although not completely at variance with the previous definitions), Myers [1], basing his discussion on Brown and Levinson’s work [10], argues that hedges can be better understood as positive or negative “politeness strategies”, i.e. as rational strategies used for dealing with the social interactions involved in publishing an article (e.g. solidarity with readers, unspeakability of direct criticisms, deference towards the scientific community).

The proponents of the other viewpoint consider that the association of hedging with vagueness or fuzziness can obscure some important function of hedging [20-21]. Instead of interpreting the use of hedging solely in this way, one could alternatively consider it as a way of being more precise in reporting results. Hedging may present the true state of the writers’ understanding, namely, the strongest claim a careful researcher can make. Referring to academic writing, Rounds argues that hedges are not used simply to cover yourself and to make things fuzzy, but that they can also be used to negotiate the right representation of the state of the knowledge under discussion, i.e. to achieve greater preciseness in scientific claims [22]. Indeed, as Tarantino explains, all along scientific writers are aware that the fragment of truth they are exploring is only another step towards the discovery of other truths which will in turn advance knowledge and understanding of nature. In their search for truth (a direction in which all scientists are moving but which is not something one ever finally achieves) and “through the attentive and painstaking organisation of their thoughts, scientists acknowledge that their contribution is a mere glimmer of light in the stream of endeavours to investigate and penetrate the wondrous mystery which include man and the universe” [23].

I partly agree with Skelton [16] that hedges should not always be considered as a problem, as a ‘cover-up’ tactic, but rather as a resource to express scientific uncertainty, scepticism and doubt. After all, scientific rationality is a myth, as Gilbert and Mulkay argue [24], and science has always been oscillating between the desire to be precise and the impossibility of accurately quantifying the world. (This is why scientists’ eagerness to accuracy is very often frustrated).

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It seems you should only ascend the Chinese Wall according to your capabilities if you have something unmentionable or brain disease. Photograph kindly sent by Christine Pavesicz.



Medical writing in a CRO: The challenges and solutions

by Shalini Dwivedi

“Team! Tell me: are we ready for this project? Let me tell you in advance, the timeline for this project is extremely rigid, and it is extremely possible that we might need to come to the office even on weekends to make this happen. But before committing to anything, think about it first and let me know by the end of the business day, so that I can promise our BD guys.... There is no pressure on anybody, but once it is fixed, we have to do it according to the agreed timelines....” Our head of department was speaking in a routine sort of way. At least once every week, we hear almost the same words and while calculating the hours we were to spend in that particular month, all team members looked mischievously into each other’s eyes as if to say ‘I told you so’.

We all knew we would say yes. What other options did we have? When you work in a contract research organisation (CRO), you realise the importance of getting new business. The management of the CRO calculates not only how much time you take to complete a project, but also the utilisation ratio. If the utilisation ratio of your team is less than a hundred, it means more work can be given to you (because you are at the receiving end), and you are expected to accept that.

In the last few years, outsourcing, especially in the pharmaceutical industry, has experienced a boom due to economic pressures on clients and favourable resource availability in various countries, including India and China. Outsourcing offers benefits to both the parties, clients and CROs, but managing projects and maintaining a flourishing relationship with clients is no cakewalk. Once an agreement is reached and the project starts, there can be various (though unexpected) challenges that come into the picture.

Business! Business! Business! (But how much is enough?)

Usually, after receiving requests for proposals (RFPs) from clients, analysing them and before sending off a quotation, the medical writing department will discuss the proposals internally in order to identify exactly what kind of work is expected and to estimate the resources required. A client and a service provider generally have a discussion about the requirements, timelines and other important project-related information. The conversation on such elements is important to assess ‘do we want this project?’ (by the CRO) and ‘can we award the project to this CRO?’ (by the client). If the project description provided by the client in the RFP is not detailed enough or is unclear for other reasons, the CRO usually has an opportunity to interact with the client and ask questions that will help to subsequently

prepare a proposal tailored to meet the client’s expectations. Conversely, the client can also ask for some clarifications concerning the CRO’s proposal to ensure that it fits the requirement. Writing a response, getting clarifications on certain issues, blending the precise technical and project management requirements and quoting an acceptable price take a lot of time, concentration and effort because the client will pick the CRO it considers most likely to provide the best service and match its project requirements and budget. It is often very difficult to work simultaneously on RFPs and manage ongoing projects. Fulfilment of contractual obligations and timelines for ongoing projects is very important. However, because RFPs give us business, these also cannot be ignored. It can happen that, when we are in haste, we make wrong assumptions and forget things that are crucial. Before responding to an RFP, it is therefore rather important to stop and reflect on two essential things: ‘who are we serving?’ and ‘who do we serve well?’ In the professional world, a rumour about bad work travels faster than honest words of appreciation. So, be cautious and aware of the projects in hand first! It is always sensible to have a dedicated individual or team that works on RFPs only, allowing the document reviewers and writers to concentrate on the assignments in hand.

Another very important observation is resource estimation. Sometimes, it is really tempting to fall for every opportunity that comes our way, especially when the department (or business) is new, and often in that temptation we make promises even beyond our capabilities. Nevertheless, before taking on a project, we should analyse our experience as well as the intricacies of the project. The best solution is to develop a metric for the team (within the team) that shows how many of us are involved in currently ongoing projects, to what extent of work and responsibilities, and how many hours we spend each day on these projects. This gives a general idea regarding the hours taken during completion of the first draft, initial quality checks, peer reviews, scientific reviews, and addressing comments received from reviewers. On the basis of this information, an assessment can be made as to how many hours will be required before sending the first draft off to the client. Resource estimation is an essential component of a service industry, and it directly impacts on the efficient handling of a project. The challenges come when timelines change for various reasons or we do not receive the source documents on time. And, in turn, we need to work for more hours than required to meet deadlines because in the meanwhile, we accept a few more proposals.

Medical writing in a CRO: The challenges and solutions

Timelines, Scope Creep and the Client-CRO Relationship: What to manage?

We never wish to default on timelines, but the biggest challenge comes when there are uncertainties at the client's level. I really find it very disheartening that even after signing a common service agreement, sometimes, certain clients unilaterally change the scope of work, often by sending an e-mail, in which the expectations are quite different from what was in the agreement initially. Despite having clearly defined processes and robust metrics, the client fails to understand that keeping the project on track is a mutual responsibility of both parties, in which the client also has to play an important role. Sometimes, we do not receive appendices for compilation on time; on top of that, we are told that they were already sent, often without any verification at their end. In other cases, it also happens that we keep receiving data right up until the last minute. Sometimes, the client is so demanding that we need to do extra analyses for them, which were not included anywhere in the agreement, but because we are a service provider and we wish to maintain a long-lasting (in fact, never-ending) relationship with our clients, we offer them discounts (even at the cost of burning the midnight oil, giving up responsibilities for our kids to our spouses and yawning throughout the day while working at office). Above all, whatever we do, we cannot ignore the timeline, even if it is unreasonably short (of course, our manager agreed to it, despite our stated apprehensions), but our efficiency should not decline either (especially, if the CRO is having a dialogue with the client about further business!).

Sometimes the client does not honour its own internal timelines (for whatever reason), but then expects us to squeeze our timelines to compensate for the lost time. In cases where the client does not keep its end of the bargain, there is always a possibility to rediscuss timelines. Likewise, if there are changes in the strategy at any stage in a project, the client must inform the CRO of this in a timely manner, and the CRO may ask for additional payment for managing any scope creep that arises due to changes in the original plan. Nonetheless, asking for additional payment may be difficult if the organisation is a start-up division in the CRO, as the priority is to establish itself and earn repeat business from the same client. Therefore, the CRO needs to make additional efforts and go extra miles when setting up a relationship with the client in order to further boost the business.

Furthermore, resource and project management at the same time is often complicated, and timelines usually slip. Sometimes this is to our advantage, but mostly this is not the case, as it is always hard to resolve timeline conflicts with other ongoing projects. If the conflicts involve projects from the same client, we may ask the client to set a priority, but if projects from different clients are involved, then resolving this issue is very much dependent on the client-CRO relationship. We must also realise that meeting timelines does not mean producing documents

with compromised quality or sending incomplete drafts on a set date. We are hired not only to meet the client's requirements, but also to eliminate their impediments, lessen their time to review and send completed drafts. A good client-CRO relationship is based on this trust, this faith, that we will provide a quality document in time. This shows our seriousness to remain in business, as well as to win the client's confidence that 'we can make it happen'.

To maintain a good client-CRO relationship, the first thing that comes to my mind is transparency: the factual status reporting of a project. To be transparent and honest are our moral responsibilities and everyone in the team must realise that these are the most significant elements for successful completion of a project. Status reporting indicates whether a project is being executed as per the project plan and is also vital for determination of any required corrective action by the stakeholders. Sometimes, the client does not stay reasonably consistent with their initial requirements and therefore it is highly likely that the project may take an undesirable route. In such a case, rather than making assumptions, the best thing is to ask for detailed instructions from the client, because if the instructions are comprehensive, thorough and cover every aspect of a project, these definitely will minimise the chances of error and failure of the project.

Project Management: What will always work? The 4 'W' Policy (What, When, Why and Who)

As most of the time, we work on multiple projects; another very important aspect is tracking the development of a project. Usually, it is not necessary to follow the tracker in a very stringent manner, but it certainly helps in managing the timelines. As we know the target date, it guides the whole team regarding the progress of particular projects, in terms of 'where we are' and 'where we should be'. It is prudent to prepare the tracker in a version for individual members and individual projects as well as in a collated version for the whole team and all the ongoing projects. It will help to analyse whether more resources are required to meet the timeline assigned to a particular project, as well as for self-analysis of the team members to improve their efficiency. Otherwise, without achieving the small milestones listed in the tracker, the team will be left with a 'to be completed' list. Each milestone achieved according to the tracker gives immense confidence to an individual, team and the project manager, that 'we are on track' and 'we will do it'. This takes a lot of stress away from a CRO.

For discipline and efficient project management, it is imperative to have standards, processes and guidelines in place. Without such tools, there is always a risk that the project will go in a wrong direction. The responsibilities should be well defined, and the person bearing a particular responsibility should know the need of following a particular process (after all, s/he cannot do it every time just because the boss has asked it to be done in that manner). However, sometimes, it is also possible that not all

Medical writing in a CRO: The challenges and solutions

- > the defined processes need to be followed in a particular project. To do something just because 'it is defined in the process' is not the right approach. Processes should always be project-specific, as these reduce time taken to complete the particular project with improved efficiency. Furthermore, it allows the stakeholders to swiftly respond to challenges, if any.

Another factor contributing to a successful client-CRO relationship is the 'team'. Clients look for the best team management practices followed in a CRO. Sometimes a project needs different cross-functional teams to come together for a solution. A team-oriented environment contributes towards the overall accomplishment of a project. The most common conflicts occur due to lack of leadership, lack of individual productivity and due to some members' 'only me' approach. The team(s) must be trained to understand that the effort and contribution of each individual is important but the efficient functioning of the individuals as a coherent, productive team is even more important. As a rule, conflicts within the team or between two teams within the organisation should not be played out in front of the client, and the team leaders should work to understand the cause of any conflict and to resolve it before it becomes a major issue. Conflicts can also have a positive effect in a project and may increase the efficiency of the team members, but only if they are discussed with the right attitude.

Warning! Haven't you trained the team?

Most projects get into trouble at some point of time. There are some measures that always need to be followed, so that we are able to save the projects from running into trouble, and in turn from souring the relationship of the organisation with a client. The whole team should be trained to predict failures before they actually occur, so that everybody in the team is able to raise the flag against the expected failure. The team also needs to learn that once a warning sign has been observed, measures need to be taken to determine what could be done to prevent failure and lessen consequences.

The training for predicting failures requires a proactive approach and participation of the whole writing team. The first thing is to make a project plan, and then there should be a brain-storming session on where things may go wrong. It is better to have a compilation of such issues (for ease of use in future projects), their probability and potential impact and actions that can be taken to mitigate such risks. Once prepared, this list should be followed in a stringent manner, and if any risk is identified, the action items must not be overlooked. The team must be accustomed to following this, and because the risks in the process will be dependent on each other, the chances of skipping any of the steps should be minimised.

The first sign of trouble is to see the team working for long hours *ad infinitum*. This might occur due to insufficient communication and an inadequate understanding of the objectives by the team members. The project manager needs to be in constant touch with the team to understand any consequences that may lead to working longer hours. Priority

should be given to resolving this because of its possible impact on the motivation of the team in future projects.

A second risk factor is the availability of items to be delivered by the client. In a medical writing project, one of the most important components that drive the project is receiving source documents from the client in time. If this does not happen, the project may get stuck at any stage. No two projects are the same and thus there should be a separate checklist for essentially required documents of every project. The team must be trained to follow the checklist for every project systematically, so that nothing is missed out and if something is missing, it can be requested from the client in time. Similarly, writing immediately without going through the source documents thoroughly may again have a negative impact on the project in hand. Discrepancies can be often seen in some tables/graphs and written data received from the client. We should not wait until the last date to inform the client of such things if they can be addressed to and clarified by the client in a timely manner.

It is equally important to train the team to learn the significance of quality checking, peer review and scientific reviews of documents. The project plan must allow an ample amount of time for these reviews. The custodians of various sections of a document must be trained to follow the tracker as per the plan. Sometimes due to apprehension within the team, some writers find these processes offensive, but the team must be educated to understand that these reviews are intended to make a document meet scientific standards and should always be constructive in nature. The team should be motivated to share their experiences and learning. Such interactions can concern scientific, technical, regulatory or operational aspects of the project. Shared learning is always helpful as people easily understand the importance of various processes; it is fun learning things together, and in turn such an activity builds a successful and intact team.

Despite all the challenges and stress, the experience gained and immense satisfaction earned after producing quality documents lessen all the pains and anxiety experienced during the execution of a project. Positive feedback on work from the client makes our day, and we start a new day with the same zeal and enthusiasm with which we worked on our first independent assignment. Recognising that 'what we produce is quality' is an important factor in helping us to receive and accept the words of thanks and appreciation confidently.....

Acknowledgements

I am thankful to Dr. Rajesh Kher, Associate Director and Head (Medical Writing and Pharmacovigilance), GVK Biosciences, who introduced me to the world of Medical Writing and whose valuable inputs helped me complete this article.

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Communicating the value of a drug: Developing a global value dossier

by Catherine E Rycroft

Introduction

A global value dossier (GVD) is a tool developed by a pharmaceutical company to communicate the value of a drug (i.e. the Value Story). It is primarily used internally, although may also serve as the basis of reimbursement submission dossiers for health technology assessment (HTA) bodies such as the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom, although it is not directly transferable to such dossiers.

The GVD summarises the burden of the disease of interest, highlights the unmet needs, then expresses the value of the drug in meeting those needs. The Value Story consists of a series of Value Messages, each supported by concise and scientifically accurate evidence. Development of these Value Messages is central to the preparation of a GVD. Table 1 presents some hypothetical Value Messages in their early and refined forms.

Table 1. Refinement of Value Messages

Original Value Message	Refined Value Message
Ask "So What?"	
Miracle Drug is a humanised monoclonal antibody produced by recombinant DNA technology, directed to an epitope in the B antigenic site of the J protein of antibody sequences.	Because of its site-specific targeting mechanism, Miracle Drug suppresses the viral infection 10 times faster than Older Drug.
Check the evidence	
Serious disease affects many people.	Serious disease affects elderly women, the fastest growing population segment in the world.
Make it simple	
<ul style="list-style-type: none"> Patients prefer the once-weekly dosing of Miracle Drug over the twice-daily dosing of Older Drug. Patients prefer the flavour of Miracle Drug over that of Older Drug. Patients prefer the size of the Miracle Drug tablet over the size of the Older Drug tablet. 	Patients prefer Miracle Drug over Older Drug.
Due to its life-saving properties, Miracle Drug reduces the number of fatal experiences, resulting in a 49.7% decrease in mortality ($P < 0.001$) because of Serious Disease and its complications.	Miracle Drug saves lives.

Structure of a GVD

A GVD typically consists of an introductory section, the Problem section (burden of disease) and the Solution section (product value), as follows:

Introduction:

- Purpose/how to use GVD
- Requirements for review before dissemination of GVD
- Contact information for internal contact point (usually internal GVD lead)

The Problem (burden of disease) section:

- Disease background
- Epidemiology (including prevalence/incidence; mortality; and comorbidities)
- Economic burden (cost of illness)
- Humanistic burden [health-related quality of life (HRQoL), functional status, symptoms, etc.]
- Unmet treatment need (competitive differentiation) with current therapies

The Solution (product value) section:

- Clinical value (efficacy/effectiveness; safety/tolerability)
- Patient-reported outcomes/QoL value (HRQoL; functional status; compliance; patient satisfaction; patient preference; and caregiver burden)
- Economic value (cost-effectiveness; budget impact; associated decrease in health care resource utilisation)

In addition, the GVD will often contain country-specific sections to enable adaptation for different markets, particularly in relation to the following:

- Epidemiology
- Economic and HRQoL burden
- Country-specific clinical considerations, including key comparators
- Country-specific economic considerations, including reference drugs
- Country-specific Value Message considerations (e.g., value may vary by country related to differences in comparators, treatment guidelines, and physician awareness of adverse events)

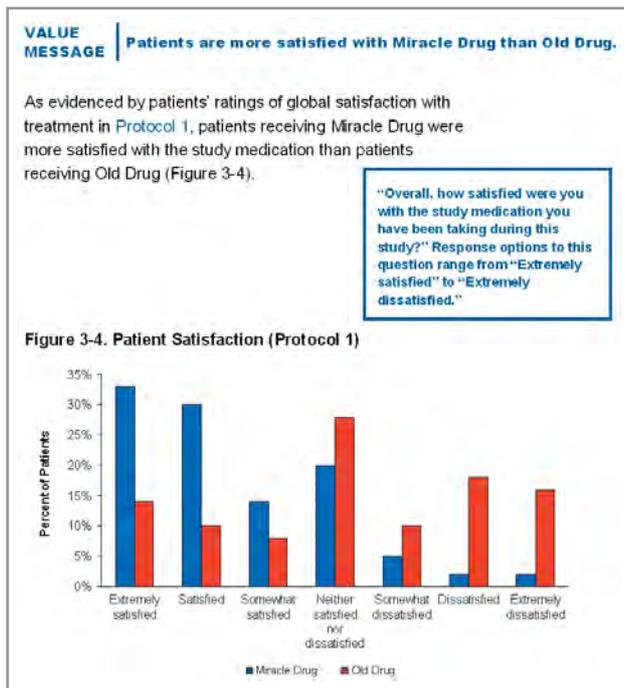
An example page from a GVD for "Miracle Drug" is shown in Figure 1 on next page.

Development process for a GVD

Several stakeholders are involved in the preparation of a GVD, including the internal team at the pharmaceutical company and several external contributors. The internal team will usually include representatives from clinical development, pricing and reimbursement, regulatory affairs, marketing, health economics, and local affiliates. External contributors may include key opinion leaders, local >

Communicating the value of a drug: Developing a global value dossier

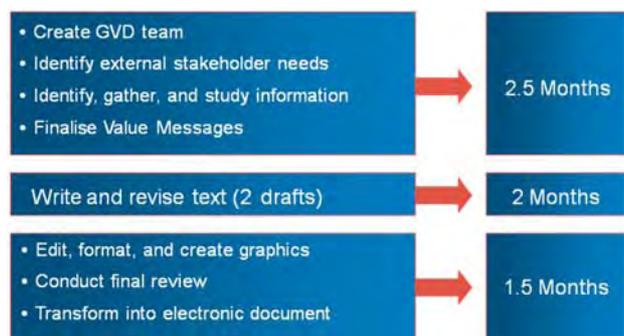
➤ **Figure 1** Sample Page from a GVD for Miracle Drug from the Product Value Section



consultants in pricing with whom Value Messages can be tested, and reimbursement, and external vendors (such as RTI Health Solutions).

The timescale for development of a GVD is approximately 6-7 months and generally begins during late phase 2 or early phase 3 drug development (Figure 2).

Figure 2 Timescale for Developing a GVD



The Problem (disease burden) section can be created quite early in the process using peer-reviewed literature, and authoritative national/international sources such as professional organisations and federally sponsored research organisations. The Solution (product value) section will be based on the outcomes of the sponsored studies. The credibility of the GVD will be increased if the sponsored studies are already published so an early start is advisable. A literature search will also identify any independent studies, which may provide further support for the product, or conversely, it may highlight any negative data for the product, that will need to be evaluated and contextualised.

Key data sources required to inform the development of a GVD include: clinical trials, observational studies, expert opinion, product inserts and monographs, market research reports, published literature, and unpublished data on file.

Benefits of a GVD

There are several benefits in developing a GVD for a product. The development process focuses the team's attention on the Value Story and Value Messages associated with the product, driving refinement of the Value Messages, and building a consensus for the global product strategy. The development process will also highlight any gaps in the evidence base, which will need to be addressed with further research, as well as highlighting any existing conflicting or counter-evidence, and helping to identify and prioritise the outcomes research plan.

Additionally, there are several benefits of the GVD itself. The GVD acts as a central repository for the most current Value Messages and the best available evidence for the product. This enables the dissemination of strategic guidance and a consistent Value Story and approach to local pricing and reimbursement activities across many countries. The GVD also presents a summary of the cost-effectiveness and budget-impact analyses in a manner that is accessible for all team members. The GVD supports the work of local affiliates, by means of supplemental tools such as presentations of anticipated frequently asked questions by payers, and prepared responses (known as Objection Handlers). Finally, the GVD may also serve as a basis for development of country-specific submissions, such as for NICE, although it will not be directly transferable.

Tips for Success!

The key factors involved in ensuring the preparation of a high-quality GVD in line with the product timelines, are as follows:

- Start to prepare early, preferably in late phase 2 of drug development, with finalisation of the GVD after the phase 3 data is available
- Develop at least two drafts of the GVD before finalisation
- Obtain feedback from local affiliates and other internal stakeholders
- When the GVD is issued to affiliates, training is advisable to provide a summary of the contents of the GVD, and an overview of how to use it
- The GVD should also be regularly updated in order to maintain its relevance

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List of medical writing articles written by EMWA members in other journals

The following is a list of articles relevant to medical writing published by EMWA members in journals other than *The Write Stuff*. It is an update of a list published in *The Write Stuff* in June 2009 (*TWS* 2009;18(2):146. Names of EMWA members are printed in bold. The list is also available on the EMWA website (www.emwa.org). Members are requested to send citations to their articles for publication in future issues of *TWS*. These citations will also be added to the list retained on the EMWA website.

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Tense matters: The preterite and present perfect in scientific texts (3)

by Alistair Reeves

In the first two articles in this series, I looked at basic differences between the preterite and present perfect, the strict division between the two tenses, the use of the preterite and present perfect in the active and passive voices, and overlap between the two tenses [1, 2]. In this third and last article, I shall be looking at the use of the preterite and present perfect for repeated actions, to herald disagreement, limitation or qualification, when writing up to a cut-off point, as continuous tenses, and how to express in writing stress on the auxiliary verb when speaking (e.g. *We have done this, but ...*).

E. Preterite and present perfect with repeated actions

8 The present perfect is used when referring to repeated actions in the past, even if the actions had a definite end and no more are planned.

[20a] *We have repeatedly examined this question.*

[20b] *Inadequate effects of drug X in horses have frequently been reported.*

Without further qualifiers, you are referring in [20a] and [20b] to any time in the past up to the time of writing. If you write [20a], the last time you examined the question would normally be fairly recent. What 'recent' means here depends on the context, of course. You might be referring to a long-term project over 15 years where a question was reconsidered every year and the last time was 1 year ago. Or it might be something that was assessed irregularly over the last 2 years, and the last time was 1 month ago or yesterday.

If a repeated activity took place within defined limits in the past, then the preterite is used as in [21a] and [21b]:

[21a] *We repeatedly examined this question in four studies conducted in the 1990s.*

[21b] *Inadequate effects of drug X in horses were frequently reported before the formulation was changed.*

F. Use of present perfect to herald disagreement, limitation or qualification

9 The present perfect is often used to herald disagreement with or limitation or qualification of a claim just made.

This is often achieved with or without linking words in the same or a subsequent clause:

[22a] *All studies so far have shown that Drug X is a potent inhibitor of enzyme Y. We were, however, unable to confirm this in the present study.*

[22b] *Although all studies so far have shown that Drug X is a potent inhibitor of enzyme Y, we were unable to confirm this in the present study.*

[22c] *All studies so far have shown that Drug X is a potent inhibitor of enzyme Y. Although we were able to confirm this in patients with Disease X, we did not observe this in healthy volunteers.*

[22d] *Anaphylactoid reactions have been reported in more than 5% of patients during the first infusion of Drug X. In our experience, this only occurs if the infusion is given too rapidly.*

[22e] *Some authors have reported that women are more likely to receive stronger analgesics. Others, however, report no preferential treatment based solely on gender.*

[22f] *While some authors have reported that women are more likely to receive stronger analgesics, others report no preferential treatment based solely on gender.*

In [22a] and [22e], after having read 'All ... have shown' and 'Some ... have reported', the reader is already subconsciously preempting a limitation or qualification that will often be expressed in a subsequent sentence. The limitation may come—or it may not—but the implication of the present perfect is that it is likely. It is frequently introduced with 'however', as in the subsequent sentence in both examples. In [22b] and [22f], the limitation has been made immediately explicit by the use of 'Although' and 'While' in the first clause in each case, and in [22c], the limitation comes immediately at the beginning of the subsequent sentence with 'Although', and in [22d] also in the second sentence with 'only'.

What is the effect of using the preterite instead of the present perfect in the above examples?

[23a] *All studies showed that Drug X is a potent inhibitor of enzyme Y.*

[23b] *Although all studies showed that Drug X is a potent inhibitor of enzyme Y ...*

[23c] *Some authors reported that women are more likely to receive stronger analgesics.*

[23d] *While some authors reported that women are more likely to receive stronger analgesics ...*

[23e] *Anaphylactoid reactions were reported in more than 5% of patients during the first infusion of Drug X.*

Tense matters...

Because there is no longer any implication of ‘up to the present’, [23a] and [23b] would have to be preceded by something for the word ‘all’ to refer back to. This would typically be a sentence describing a formal series of studies or studies conducted by different groups over an unspecified duration, such as *Drug X was investigated in five Phase II studies* or *Many authors have published reports on the effects of Drug X on enzymes Y and Z*. This would mean that the statement refers to actions finished in the past, and therefore the preterite is appropriate. [23a] could still be followed by the subsequent limiting sentence in [22a]. It is similar with [23c] and [23d]: a specific set of authors would have to have been mentioned in the previous sentence. [23e] is reporting on the incidence of adverse events over a defined period in the past, usually a study or series of studies.

G. Writing up to a cut-off point

10 Although the present and present perfect tenses may be appropriate for ‘Methods’ and ‘Results’ sections in interim reports, it is usually better to regard your cut-off point as a final endpoint in the past and use the preterite, as in a final report.

When writing up to a cut-off point, things are complicated by whether you regard the cut-off point as ‘now’ [24a]—even though it may be a few months before—or as a time-limiting point in the past [24b]:

[24a] Now: *7 patients (so far) have developed paraesthesia.*

[24b] Time-limiting point in the past: *(Up to the cut-off point), 7 patients developed paraesthesia.*

Some would argue that [24b] should read *Up to the cut-off point, 7 patients had developed paraesthesia*, using the past preterite, and this is certainly grammatically correct, because the paraesthesia developed before the cut-off, and the cut-off was already in the past. However, again to keep things simple, I usually prefer to regard the cut-off as a time-limiting ‘endpoint’ in the past and stick to the preterite in this situation, at least in the methods and results sections. In your introduction, summary or discussions, you might prefer to use the present perfect, which means that you cannot add the time-limiting statement ‘up to the cut-off point’. Also, if it is obvious that it is an interim report (and it should be), there is no need to keep repeating ‘up to the cut-off point’, because this is very wearing for the reader.

H. Use of the preterite continuous and present perfect continuous

11 The continuous forms of both tenses are frequently used with adverbials that indicate whether the activity was continuous or intermittent, if this important.

The present perfect continuous and preterite continuous are almost always qualified by some sort of time phrase indicating *duration* of the activity up to the present—and *not*

location of the activity as an event in the past (as we know from the first article in this series, the present perfect does not permit a time-limiting element in the past).

[25a] *We have been monitoring expenditure for about 10 years.*

[25b] *We have monitored expenditure for about 10 years.*

[25a] can mean two things: (i) you have been monitoring expenditure without interruption up to the present and are still monitoring it, or (ii) you have intermittently (regularly or irregularly) monitored it up to the present, and your last investigation might be some time ago. This is similar to the use of the present perfect for repeated activities. In both cases, your next sentence could say that you have decided to stop or continue, or report on what you have found. Despite the use of the present perfect *continuous* for [25a], when we compare the implications of [25a] and [25b], we see that they can both have these two meanings, but that [25b] more strongly suggests that the activity was continuous (in the sense that it was *not considered* intermittent) and is more likely to mean that the activity is now finished. It depends on the nature of the activity, of course: e.g. *I have been brushing my teeth with fluoride toothpaste for the past 10 years* is unlikely to be continuous in the sense of uninterrupted. *I have been shaking this tube for about 5 minutes and substance X has still not dissolved* would, however, be very unlikely to mean that you had shaken the tube intermittently for 5 minutes; it could, but it is unlikely. Often it is not important whether the activity was truly uninterrupted or intermittent, and if it is important, this is usually made clear by the use of adverbs or adverbial phrases. For example, you could add the adverb *periodically* to [25a] and [25b] to clarify that the activity was intermittent but was regarded as continuous. When speaking, you might add a more informal adverbial, e.g. *on and off*, to indicate this.

The preterite continuous sounds strange if combined with time phrases indicating *duration* of an activity:

[25c] *We were monitoring expenditure for about 10 years.*

There is an exception to this—a special, informal use of the preterite continuous to indicate intention, e.g. *We were (originally) staying for 2 weeks, but the first week was so wet, we decided to go home early* (a common formulation is also: *We were (originally) going to stay ...*). The speaker here will normally stress the word *were* or will often add the word *originally* before *staying* and stress *originally* instead of *were*. This is a colloquial way of saying *We intended to stay for ...*, and is not suitable for formal writing.

The preterite continuous is often used with time phrases that indicate *when* in the past a continuous activity was being conducted, often combined with information on a single event that occurred while the continuous activity was ongoing.

Tense matters...

- > [25d] *We were monitoring expenditure at that time/between June and December 2006/before introduction of the euro and discovered that Group A was spending far too much.*

In [25d], the preterite continuous has exactly the same function as the imperfect in French and other languages, describing an event that occurred using the preterite while another activity was ongoing using the preterite continuous.

The differences between the preterite and present perfect and their continuous forms are complex. The continuous forms are more often used when speaking, when it is easy to indicate and shift stress by intonation, and to qualify meaning with informal phrases. This means that the continuous forms of these tenses are not used frequently in regulatory writing, and are usually restricted to introductory and discussion sections of documents. They are used more widely in publications and in the area of medical communications, and are often combined with adverbs and adverbial phrases to make their meaning more precise.

1. Reflecting stress on the spoken auxiliary verb when writing

12 Stressing the auxiliary verb is a spoken device used to herald disagreement with or limitation or confirmation of a claim just made.

If you are involved in a discussion and one of the speakers says:

[26a] *Yes, we **have** examined this ...* (present perfect with stress on the auxiliary verb), or

[26b] *Yes, we **did** examine this ...* (using 'did' is the way to make the preterite emphatic)

they will almost always immediately follow this with 'but ...' to limit or 'and ...' to confirm. So this use is like Point F above, but also includes the idea of confirmation. However, this spoken device is difficult to render when writing and is usually only required when reporting on things people have said, often in discussions or proceedings, as in [27a].

[27a] *Live conversation at a congress discussion:*

Speaker 1: We had several patients with interstitial lung disease. I don't think you've examined this yet.

Speaker 2: *Yes, we **have** examined this, but the data are still being evaluated/and we have also seen cases.*

[27b] *Report prepared afterwards:*

Speaker 1 commented that she had seen several patients with interstitial lung disease and that she thought that Speaker 2 had not yet examined this in his patients. Speaker 2 said that his group had indeed examined this, but that the data were still under evaluation/and that they had also seen cases.

In [27b], the stress was rendered by adding the word 'indeed'. Other confirmatory adverbials may be appropriate,

e.g. *definitely* or *certainly*, but this obviously has to be suited to context. Sometimes the verb 'to stress' or 'to confirm' can be used: *Speaker 2 stressed/confirmed that his group had examined this ...*

Summary of aspects of use of the preterite and present perfect in scientific texts covered in this series:

1. The preterite does not permit time elements in a sentence that extend to the present or into the future.
2. The present perfect does not permit time-limiting elements in the past in a sentence.
3. Context determines whether the preterite or present perfect is appropriate with other limiting factors.
4. The preterite is the appropriate tense for reporting on methods in the 'Methods' section of a document.
5. The preterite is the appropriate tense for reporting on results in the 'Results' section of a document.
6. The basic differences between the preterite and present perfect are the same whether the active or passive voice is used.
7. Unlike 'Methods' and 'Results' sections, those that introduce, discuss or comment make use of the full range of tenses, and context determines whether the preterite or present perfect is appropriate.
8. The present perfect is used when referring to repeated actions in the past, even if the actions had a definite end and no more are planned.
9. The present perfect is often used to herald disagreement with or limitation or qualification of a claim just made.
10. Although the present and present perfect tenses may be appropriate for 'Methods' and 'Results' sections in interim reports, it is usually better to regard your cut-off point as an endpoint in the past and use the preterite, as in a final report.
11. The continuous forms of both tenses are frequently used with modifying adverbials that indicate whether the activity was continuous or intermittent, if this is important.
12. Stressing the auxiliary verb is primarily a spoken device used to herald disagreement with or limitation, qualification or confirmation of a claim, and is often rendered in writing using a confirmatory adverbial or a verb including an idea of confirmation.

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Some comments on the 'Compilation of QRD decisions on stylistic matters in product information' from the EMA

by Alistair Reeves

The URL <http://www.ema.europa.eu/htms/human/qrd/docs/stylisticmatters.pdf> conceals a useful document for those involved in the preparation and translation of product information in the EU and associated countries. It contains the European Medicines Agency's (EMA) advice on 'stylistic matters' (and other matters) in the form of detailed Quality Review of Documents (QRD) suggestions—unfortunately only suggestions. I wish they were requirements, because suggestions always leave room for interpretation and discussion, and several of the issues should just be regulated to avoid time-wasting discussions.

Those responsible at the EMA might like to consider these comments when issuing a new version. The valid version is Version 11 from 2008. It covers 22 points. The last point simply provides translations in all languages for the term 'perforated unit dose blisters'. 8 of the remaining 21 issues are not style issues and do not belong in this list, important as they are, i.e. caution with dietary recommendations, inclusion of general health information, use of combined printed package leaflets for different dosage forms and strengths, various issues surrounding the use of trade names and INNs, and how to express strengths for single- and multi-dose preparations.

That leaves us with 13 issues, all of which give sound advice that could be improved in some cases. For each point, I have summarised the EMA advice in normal typeface. My comments are in italics. The main message from the EMA is that they want consistency.

Three of the points are concerned with abbreviations and acronyms.

Abbreviations and acronyms

Avoid non-standard abbreviations. If you can't, all abbreviations and acronyms are to be explained at first mention.

Fine. But what does 'non-standard' mean? And how about some guidance on whether units of measurement should be included and whether a brief list of abbreviations must be supplied with each product information document.

Subscript and superscript are sometimes used inconsistently (sometimes! Here the EMA is being kind).

You could not give more sound advice. Almost all abbreviated units have a 'standard' form, and if they don't, a definition should be given in each document. C_{max} and m^2 are not written as they are for fun—it is because they follow universal conventions that help the reader understand what they are reading.

For abbreviations of antiretrovirals, some countries require the full term and abbreviation in the national lan-

guage and other are happy with the full term in the national language and the English abbreviation.

See the above URL for details. The suggestion seems rather complex to me, but I do not have much experience with antiretrovirals, which may explain this.

Use of 'should'

You must not use 'should' when you mean 'must'. You must say 'must' or use a 'to be' formulation, e.g. NOT 'X should be taken with food' BUT 'X must be taken with food' or 'X is to be taken with food'. Not only is this clearer in English, but it also makes translation much easier.

Sound advice—and must also be observed for study protocols.

Consistency

Once a particular style or house style has been selected it must be used consistently throughout the text.

A principle we must always observe in any document, not just product information documentation.

It would be worth clarifying here that this means (I hope) within one self-contained text, i.e. a single package leaflet, and not across an entire dossier or variation. It would also be useful if the EMA would confirm that text with American English spelling (house style) and safety tables with British English spelling (because the British English version of MedDRA was what the company bought), or vice versa, are acceptable. I have had to change spelling in tables several times because of this, and this is really an absolute money and time waster. Not really an issue for product information, but if this were answered somewhere by the EMA, it would also banish a lot of uncertainty and avoid much discussion.

Foreign terms

Foreign terms must be written in Italics; e.g. *in vivo*, *in vitro*, *Helicobacter pylori*.

What is a foreign term? Pancreas? Duodenum? Scenario? Angst? Déjà-vu? And what purpose do the italics serve? Organism names are not foreign terms, they are names that are italicised according to the best observed universal linguistic convention I know, and even if you were writing a text in Latin you would italicise them. It is an absolute time waster checking that 'foreign' terms are italicised, and italicisation does not contribute to comprehension at all. American journals jettisoned italicisation of this sort years ago (except for organism names) [1], and it is increasingly the case in British journals. I think the EMA should revise their 'suggestion' for this one and decree that italicisation is definitely passé ('passé' here is written in italics only because all of my comments are in italics). >

Some comments on the Compilation of QRD decisions...

- > A salutary side effect of this would be that this suggestion from the EMA would no longer contain the strange capitalisation of 'Italic', nor would we have to puzzle over the meaning of the unusually placed semicolon before 'e.g.'.

Gender

"He/she" should be used if no other neutral gender locution is possible. Patients can be referred to as "he" or as "she" when the medicinal product is exclusively for use by males or females.

In 99% of cases, it is possible to avoid this in English—so the use of he/she and lookalikes (e.g. s/he) should be the absolute exception. Use the plural where you can and don't worry about using 'they' as a pronoun for a singular subject. We do it all the time when we speak, and it is increasingly gaining acceptance when writing. The second sentence of the EMA text is common sense. But sometimes we—and I am no exception—need reminding about common sense. But I have to say, I'd much rather see 'men or women' rather than 'males or females' [2].

Imperial measures

Include these only in English texts and only if elderly patients might use the products.

Who can disagree with that? The sooner we get rid of imperial measures, their US American variants, a.m. and p.m., and Fahrenheit, the better!

Number separators

The appropriate decimal (. or ,) and 'thousands' (. or , or other) separators for each country are listed.

This is a bore but is very important. As hard as authors from countries that use a comma as a decimal separator may try to use the decimal point in English, one or two usually slip through in publications I edit. Tables in product information documents, for example, are often just copied in from the original with commas for decimals and dots for thousand separators. Searching 'anydigit'-comma-'anydigit' and 'anydigit'-full stop-'anydigit' using 'search and replace' should be a last step when working on any document you write or edit, and not just product information—and, as ever, do not 'replace all'.

Strength of normal saline

Reference in SPC, package leaflets: 'sodium chloride 9mg/ml (0.9%) solution for injection'

Label for the vial of solvent: 'sodium chloride 9 mg/ml <solution for> injection'.

Clear instructions. Great.

Four of the points are concerned with units.

General format

Preferred style is 'figure-nonbreaking space-unit'.

A nonbreaking space is achieved by pressing <CTRL + shift + spacebar> and is shown as a degree sign if you have this sort of symbol switched on in Word (under Options, View, turn 'spaces' on). A nonbreaking space is necessary to avoid the unit being split off onto the next line. Also a clear instruction from the EMA, which is great, and I have always agreed with this one—but what about the huge number of people who think that there should be no space? I recently trained a bunch of British mechanical

engineers working on medical devices, and was shouted down when I said that there should be a space. Apparently, a space is not used in the engineering world (confirmed by my son and father, who are both engineers). I suspect that your drug or device application will not be turned down if you do not leave a space. Not leaving a space has the positive spin-off that you don't have to bother with a nonbreaking space. I am beginning to wonder why I have always been a proponent of the space ... but I just think it looks better. Whatever—leave a nonbreaking space and the EMA will be happy!

The EMA also want a space between '>' and '<' and the number following them.

I suppose this also extends to '=' and '±'. Nonbreaking spaces should also be used.

Degrees of temperature

° and C have no space between them but you may write either 10°C or 10 °C.

I disagree. Giving choices is bad as it leads to fruitless discussions. I would rather see: use only 10°C (or F).

Standard abbreviation for litre

When abbreviated, litre must always be written lower case.

It has been interesting to watch how the upper case L has gradually replaced the lower case l for litre over the past 5-10 years. And I actually think it is a good thing [3]. The EMA is fighting a losing battle here and should either decide to say 'Either is OK as long as you are consistent in one document' or capitulate fully and say 'Use L'. In serif fonts like the Times group, the l (ell) is almost identical to the 1 (one), and for this reason, I think the advent of 'L' for litre is a good thing: which do you prefer, 1.0 l or 1.0 L? If you don't use a space before the unit, this is definitely confusing.

Use of microgram

Micrograms should always be spelled out for safety reasons. If there are no safety concerns, the accepted abbreviation 'µg' may be used. 'µg' may be used throughout the SmPC, except for the name of the medicinal product in Section 1 to ensure consistency with the name on the label and the package leaflet.

Sounds like good advice to me. The EMA also says "there may be Member-States where this abbreviation is not used". These states may use 'mcg', so that should be borne in mind. (Oh, and by the way, member states does not need to be capitalised, nor does it need a hyphen!)

All in all, good, time-saving advice for those preparing (not only) product information—and it would be even better with some refinement.

Alistair Reeves

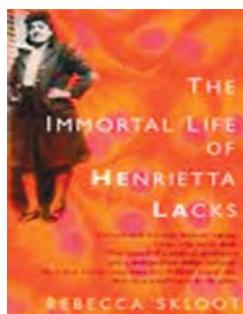
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In the bookstores ... ■

The story of the world's most successful cells...and more



Rebecca Skloot. *The Immortal Life of Henrietta Lacks*. Macmillan, 2010. ISBN 978-0230750210. 13.99 GBP. Pages 384.

Rebecca Skloot's *The Immortal Life of Henrietta Lacks* is the product of the science writer 20-year obsession with the woman whose cervical cancer cells became HeLa, the first successful

cell culture line and one of the most commonly used. Her book chronicles both the lives of the African-American farm worker and the family left behind by her early death from aggressive cervical cancer and the author's story of writing the book. Skloot uses the parallel narrative structure characteristic of creative nonfiction to tell the public story of Henrietta and her cells and the private story of the author and Henrietta's family. In Skloot's words, "It's not only the story of HeLa cells and Henrietta Lacks, but of Henrietta's family...and their lifelong struggle to make peace with the existence of those cells, and the science that made them possible."

Henrietta Lacks presented at Johns Hopkins Hospital in 1951 with a lump on her uterus and blood in her urine. Her cervical cancer was treated with the standard treatment of the day, tubes of radium sewn inside her cervix, but she died in great pain within a few months. Just prior to her treatment and at autopsy, samples of her cancer cells were taken and sent to George Gey's cell culture laboratory. Gey and his team had been trying for 3 decades to grow cells outside the body, hoping to find the cause of cancer and its cure. Cervical cancer cells were of particular interest to his colleague Richard Wesley TeLinde, who wanted them for experiments to prove his then radical assertion that cervical carcinoma in situ is a precursor to invasive carcinoma and should be treated to prevent the more serious disease. Within 3 weeks Gey appeared on television announcing, "Tonight we will learn why scientists believe that cancer can be conquered" and demonstrating the success of the HeLa cell line. Gey supplied the cells to researchers all over the world, and a facility was set up at Tuskegee Institute to manufacture the huge amount of cell culture required to produce and evaluate Jonas Salk's groundbreaking polio vaccine. HeLa went on to dominate the biomedical world, both metaphorically through its ubiquitous use in research and literally through its widespread contamination of other cell culture lines. Skloot estimates that 60,000 scientific articles have been published about research done with HeLa—a number that increases by 300 a month—and that HeLa contamination causes several million dollars of damage a year. Henrietta's widower and four surviving children were not aware of the use of their wife and mother's cells and her "immortality" until 1973

when Henrietta's daughter-in-law found out about HeLa from a neighbour's relative and the family were contacted by Hopkins researchers requesting blood samples. Since then the family have tried to make sense of what HeLa means to and for them while they have also struggled with issues of poverty, poor education, and ill health.

Moving back and forth in time over a period from the 1920s to the present, Skloot uses the story of Henrietta Lacks and HeLa as a framework for pursuing many interesting themes, among them African-American social history, ethics of biomedical research, public understanding of science, and the current American health care system. Henrietta and her family were part of the Great Migration, the mid-twentieth-century movement of African-Americans from the farms of the southern United States to the factories and ghettos of the North. In their black steel-worker neighbourhood, stories of the "night doctors" who stole children for medical experimentation at Hopkins had been common for generations. Although these tales may seem bizarre in the context of the philanthropy of the Quaker entrepreneur and abolitionist Johns Hopkins, who endowed a hospital specifically charged with treating the poor of Baltimore regardless of race as well as a school to educate orphaned black children, they do graphically demonstrate the very real legacy of segregated medical care and of the appalling ethics of medical treatment and research in twentieth century America. These two phenomena are brutally exemplified in the chapter recounting a visit by the author and Henrietta's younger daughter Deborah to a mental hospital (formerly called The Hospital for the Negro Insane) to learn about the death of Henrietta's older daughter Elsie.

Skloot also describes the abuses of medical research performed using HeLa cells in the 1950s and 1960s, including research on prisoners and the withholding of information that the test product being administered to patients awaiting gynaecological surgery was in fact cancer cells. Revelation of these practices by Jewish doctors horrified by the parallels they perceived between Nazi research and the instruction they had received to give injections of HeLa to uninformed patients resulted in new rules set by the US National Institutes of Health for independent ethical review and informed consent. The new rules challenged researchers; one of them wrote to the editor of *Science*, "When we are prevented from attempting seemingly innocuous studies of cancer behavior in humans...we may mark 1966 as the year in which all medical progress ceased."

Skloot's private narrative is an effective tool for contrasting Henrietta's family's understanding of the HeLa cells with that of the scientists and doctors in the book. One of the most thought-provoking episodes she relates is a visit with two of Henrietta's children to a Hopkins cancer researcher who carefully explains to them what DNA and cells are and shows them HeLa cells dividing under a microscope. He patiently answers all their questions such as

In the bookstores ...

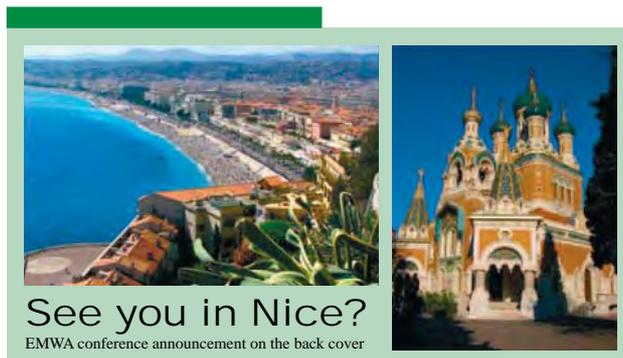
- > “If those our mother’s cells, how come they ain’t black even though she was black” and dispels some of Deborah’s misapprehensions; she had been afraid that normal, noncancerous cells from her mother are still living and that she has directly inherited her mother’s cancer and the “the thing that made her cells grow forever.”

Despite the historical nature of the book, contemporary issues of equity and ethics in the American healthcare system are never far out of the picture. Henrietta’s poor descendants have no health insurance and thus little access to the benefits that research using her cells created—with particularly dramatic effect at the book’s climax. As advances in medical care over the last 60 years may not have materially affected health outcomes for families like Henrietta’s, Skloot argues that the more rigorous ethical standards and regulation for biomedical research and use of human tissue in the same time period have not meaningfully changed the ethical outcomes for anyone. Cells taken from a patient’s body in blood samples or removed tissue can still be used for research and commercialized without consent from or compensation to the patient. Although the details she supplies are specific to the United States, recent revelations elsewhere—such as at Alder Hey Hospital in Liverpool—indicate this is unlikely to be a purely local phenomenon.

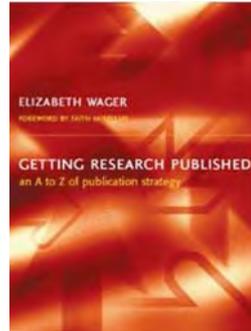
The devices of creative non-fiction Skloot uses deliver a compelling narrative along with fascinating social and scientific history, but the book does suffer from the heavy presence of the author in the story and her cloying self-congratulation on her ability to assimilate herself into Henrietta’s family. Prolonged descriptions of her challenges in getting them to talk to her, passages such as her description of her own reactions when a mental hospital official presents Elsie’s medical records to Deborah, and lines like “Oh my god...I did this to her” at a time of crisis in Deborah’s physical and mental health distract substantially from the successes of the book. Despite these authorial excesses, I recommend *The Immortal Life of Henrietta Lacks* heartily. As medical writers, we can never be reminded enough of the real people behind the research and of the people to whom its benefits are due.

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Another successful book on publishing research from Radcliffe Publishing



Elizabeth Wager. *Getting Research Published: An A to Z of Publication Strategy* (2nd edition). Radcliffe Publishing, 2010. ISBN 978-1846194085 (paperback) 25.00 GBP, 31.00 euro. Pages 191.

Radcliffe Publishing has a formula for their books and it is a successful one: find a top-notch expert on a topic, have them write a very well organised and to-the-point book, and then sell it at an affordable price. This time the author is Elizabeth Wager, who is a freelance publications consultant and developer of the Good Publication Practice, as well as chairperson of the Committee on Publication Ethics. The book is *Getting Research Published: An A to Z of Publication Strategy* (2nd edition), available in the paperback edition for about £25.

The book begins with four short chapters about the basics of publication strategy. This part of the book is a practical guide with directed information which is not weighed down by a lot of unfamiliar jargon. Important terms are written in bold type and are elaborated on in the following A-to-Z part of the book. This format makes it very easy to grasp the essential information. After reading the first chapters, I quickly understood the basics of a publication strategy, including what steps I need to follow, how to develop a plan, and how much time I might need to execute my plan. The fifth chapter is the very hilarious tale of Dr. Seymour and the disappearing paper, which is a tongue-in-cheek, albeit sadly realistic, story of how things can go wrong such that your paper never sees the light of day. The point is: have a strategy, develop a plan and stick to it so this doesn’t happen to you!

The A-to-Z part of the book is useful for anyone interested in publishing research, whether you have any interest in a publication strategy or not. In addition to explaining common terms like impact factors and open access journals, more elusive secret mystery knowledge information, typically known mostly to experienced insiders, is included. Two examples are the often confusing conventions of authorship order and the bold truth about vicious reviewers. After reading the A-to-Z section, I wished that I would have read this book before my first EMWA conference, then terms like STROBE, CONSORT, and the Vancouver group would have been more meaningful. Well, there is still time to pack the book in my suitcase for the next conference, *if* I can get it back from my colleagues!

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Phytotherapy—Regulatory peculiarities

by Karin Eichele

The regulatory process for herbal medicinal products has some peculiarities. In 2004, a EU Directive on licensing of traditional herbal medicinal products was introduced and provided a framework to harmonise the control of the quality and safety of herbal medicines in the EU (http://ec.europa.eu/health/files/eudralex/vol-1/dir_2004_24/dir_2004_24_en.pdf). Now, all herbal medicinal products will need to obtain a marketing authorisation. Three categories of applications with distinct requirements exist as outlined below:

Simplified registration procedure: The EU Directive introduced a simplified registration procedure for “Traditional Herbal Medicinal Products”. For these traditional registrations, it is necessary to demonstrate 30 years of use, including at least 15 years in the EU. The application must be supported by bibliographic references or expert reports on the safety of the product. In the label, it has to be clearly stated that the product has been approved on the basis of long-standing traditional use only.

Well-established use procedure: A well-established use application is another option for herbal medicinal products which have a history of medical use in the EU for at least 10 years. The documentation has to be submitted in the Common Technical Document (CTD) format and should cover all aspects of the safety and efficacy assessment. For this type of application, efficacy and safety requirements can be answered by reference to scientific literature (‘bibliographic dossier’). A well-established use application is only possible for the indication in which the respective product has already been used. Applications for entirely new therapeutic indications do not fall under this regulation. You will find a good article by Iain Colquhoun on this procedure in a previous issue of *The Write Stuff* (Vol. 18, No.1, 2009).

New application procedure: For new herbal medicinal products without adequate history of use in the EU, a complete clinical and preclinical development programme resulting in a full dossier in CTD format is required by the authorities.

Like all medicinal products for human use, herbal medicinal products have to be manufactured according to GMP. For all the above mentioned regulatory categories, full quality documentation is needed. Some special requirements for herbal medicinal products are specified in further guidance documents. One of the characteristic features of herbal medicinal products in a quality dossier is

the differentiation between ‘herbal substance’ which is the herbal drug (raw material) itself, and the ‘herbal preparation’, which is the active pharmaceutical ingredient prepared from the herbal drug. These characteristic features of herbals will be described in Module 3 of the CTD, as outlined in a separate section on herbals in Vol. 2B of the Notice for Applicants (http://ec.europa.eu/health/files/eudralex/vol-2/b/update_200805/ctd_05-2008_en.pdf).

The following links will cover some of the peculiar aspects of herbal medicinal products regulations:

<http://traditionalmedicines.info/EURegulatory.pdf>

This document summarises the requirements for traditional use registration in the EU.

<http://www.bfarm.de/cae/servlet/contentblob/1014546/publicationFile/66207/escopbonn2001.pdf>

This presentation from 2001 summarises the requirements of the well-established use procedure with respect to herbal medicinal products.

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000217.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac0580033a9e

Here you will find links to guidance documents related to quality, non-clinical data and clinical data specific for marketing authorisation applications for herbal medicinal products.

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000212.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac058003380a

For well-established use and traditional use applications, reference can be made to the community monographs. These monographs are established by the Committee on Herbal Medicinal Products (HMPC). From the clinical and non-clinical point of view, reference to a community monograph can be sufficient to obtain a marketing authorisation. This link gives you further information on the role and the development of these community monographs.

If you have any further questions on the regulatory process for herbals, or you have any other comments or suggestions, please e-mail me at: karin.eichele@bionorica.de.

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Journal watch



Science and the media, the importance of putting results into context, and a new register for systematic reviews

by Nancy Milligan

Bridging the communication divide between science and the media

The general public have a keen interest in science and technology particularly if it is related to their health. Given the numerous sources for healthcare-related information and news now available (for example, magazines, newspapers, television programming, and the internet), it is important that scientists and others involved in the biomedical field know how to communicate the latest research findings to the media. The authors of a recently published editorial in the *Journal of Translational Medicine* suggest that it can be difficult for scientists to get information about their research across in the media for two main reasons, firstly because the format of much of today's news coverage does not allow detailed reporting of study results and secondly because of the media's and the general public's limited understanding of scientific terminology [1]. They argue that it is important for scientists and journalists to bridge this communication divide that exists between them, and in doing so scientists will not only be able to help educate and guide the public in their medical decisions but also benefit themselves through greater awareness of their work which can help to increase funding and potentially enhance career opportunities.

The authors go on to offer practical tips for scientists to keep in mind when working with the media: (1) know who you are dealing with; reporters and editors are looking for stories that their readers or viewers will find interesting; therefore, you should be able to explain quickly to a journalist the main results of your research, why it is interesting and exciting, and why people should know about it; (2) communicate simply and clearly, e.g. start with a well-written executive summary to outline the key findings, organise the content using informative headings and sub-headings to ease understanding, and use 'plain language' such as writing in short, clear sentences with common every day words rather than complex scientific jargon; and (3) build relationships with key reporters covering your field in the media.

Putting research results into context

In a comment in the July 3rd issue of *The Lancet*, the editors have requested that authors of all research reports submitted to the journal from August 1st 2010 include a panel in the discussion section of the report putting their work into context of what has gone before [2]. Previously (July 2005), *The Lancet* required that submitted papers included

a clear summary of reported research findings and an explanation of how the trial's results affected this summary [3]. They also suggested that the relationship between existing and new evidence was referenced to a published systematic review or meta-analysis of the subject. However, subsequent monitoring of the five main high-impact journals (*Annals of Internal Medicine*, *British Medical Journal*, *Journal of the American Medical Association*, *The Lancet*, and *The New England Journal of Medicine*) found that only one in 24 reports that were not first trials placed the results in the context of an updated systematic review in the discussion [4]. This is important as authors need to express what their research adds to other work and therefore what this means for patients and clinical practice. *The Lancet* suggest that a panel in the discussion section would help to summarise the totality of evidence (for example, 'authors should outline how they searched for previous evidence and assessed its quality and what their findings add to previous work') and to put their results into context (for example, 'authors should either report their own, up-to-date systematic review or cite a recent systematic review of other trials'). They suggest a systematic review (but not necessarily a formal meta-analysis) is the key component of putting research into context. This all sounds like a good idea, as seeing research results in context will make it easier for people to judge the value of the study; however, if no recent systematic review is available and authors are expected to carry out their own systematic review to include, this could add substantial time and costs onto publishing a study.

New register of ongoing systematic reviews

Well conducted systematic reviews are widely seen as the best quality evidence to inform policy and clinical practice; however, as with primary research, there are concerns about publication bias and selective outcome reporting associated with systematic reviews. In response to these concerns, the Centre for Reviews and Dissemination (CRD), with the help of their Register Advisory Group, are developing an international register for ongoing systematic reviews with health-related outcomes [5, 6]. The web-based register, to be launched later this year, will be similar to clinical trials registers, prospectively recording key features of systematic reviews, and 'will offer free public access, be electronically searchable, and open to all prospective registrants'. Registration will require the provision of

a minimum data set, and once accepted the protocol can be uploaded on the database, a unique permanent identification number issued, and an audit trail for amendments to the protocol and updates will be available.

According to the CRD website, their intention is 'to promote transparency and discourage discrepancy between what is planned in a systematic review and the results that are ultimately reported. Quoting the unique registration number in all manuscripts should help avoid duplication of publications and aid the peer review process: manuscript details can be compared to the permanent registration record including an audit trail of subsequent amendments. This should reduce the likelihood of reporting biases and improve reliability of the evidence upon which decisions and patient care are based. The register will also form a valuable tool for commissioners enabling them to avoid funding duplicate reviews'.

A Delphi consultation exercise has been launched in order to gain the opinions of journal editors and international experts in systematic reviews and guideline development in order to agree on a minimum data set for registration. For further information go to www.york.ac.uk/inst/crd/projects/register.htm or contact Alison Booth at crd-register@york.ac.uk

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See you in Berlin?

EMWA conference announcement on page 200.



You never know what is round the next corner ...

A sign in the garden of the magnificent Gulbenkian collection in Lisbon.

We decided to turn left (...) to see what further delights awaited us after visiting the exhibition!

Alistair Reeves

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Big country health spenders

The OECD has recently released data showing that healthcare spending has increased from an average of 12% of total government spending in 1990 to an average of 16% in 2008. As a percent of their GDP the US, Switzerland, France and Germany are the biggest spenders on health with Britain spending almost half that of the US in relation to its GDP.

Source:http://www.economist.com/node/16473122?story_id=16473122&fsrc=nwl

Out on our own

Out on our own

After a swathe of different contributions in the last issue, we are down to one article in this issue—an amendment to the report of the 2010 Freelance Business Survey that includes corrections to the first three tables because of calculation errors. No corrections to the tables covering details of fees were necessary. The original PDF of the survey in the TWS area of the website will be updated so that anyone accessing the survey will be able to view and download the amended version.

This issue of TWS is about publications. The sometimes unsung heroes and heroines of publications and other documents (and certainly not only in our field) are author's editors, who play an important role in their creation. Their input ranges from basic editorial review to complete rewriting, and often goes even further, as described in Karen Shashok's excellent article in *Learned Publishing* from 2001 [1]. I have the impression that freelance writers find themselves in this role more often than salaried writers, especially in countries where English is not the first language. Indeed, many of us market ourselves as such—and over the past 8 years, author's editing has come to be my major activity. Karen was unable to attend the Lisbon Conference, but in absentia, suggested that a topic for the Freelance Business Forum might be whether author's editors should be acknowledged on publications, and if so, how. She is convinced that they

should always be acknowledged and will not work for a client if they are not prepared to. This may be a luxury many of us cannot afford. This was briefly discussed in Lisbon, with three broad groups: (i) "Maybe it is better not to be acknowledged, because we never know what happens to the manuscript after we return it."; (ii) "I always add my name under the acknowledgements to anything I edit, and sometimes it gets taken off, but there's not much we can do about it."; (iii) 'Yes, of course the author's editor should always be properly acknowledged and this is something we should fight for'. So let's have a debate here in these pages about this. If you would like to defend—or attack—the opinions of one of the groups above, please let us know so that we can plan this in for the December issue. Karen set the scene for us in her article in *Learned Publishing* and looks at these different points of view in a short contribution to TWS in this issue. So don't hold back—please let us know what you think!

And, of course, we look forward to receiving any other contributions you would like to make to Out on our own.

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Reference:

1. Shashok K. Author's editors: facilitators of science information transfer. *Learned Publishing* 2001;14(2):113-121.

Changes to report on Freelance Business Survey

Thanks to Adam Jacobs for pointing out that there must have been an error in the way some of the percentages were calculated in the report on the 2010 Freelance Business Survey. In both 2007 and 2010, these were taken directly as calculated by SurveyMonkey. That the calculations had been made excluding zeros did not become obvious until the 2010 results were ready. This affected only the three sections below, so all the information on charges and fees remains unchanged. There were no major changes to any of the main findings and the text below has been adjusted accordingly. The PDF of the entire article in the last issue of TWS available on the website has been revised.

Sources of work

Respondents were asked to indicate their sources of work (totalling 100%) from the categories given in Table 1, which shows the mean percentage of work obtained from each source.

The pattern in 2010 was similar to those of the 2003 and 2007 surveys with longstanding customers accounting the highest mean percentage of work (46%), followed by referrals from colleagues (16%). It is worth noting, however, that the mean percentage of work from CROs and agencies decreased from 15% in 2007 to 5% in 2010, possibly

reflecting the economic crisis from 2009 onwards. The volume of work derived from the EMWA Freelance Directory did not change at 7% for 2007 and 6% for 2010.

Types of activity

Respondents were asked to indicate their types of activity (totalling 100%) from the categories given in Table 2, which shows the mean percentage of each type of activity.

Writing was the major activity in 2003 (57%), 2007 (62%) and 2010 (55%), followed by editing and translation.

Types of documentation

Respondents were asked to indicate the type of documentation they generally work on (totalling 100%) from the categories given in Table 3, which shows the mean percentage of each type of document worked on. These categories were simplified and regrouped so direct comparison with 2007 and 2003 is not possible.

As in 2003 and 2007, the mean percentages of time spent on documents used for drug approval and peer-reviewed journal articles for the medical and scientific press were greatest. The 2007 survey did not include the category 'medical communications materials' which accounted for a mean of 14% of work in 2010 (the closest category in 2007 was 'marketing materials' at 8%).

Table 1: Sources of freelance work (N=123)

Source	Mean % of work	
	2010	2007
Longstanding customers	46	44
Referrals from colleagues	16	16
Referrals from customers	13	9
Own advertising	7	6
EMWA Freelance Directory	6	7
CROs and agencies	5	15
Other freelance directories	3	1
'Looking for a medical writer' ^a	-	1
Networking with EMWA colleagues ^b	2	-
Other	2	1

Table is sorted on 2010 column except for category 'Other'

CRO=contract research organisation

^a Category not present in 2010 survey

^b Category not present in 2007 survey

Table 2: Types of freelance activity (N=122)

Type of activity	Mean % of work	
	2010	2007
Writing	55	62
Editing	14	14
Translation	11	7
Consultancy work	8	4
Training events	4	4
Quality control	4	4
Proofreading	3	3
E-publishing	1	1
Other	2	2

Table is sorted on 2010 column except for category 'Other'

Table 3: Types of document (N=122)

Type of documents	Mean % of work
Regulatory documentation	35
Peer-reviewed articles for journals	29
Medical communications materials	14
Articles for the scientific press	6
Consultancy documentation	4
Medical and scientific text books	3
Training documentation	3
User manuals	1
Other	5

The Acknowledgements dilemma: An opinion

Ethical behaviour and transparency should apply to everyone, so calls for communication professionals to be named along with authors are to be welcomed. But you can't force people to do something they don't want to do if they don't see any benefit to themselves, or if they feel that doing it may harm their interests.

The situation for freelancers and non-public-sector employees is very different from the situation for tenured academics (most gatekeepers and many researchers), whose decisions about the most ethical thing to do are not constrained by possible threats to their income. It creates a dilemma when editors (many of whom have tenured day jobs) criticise self-employed colleagues for unethical behaviour and 'demand' that freelance professionals 'require'

that our name appears. Everyone wants to do what's right but first you have to eat. Those who need to take care of their income first will not be motivated to put their income at risk by scaring off a reluctant client with 'demands' for acknowledgment. For a freelancer, one instance of 'being difficult' about appearing in the Acknowledgments section can be communicated to other potential clients through the grapevine, where it can damage the freelancer's chances of landing future jobs.

Where the tipping point comes between 'needing' to put income at the top of the list of priorities and 'not needing' to (being able to afford to risk losing some clients you can't convince to improve their ways) is a personal and professional matter each person should decide for himself or herself. Maybe some colleagues, once freed from large recurring expenses such as mortgages, cars and caring for younger or older family members, will put the question to themselves: "Has the time finally come when I can afford to say no to clients who won't acknowledge my work?" That's perhaps a more realistic goal—getting colleagues to ask themselves if they can afford to change their personal policy regarding acknowledgement—than simply saying, "The rules have changed and now, if you don't demand acknowledgment, your behaviour is not ethical". Opting out of acknowledgment is important for professionals who don't want their name and reputation associated with work that does not reflect their normal quality standards. Many different people are involved in manuscript editing and revising, and the translator, medical writer or author's editor is not always called in again to check the English language, writing, reporting or compliance with ethical guidelines after others have made changes. So the risk that what gets published will contain things that make the communication professional uncomfortable can be considerable. For academics and other permanently employed people it's no problem since their income is assured no matter what they do. For freelancers it's completely different. You spend your whole life cultivating your skills and your reputation, and you get work by reputation and word-of-mouth, not by being on a payroll, so your income is never totally secure. One substandard article in the public domain with your name on it can damage a freelancer's reputation (and income) badly. If the communication professional is not allowed a final sign-off option on material that is to be published, that professional cannot in good conscience assume public responsibility for the content.

Now that ethical issues in STM publishing are attracting so much attention, it's great that there are calls to make the roles of different authors and other contributors transparent. Transparency means public responsibility and accountability for everyone involved in research publishing. Perhaps it's also time for academic gatekeepers (who enjoy the economic security that allows them to take a stand with no risk to their livelihood) to come out of the shadows too. Putting an end to anonymity in peer review and anonymous editorials may be a helpful way for gatekeepers to use their power to lead the way towards greater transparency and accountability.

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Linguistics corner

Current medical discourse research

The Linguistic corner aims to publish abstracts of papers related to oral or written medical discourse of interest to the TWS readership. Abstracts are numbered consecutively to build into a series that can be saved as a collection. Contributions should be in English but can relate to papers published in other languages. Françoise Salager-Meyer invites you to send abstracts to her at: francoise.sm@gmail.com.

Étude des termes relevant des champs sémantiques de l'essai et de l'erreur en anglais médical

(A study of terms related to the notions of trial and error in medical English)



François Maniez (francois.maniez@univ-lyon2.fr) is a professor of English linguistics and has been teaching English for Specific Purposes for the past 20 years at Lumière Lyon 2 University (France). He has directed the Centre de Recherche en Terminologie et Traduction since 2007, and was the coordinator of the translation of the bilingual (English-French) version of Dorland's

pocket medical dictionary in 2008. His main research interests are corpus linguistics, lexicology, lexicography and English for Specific Purposes, with a particular focus on the syntactic and lexical aspects of medical translation.

Darwin's secret garden

A fascinating article in BBC news explains a secret venture between Charles Darwin and his friend the botanist Joseph Hooker after Darwin's and then Hooker's visit to the volcanic Ascension Island in the South Atlantic Ocean. Ascension Island had no trees or fresh water at the time. Rain water quickly evaporated. The pair figured that planting trees on the island would capture rain, reduce evaporation and create fertile soil. Conveniently, Hook's father was the director of Kew Gardens. Arrangements were made in 1850 to start shipping trees and plants regularly to the island. This resulted in an ecosystem of incongruous plants in a cloud forest that captures sea mist. Normally such a system would take over a million of years to evolve. Dr Dave Wilkinson, an ecologist from Liverpool John Moores University, thinks that useful information could be obtained for creating future colonies on Mars but so far nobody has set about studying the Garden of Eden on Ascension Island.

Source: <http://www.bbc.co.uk/news/science-environment-11137903>

Abstract 7

Maniez F, *Asp*¹ N° 56, 2009, pp. 89-104.

Striving to avoid future mistakes by using knowledge acquired from previous unsuccessful attempts has always been one of the basic principles that underlie any scientific activity. However, the subject addressed in this article is not that of empiricism in science (as the juxtaposition of terms such as *trial* and *error* might suggest), but rather the various ways in which the corresponding notions are expressed in the English medical vocabulary and how they translate into French. Both terms are indeed closely linked with the concept of medical research, as the aim of any new clinical trial is to reduce the margin of error of the therapies under scrutiny.

The first term (*trial*) refers to one of the mainstays of evidence-based medicine, and leads to a description of the various categories of medical trials and the French translations used for the corresponding terms. The French equivalents for such terms as *controlled trial*, *crossover trial*, *double-blind trial*, *randomized trial* and *multicenter trial* are thus discussed, and their usage in a 23-million word corpus composed of medical research articles is compared to the recommendations of well-known lexicographical sources such as the *Grand Dictionnaire Terminologique*.

The second part of the article is somewhat longer and describes the various uses of the term *error*, with a particular emphasis on medical error. The author has chosen to focus on a few of the terms that belong to this particular semantic field, among which the words *error*, *mistake*, *slip* and *lapse*. The difficulties that arise in distinguishing between such terms within the context of ESP are examined, and a comparison is made between the use of such expressions as *near miss*, *close call* or *sentinel event* in the fields of medicine and air transportation as the terminology of these two fields are found to overlap to some extent. The notions of negligence and oversight (as well as the related notion of malpractice) are also discussed, as are the translational difficulties created by such hypallages as *negligent adverse events* or *negligent injuries*.

The author concludes that the terminology of the field of medical trials is predictably stable both in English and French, even though a small degree of variation is noticeable in the French translations of such words as *randomize* or *randomization*, for instance. In the field of medical error, the relative paucity of the French vocabulary makes it difficult to distinguish between mistakes, slips and lapses, whose specific definitions are clearly laid out in the literature, but which may seem interchangeable terms to the layman. The relative lack of transparency in the way the medical profession sometimes communicates with patients about past errors might also play a role in the comparative 'fuzziness' of the corresponding notions.

¹ *Asp* is the journal of GERAS (Groupe d'Étude et de Recherche en Anglais de Spécialité), an association whose aim is to promote ESP research.

Students' plagiarism: Heralding change?

Plagiarism by students has been receiving some press recently because one way or another its prevalence might be acting as a force for change. The first change that it could bring about is the demise of the personal statement as part of the higher education application process.

I recently read a student's personal statement, which was part of his application for medical school in the US. The student suffers from a hereditary medical disorder and explained that he wanted to become a doctor to help others who suffer from disabilities. He came over in his statement as a compassionate, ambitious and capable young man—just the sort of doctor you would wish to consult. What then are his chances of acceptance by the medical school? This will of course depend on the competition for places. What if that competition is unfair? Then society is deprived of a doctor with the optimal qualities.

A study of 4975 residency application essays received by a hospital in Boston found evidence of plagiarism in 5.2% of the essays [1]. The study used an Internet-based tool to analyse the essays and plagiarism was defined as a match to an existing work of more than 10%. Prevalence was higher among non-US citizens and those who had attended medical school outside the US and Canada. Some applicants who had plagiarised material had achieved high academic grades.

When asked why he thought there was so much plagiarism, the lead author of the study, Scott Segal, listed increasing competition for places, a failure to see copying from the Internet in the same light as copying from print sources, the relative low risk (until now) of being caught and cultural differences in attitudes towards the seriousness of plagiarism [2]. He also mentioned that the applicants could have received bad advice from people who had assisted them or from unscrupulous corporate services catering to applicants. An editorial in the same issue of the journal suggests that personal essays should be abandoned if they are “increasingly being polluted by Internet samples or hired consultants”.

Another article published in *The New York Times* [3] supports Segal's explanation that copying from the Internet is viewed differently. Furthermore it quotes Susan Blum, who has researched students' plagiarism in France, as saying that the traditions that an author's singular effort creates an original work and the Western concept of intellectual property rights are under challenge. The discipline officer at the University of California affirms that most students who engage in plagiarism are not ignorant but know that it contravenes university rules. It seems that undergraduates now are less interested than those who grew up in the 1960s in cultivating a unique and authentic identity. Young people adopt many personas through social networking and do not see the need to present themselves or respect others as unique. Text, images and music are so easy for

them to download from the Internet with their own computer that they assume ownership of the downloads rather than crediting them to some unnamed author (e.g. sources like Wikipedia). Surveys of students from 2006 to 2010 found that in only 10 years the average percent of students who think copying from the Web is 'serious cheating' has dropped from 34% to 29%. Of students surveyed 40% admitted that some sentences in their written assignments had been copied from elsewhere. The article gives Helene Hegemann's novel about Berlin club life as an example of changing attitudes. The book contained several passages which were known to be plagiarised, but was still listed among the finalists for a book prize.

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Declarations of funding or declared conflicts of interest (COI) should be published

Between a quarter and a third of academic investigators have some form of financial interest in the studies they report [1, 2]. Given that readers' belief in the soundness of the results reported are known to be affected by statements of COI [3], it's odd that although 93% of biomedical journals require authors to state their sources of funding and declare their potential COI [4], many fail to publish this information with the articles they publish.

To be aware of possible bias readers need to know if authors have funding and/or potential conflicts or not. Robert Klitzman and colleagues, authors of research published in the current issue of the *Journal of Medical Ethics*, have called for the International Committee of Medical Journal Editors (ICMJE) to include a stipulation in their guidelines that journals publish funding and COI disclosures made by authors.

Their call came as a result of their investigation related to research conducted in developing countries. They looked at disclosure from the readers' point of view and therefore did not question journals as to whether declarations had been made or ask authors whether they had in fact received funding or had potential COIs. Instead they searched Medline for all English articles relating to HIV research in humans published in 2007 where the research was sponsored by a developed country but conducted in India, Thailand, Nigeria or Uganda. They found that more than 33% of the articles did not disclose funding and 80% did not report if there were COIs. Funding was more likely to be disclosed if at least half of the authors, the corresponding author or the journal editors were from the

Biomedical publishing shorts

- > sponsoring countries. Ultimately, however, journals must require disclosures and it should be the norm that they publish the disclosures.

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Editor changes misleading sentence in published article

Reuters Health reports that the editor of *The British Journal of Dermatology* changed a sentence in a paper it had already published in response to an article by an investigative journalist in the popular press. The paper was company-sponsored study and related to L'Oreal-Nestle tanning pill. No conflicts of interest had been declared by the authors. The sentence had said that the "results support the use of this nutritional supplement." The report in Reuters quotes Peter Schalock, a dermatologist at Massachusetts General Hospital in Boston, as saying he had a "hard time seeing that statistically or scientifically (the researchers) have proven it." The paper had been peer-reviewed.

Source: Joelving F. Editor changes industry-backed tanning pill study. 30 July 2010. Available at <http://www.reuters.com/article/idUSTR66T4DG20100730>

Adding favours: Can authors be added to the manuscript after submission?

Bearing in mind that to be an author someone must have made a substantive intellectual contribution to a published study and approved the final version of the manuscript to be published [1], it seems strange that situations arise when the original manuscript submitted to a journal fails to list all the authors. A legitimate circumstance in which this might happen is when more experiments or analyses are conducted in response to reviewers' comments. The new experiments might involve a substantive intellectual input from someone who was not involved in the previous work or a statistician might be commandeered. Otherwise journal editors should view requests to add authors with grave suspicion of honorary authorship, they should at least ask why. The Committee of Publication Ethics (COPE) has produced a flow chart in which editors are advised to clarify the reason for the change in authorship and secure the agreement of all the authors to the change [2].

If the authors fail to agree the review process/publication should be suspended. However, on the occasions when I have asked for authors to be added just before (in one case even after) publication the journal did not bat an eyelid.

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1. http://www.icmje.org/ethical_1author.html
2. http://publicationethics.org/files/u2/04B_Author_Remove_Submitted.pdf

How a copyeditor can deal with plagiarism and authors who plagiarise

Mary Ellen Kerans and Marije de Jager who edit manuscripts for biomedical journals have written an interesting article on detecting and dealing with plagiarism [1]. Mary Ellen Kerans found that 30% of accepted manuscripts which she edited for a well-indexed medical journal over a 2-year period had plagiarised text. Sometimes as much as 90% of the text was plagiarised. The COPE flow charts can assist journal editors in dealing with plagiarism after it has been detected [2] but these authors set out the procedures they use to detect plagiarism before publication for journals that are not yet using CrossCheck software [3]. Although they encourage journals to use CrossCheck where they can afford it they recommend that the uncritical use of detection software is in any event to be avoided.

The article sets out 6 steps that these copyeditors use during the editing process. They start by checking the introduction and discussion for red flag indicators of plagiarism such as uneven style, choppy text and a mixture of British and American English. Next they use Google for determining the amount of plagiarised material and to trace the original text. Dependent on their findings they might return the article to the editor with a recommendation that the acceptance be rescinded if there is considerable plagiarism (90% or more), ask the authors to rewrite specific parts of the text or rewrite patch-written fragments themselves. The authors are always consulted about the edits and Kerans and de Jager emphasise that care should be taken to speak to authors in ways which do not dishearten them. They give tips on how to deal tactfully but firmly with authors and also discuss the special circumstances relating to authors whose first language is not English. The article also contains a useful list of terms used when discussing plagiarism.

The final step of their 6 steps is to check the revised manuscript following the editing and possibly if it differs extensively from the original manuscript returning it to the editor with a suggestion that it be peer reviewed again.

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Classic overwriting

It is always worth bearing in mind what the reader already knows and needs to know to get your message. Less experienced writers—and unfortunately quite a few experienced writers—often forget this and ‘overwrite’:

Vital signs and physical findings

With respect to the evaluation of vital signs and physical findings, values were determined in all studies at the screening visit, with the exception of studies X and study Y, where these evaluations were not carried out.

The reader knows from the subheading above that we are talking about vital signs and physical findings in this subsection, so the introductory prepositional phrase is superfluous. And if you say something was done in some studies except in two of them, there is no need to underline this with a further clause with exactly the same information. In terms of words, therefore, the above sentence can therefore be reduced by 66% without any loss of information:

These were determined at screening in all studies except studies X and Y.

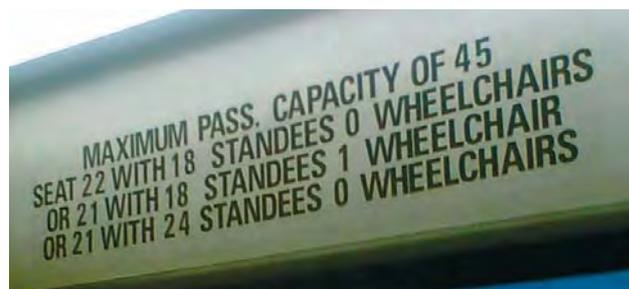
Verbal arithmetic muddle with an important message

Last time I was at Heathrow Airport, I had to stay the night near the airport, and the bus on the way to the Premier Inn broke down. That gave me time to contemplate this notice to passengers. Apart from the wonderful new word ‘standee’ (which I can pretty well guarantee won’t enter my active vocabulary), how many people end up standing on one seat according to the last line? Somehow the statistics here just don’t work out.

There is an important message for us here, however: in English, the use of the plural with ‘no’ represented here by ‘0’ when using countable nouns (0 wheelchairs). Hence: *No adverse events were observed* and not *No adverse event was observed*.

PS: The bus also broke down on the way back to airport the following morning. Which gave me the chance to capture this on my mobile for your enjoyment.

PPS: I thank Guy Whitehead of the American Medical Writers Association for inventing the term ‘verbal arithmetic muddle’.



Enforcing consistency

Sick of wasting time checking the consistency of the use of hyphens, a client of mine recently found a neat solution to two hyphenation problems: (i) do you need a hyphen after ‘non’ (e.g. non-clinical), and (ii) if you do, in a section heading, do you capitalise the element after the hyphen (e.g. Non-Clinical Studies). They decided not to hyphenate ‘non’, which also solves the capitalisation problem. It was enforced using Word: under Tools/Autocorrect, Replace: enter ‘non-’, and under With: ‘non’. All those working on the document were requested to make this setting on their computers. This makes it impossible to put a hyphen after ‘non’ and it happens automatically while you type (try it out). The only problem is that it is a global Autocorrect function. Whilst I generally agree about no hyphen after ‘non’, there are some instances when I think you need one (e.g. ‘non-native’ and non + abbreviation, as in ‘non-ICH study’). So if you make this Autocorrect setting, you have to go back and insert a hyphen if you think it is necessary. My client still feels this change represents a net time gain, as long as you store all the ‘non’ words in your custom dictionary for the spellchecker so you’re no longer asked about them. I am still deciding whether I can be bothered to check whether there is a time gain or not, but I’m increasingly thinking that I will not bother. I am a great proponent of consistency—but life is too short to look for that last (missing) hyphen.

We all know what it means, but ...

... I find this very sloppy, and it should never be written: *The MCS score was not significantly different before and after surgery.* So what does it mean? It means: *The MCS scores before and after surgery did not differ significantly,* and that is what should be written.

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Don’t go calling people nutty fruits

Shirley Brown, a councillor in Bristol in the UK, has been convicted of a criminal offence under the Public Order Act for using “threatening, abusive or insulting words, with intent to cause a person harassment, alarm or distress”. She called a fellow councillor, Jay Jethwa, who is Asian, a coconut. Apparently coconuts are not only fruits (more precisely drupes) that fall on your head in the jungle but are also a term of abuse for people who have disregarded their cultural roots. They are compared to coconuts as being brown on the outside but “white” on the inside.

Source: http://news.bbc.co.uk/2/hi/uk_news/magazine/8771721.stm



Words, Grammar & Co

A storm in an English teacup: American English as standard English

Some people claim to be able to foretell the future from tealeaves in a cup—a pastime about as futile as debating the future of English. Nevertheless the online *Economist* recently took to debating this very subject. The proposal was “This house believes that the English-speaking world should adopt American English.” Imagine such a suggestion in a British magazine!

Michael Agnes, editor-in-chief of Webster’s New World Dictionaries, defended the motion and Robert McCrum, associate editor of the *Observer* and author of the book *Globish* opposed it. Michael Agnes claimed that American English could become the global standard because it is “seductive and intrinsically capable”. No, I didn’t quite follow this argument either. Easier to follow was his camp’s line that computers nowadays are usually set to American English and few people (apart from the British, I presume) can be bothered to change their computer settings. Robert McCrum proffered that rather than American English, Globish, a very basic English which allows all people with even a splattering of English to communication, is becoming the standard. Michael Agnes could not accept this. Globish, he countered, is by no means becoming adopted as a standard among those whose first language is English, and certainly not by native North American English speakers. Both arguments came over as rather weak. The motion failed with 30% of participants voting for and 70% voting against. But many ‘speakers’ from the floor discarded the Globish concept too, believing that English will continue to expand and change as it has done already for hundreds of years.

It was pointed out that there are comparatively few differences between UK and US written English and these differences hardly hinder the reader’s understanding of the text. There is therefore no need for any standard. The big differences are in the spoken languages but here there is also tremendous variation within the countries where English is spoken (soon to include Mongolia and Chile who have recently pronounced intentions to become bilingual in English). Differences in spoken language are inevitable because when members of a community speak with one another they develop their own ‘rules’ dependent on their culture, socio-economic class, age group. As one commenter, Manuel Moldes, put it, language includes “not only words but pronunciation, speed of speech, tonality and rhythm.” Accordingly “language must be spoken differently between different communities, because it must evolve with societies to reflect their ever increasing complexity and differentiation needs, and nobody can command otherwise.” Indeed the board that acts as a watch dog for Spanish have had no choice but to incorporate all new words and idioms that evolve in Spain and Latin America into ‘standard’ Spanish. Actually, *Wordnik*, an English online dictionary, has set itself the mammoth task of covering all varieties of English.

Medical writing also had a fleeting moment in the debate when a UK healthcare scientist complained of witnessing constant erosion to Americanistic English, i.e. shorter, simpler and quite thoughtless (which could equally well apply to UK English in my view). As a consequence he or she, a pseudonym was used, wrote “words become too simple, too easy to confuse. I wonder if Americans will soon know the difference between anaemia and enema.” Something to contemplate over a cup of tea.

Source: <http://www.economist.com/debate/days/view/537&fsrc=nw1>



A Danish dinner

Grammar nerds win the day

A delightful story for grammar nerds is that about two country folk who had to attend a courthouse at Spokane County in the US. They drove into town but had trouble finding a parking space. Eventually they thought they were in luck. They parked by a sign which read “NO PUBLIC PARKING PERMIT REQUIRED”. When they returned they were somewhat surprised to find a ticket on the car windscreen with a fine of \$30. They contested the fine on the grounds that there was no comma or dash or semicolon or full stop between NO PUBLIC PARKING and PERMIT REQUIRED. The judge agreed with their argument even though there is no such thing as a public parking permit.

With thanks to Adam Jacobs for sending TWS the URL: <http://www.spokesman.com/stories/2010/aug/04/drawing-a-line-between-law-and-grammar/>

Proof of a good proof-reader

You would be forgiven for thinking that the proud winner of a school magazine prize had written a stunning article that had captured the judge's imagination. But this is not always the case. In Neville Goodman's article 'The proof of the pudding is in the reading', he describes how he won the esteemed prize in his school days. He had the task of chief proof-reader, checking the galley proofs of every issue of the school magazine for 3 years. Although the author and editor had seen the proofs of a particular article 'The Viennese Public Transport System' before him, they had failed to spot that the 'L' was missing from the title.

Source: Goodman N. The proof of the pudding is in the reading. *Anaesthesia Points West* 1993; 26(1):34-35.

Copyeditor (or copy-editor) afflictions

The *Economist's* Language Johnson blog run by R. L. G. had him marvelling at both the care taken by the copyeditor of his new book and the confusion she sometimes introduces. This prompted him to read Lori Fradkin's article 'What It's Really Like To Be A Copy Editor'. Although he recommends reading it, he takes great exception to her pronouncement that *douchebag* is not one but two words: *douche bag*. It's not that he has a thing about *douche bags* but that she bluntly states that *douchebag* is wrong, because the dictionary says so. This he thinks is an all too common attitude among copyeditors. Which dictionary he demands because his 1999 edition of Webster's College Dictionary has *douchebag*? So what kind of an explanation would R. L. G. give if he were a copyeditor? Taking the example 'interest-rate hikes', he declares that he would say something interesting like the hyphen is included because when the reader sees two nouns in a row he should understand them as a compound modifier, and another noun is coming up. There are some nice reader's comments attached to R. L. G.'s article—the first one asks if R.L.G realised his example of 'interest-rate hikes' violates the *Economist* style guide and referred to a sentence he had quoted 3 weeks before "hikes are walks, not increases". There's always someone who notices mistakes and they can't really help it because, as a copyeditor reader wrote, "once you train yourself to spot errors, you can't not spot them. You can't simply shut off the careful reading when you leave the office. You notice typos in novels, missing words in other magazines, incorrect punctuation on billboards. You have nightmares that your oversight turned Mayor Bloomberg into a 'pubic' figure."

Source: What it's really like to be copy-edited by R.L.G. 26 July 2010 available at: <http://www.economist.com/blogs/johnson/2010/07/copy-editing&fsrc=nwl>

Peer review is as old as...

Elsevier has set out an interesting history of peer review on its website as reproduced below:

- It is thought that review by peers has been a method of evaluation since ancient Greece, although it was not standard practise in science until the mid-20th century.
- The physician Ishaq bin Ali al-Rahwi (854-931 CE) of Syria first described the peer review process. He stated that a physician must make notes of a patient's condition on every visit. When the patient was cured or had died, the notes were examined by a local medical council to decide whether the physician had met the required standards of medical care. If their reviews were negative, the physician could face a lawsuit from a maltreated patient.
- As early as the 17th century, scientific clubs (or societies) of gentleman scholars argued over the origin and validity of different theories and discoveries, and helped establish a formal process for announcing, validating and accrediting scientific discovery to the appropriate person.
- Peer review has been a formal part of scientific communication since the first scientific journals appeared more than 300 years ago. The *Philosophical Transactions of the Royal Society* is thought to be the first journal to formalize the peer review process.
- Albert Einstein's "Annus Mirabilis" was not peer reviewed except by the journal's editor in chief and co-editor.

Source: <http://www.elsevier.com/wps/find/reviewershome.reviewers/history>

Another useful site for anyone interested in the history of peer review is http://www.ehow.com/about_4696702_history-peer-review.html#ixzz0wQazTYYG

With thanks to **Françoise Salager-Meyer** (francoise.sm@gmail.com) for pointing out these sites.

Blots

Did you know that Southern blot is named after Edwin M. Southern, the originator of the technique, but no Dr Western was associated with the western blot? Western blot was only so named because it has similarities to a Southern blot. So should it be written western blot or Western blot?

■ For regulatory writers

What makes for a successful marketing authorisation application?

An interesting article appeared in the May issue of *Nature Reviews Drug Discovery* [1]. The article, signed by senior staff of the EMA, analysed the rates of successful regulatory approvals for 2009. The recent (and welcome) drive towards transparency requires the agency to publish the outcomes of MAAs submitted through the centralised procedure, regardless of whether approval was granted or not.

According to the authors, decisions were published for 48 new active substances (for the purposes of their analysis, biosimilars were excluded although technically these should be considered as new active substances). Approval was granted for 29 (60%) and denied for 19 (40%); that is, failure came right at the very end of the development procedure.

Orwellian rules

A well-known example of a somewhat absurd result of taking compliance with guidelines to an extreme was when some companies interpreted ICH E3 guidelines on clinical study reports as a template and listed the title page of the clinical study report as chapter 1 of the report. Compliance with style guidelines can also lead to strange results. For example, if the corresponding style guide demands that you spell out numbers under ten, and you want to express a range, e.g. “9-11 hours”, could you put “nine-11 hours”? This brings to mind George Orwell’s set of maxims for clear writing:

1. Never use a metaphor, simile, or other figure of speech which you are used to seeing in print.
2. Never use a long word where a short one will do.
3. If it is possible to cut a word out, always cut it out.
4. Never use the passive where you can use the active.
5. Never use a foreign phrase, a scientific word, or a jargon word if you can think of an everyday English equivalent.
6. Break any of these rules sooner than say anything outright barbarous.

It’s unlikely that applying style guidelines (or any other types of guideline for that matter) will lead to anything “outright barbarous”. Rule 6 should perhaps serve as a warning against overly zealous and unthinking application of guidelines, while recognising that they should be followed as far as possible.

As an aside, these rules are taken from an essay called “The Politics of the English Language” published in 1946. Orwell was complaining that much political writing was intended “to make lies sound truthful and murder respectable, and to give an appearance of solidity to pure wind.” I would hope the same can’t be said of medical writing!

Reading between the lines of the assessment reports, in many cases regulatory failure was not because the drug was not good enough but because the efficacy or safety had not been adequately demonstrated, that is, a “failed development strategy or immature application”. The authors then inferred that many of these applications may have had a better outcome with a more appropriate development plan. Obviously, late-stage failure is a huge waste of resources (and time), and if it is the development strategy rather than the drug itself that is at fault, then the public is also being denied access to a potentially useful drug.

Some have suggested that lack of resources and experience in biotech companies may often be responsible for failure [2]. Indeed, an association between company size and successful MAA has been reported [3]. Part of the remedy, according to the authors, would be greater interaction with the agencies through obtaining (and complying with) scientific advice, preferably from early on in the development process. Another factor potentially responsible for failure is an “overly conservative, risk-averse regulatory assessment”. However, they also assert—when discussing how to increase regulatory success rates—that “lowering the evidence requirements or the balance of benefits versus risks ... is not a realistic option”. The conservative approach is understandable in the current risk-averse climate, not just within regulatory agencies for drug products but in a wider context (where for example thousands of flights were grounded earlier this year because of concerns about volcanic ash and where travelers have to endure long lines at the airports due to onerous security checks).

Something needs to be done, though, because in certain therapeutic areas, such as antibiotics, there are very few new drugs coming through the pipeline. This bare pipeline has partly been attributed to the heavy burden of proof (studies are needed for each different kind of infection) and complex regulatory issues that discourage pharmaceutical companies from developing a product for what is essentially a moving target (resistance patterns change and it is hard to predict medical need so far in advance). The authors do suggest that innovative approaches such as conditional approval with stringent post-marketing requirements can go some way towards increasing approval rates and encouraging companies to move forward with drug development.

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Questions of style in regulatory writing

On page 217 of this issue of *The Write Stuff*, Alistair Reeves discusses the new style guidelines published by the EMA for Quality Review of Documents (QRD), applicable to product information such as patient information leaflets (PILs). As some of these documents are intended to be read by people outside the medical profession and the pharmaceutical sector, it is not surprising that there is a strong emphasis on readability.

This got me thinking about style guidance for regulatory documents in general. There is of course plenty of guidance as to the structure and content of regulatory documents, and regulatory writers are generally keen to follow guidelines to ensure greater compliance (see Box). Although I have come across plenty of in-house style guides for regulatory documents, a look around the EMA and FDA websites uncovered very little reference to any style matters. Indeed, the only mention of style I could find (and I stand to be corrected) was a recommendation to use International Committee of Medical Journal Editors style in some of the FDA guidance documents.

On reflection, this lack of style guidance is perhaps not surprising. After all, unlike PILs (or journal articles for that matter, where most journals have their own style guides) very few of these documents will be available in the public domain, and the target audience is the regulatory authorities. Moreover, many documents such as clinical study reports will be used in submissions to both the FDA and the EMA, so unless any hypothetical style guidance was the same for both regions, ensuring style compliance could be a big headache.

In any case, I should imagine the reviewers at the regulatory agencies are more interested in being able to locate information quickly rather than stylistic consistency. That said, consistent application of style guidelines (in-house or otherwise) will also make the documents feel like they have been more carefully prepared and so more likely to inspire confidence. Finally, as mentioned earlier, one of the main intentions of the QRD guidelines is to ensure readability. Although such readability is not as critical for regulatory documents in general, I don't think regulatory writers are exonerated from making an effort to produce clear, well-written documents. The reviewers would, I'm sure, appreciate it.

Call for silly signs

If you ever come across a perplexing sign like those on pages 207, 223, 229 and 230, please be sure to take a photo (even if only with a mobile phone) and share some language fun by sending it to *TWS* (editor@emwa.org).

Errata

Erratum in Wimalasundera S. Patents: Converting technology into a business asset. *TWS* 2010;19(2):110-111.

On the last line of page 110 and the first two lines of page 111 the sentence "Genentech in 1994 were able to obtain a patent for the gene sequence for Relaxin based on these grounds" should be deleted. This is incorrect for 2 reasons:

1. The patent for Relaxin was filed by Howard Florey Institute and not Genentech and was issued in 1991 by the EPO.
2. Relaxin is given as an example of a patent obtained under the Biotech Directive. This is incorrect because the Biotech Directive came into force in 1998 after Howard Florey Institute's Relaxin was approved in 1991 by the EPO and opposed in 1992. However, the ethical issues raised regarding the patenting of human gene sequences in this case were influential in paving the way for approval of patents such as Myriad's patent for BRCA1 in 2001 by the EPO under the Biotech Directive.

Erratum in Reeves A. Everything has its place: Word order in English. *The Write Stuff* 2010;19(2):124-127. A small error occurred in the table illustrating word order in simple passive sentences on page 125. The entry in the middle column was 'Sentence (V)' and should have been 'Verb (V)' as in the table below.

[2] Passive voice

Subject (S)	Verb (V)	Prepositional phrase with adverbial function modifying the sentence; the agent (A)
The car	was damaged	by the man

More science quotations

The great tragedy of Science—the slaying of a beautiful hypothesis by an ugly fact. Thomas Henry Huxley

I'm all in favour of the democratic principle that one idiot is as good as one genius, but I draw the line when someone takes the next step and concludes that two idiots are better than one genius. Leó Szilárd

To err is human, but to really foul things up requires a computer. Anonymous

No matter what side of the argument you are on you always find people on your side that you wish were on the other. Thomas Berger

Gained in translation

Science at the multilingual crossroads

Einem Text in einer fremden Sprache Gehör verschaffen, wird oft genug einen neuen Text eher als eine Übersetzung im landläufigen Sinne verlangen.

Jürgen Habermas (*1929)

According to Habermas, making a text heard in a foreign language will often require a new text rather than a translation in the ordinary sense [1]. Among translation theorists, there has been debate about when a text is still a translation and when it is the result of a different textual operation. While this question may be of academic interest, it has little merit for modern translation practice—where translation comes in many shapes and forms and covers a wide range of diverse activities, including adapting or rewriting a text in the target language to reach a specific audience.

How the translator goes about transposing a text will depend on which purpose the text is to fulfil in the target culture. Should the translation be recognised as such (something which has been referred to as ‘overt’ translation [2]), or should the translation not read like one, effacing any differences between the source and target cultures (analogously referred to as ‘covert’ translation [2])? This will either be explicitly specified by the client—or it will be implicit from the type of text to be translated.

The feature article in this issue’s translation section is a good example of a text calling for a ‘covert’ translation, one which is specifically tailored to the target reader’s situation. The article shows translation to be a complex of decisions rather than mere linguistic recoding. Language is not the goal of translation, it is only a necessary instrument. Language competence, such as knowledge of

grammar, correct usage, and appropriate terminology, is important, but it is not what translation is about.

The purpose of an informed consent document (ICD) is to enable potential study participants to make an informed decision about whether or not to participate. To achieve this, the text will have to be adapted to whatever it is a German, Spanish, Dutch, or Polish patient should know about studies performed in their specific countries, which may differ substantially in their cultural and social backgrounds, legal requirements, health care systems, infrastructures, beliefs, religions, and value systems.

The English-language ICD, therefore, basically serves as raw material for the translation. We read that the target-culture recipient has to be addressed differently than his source-language counterpart, units of measurement have to be converted and country-specific legal provisions added. Icons, images, or even entire graphical layouts may have to be adapted to the conventions prevailing in the target culture to facilitate understanding.

Consisting of a series of decisions to be taken, then, translation ideally includes all parties involved in either producing or receiving a text, e.g., the author (or the party commissioning the translation), the translator, and the reader. The translation process will be most successful if based on teamwork—the magic behind many a successful project. In this, translation is no exception.

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METM—An abbreviation translators should know

Mediterranean Editors and Translators, or MET for short, is an association of language service providers (LSPs) who work mainly into or with English. So far, there have been 5 MET meetings, or METMs: METM05 and METM06 in Barcelona, METM07 in Madrid, METM08 in Split, and METM09 in Barcelona. In addition to plenary and poster sessions, METMs offer a wide range of workshops relevant to LSPs. Although not specifically directed to medical language professionals, many of the MET workshops do have a medical spin.

Last year’s METM was entitled *Translation, Editing, Writing: Broadening the Scope and Setting Limits*, reflecting the wide variety of services provided by language experts. In this, as the conference title aptly suggested, we are constantly challenged to not only expand our thinking, knowledge, and skills but also to define our personal limits. A number of reports on METM09 have been published, each

providing a personal, insightful, and entertaining account of the meeting and giving it broad coverage [1-4].

METM10 in Tarragona, Spain

METM10, which will take place from **28–30 October 2010** in Tarragona, Spain, bears the title *Facilitating knowledge transfer—through editing, translation, coaching*, with workshops covering topics as diverse as practical statistics (regression and multivariate analyses), editing and revising, correct referencing, plagiarism, effective paraphrasing, or genre analysis of research articles.

MET—a knowledge-sharing and peer-teaching network. METM—an abbreviation to remember.

For more information, go to <http://www.metmeetings.org>.

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Generating informed consent documents for multinational clinical trials in Germany: Where medical writing and translation meet

by Susanne Geercken

Have you ever been sick and yet had to make a difficult and far-reaching decision?

This is the situation patients¹ find themselves in when they consider taking part in a clinical trial. It is a sign of respect to the patients, then, to dedicate special effort to writing patient-friendly informed consent documents (ICDs) for clinical trials. The following article gives an example of the steps involved in achieving this goal.

Stakeholders

Of course, first and foremost, ICDs are targeted at patients. Apart from this, however, we need to look at two further stakeholders, namely investigators and ethics committees.

Patients

As mentioned above, patients who consider clinical trial participation will typically be sick (unless they are healthy volunteers in early development studies), a situation associated with increased vulnerability. Particularly patients with chronic diseases may have gone through an ordeal of previous, potentially unsuccessful, treatment attempts. Whether or not to participate in a trial will mean yet another difficult health-related decision with uncertain outcome [Box 1].

Interestingly, the questions that are on patients' minds when they consider their choices go far beyond the purely medical:

- How long will the study take and how often will I have to come to the study site? Will there be any unplanned visits that may be difficult to fit into my daily routine?
- Will I have to travel far to get to the study site? Do I need to find somebody to take me there?
- Does it involve any overnight stays in the hospital, so that I need a babysitter for the kids?²
- What kinds of treatments, examinations and tests will have to be carried out? Compared to the standard treatment, will the treatments be more painful or more time-consuming?³

- What will be the patient's responsibilities in the study? What will the treatment cost and will all the costs be covered? ... Will travel expenses be reimbursed?³

Apart from this, the medical details will have to be considered. To tackle the difficult task of weighing the potential benefits of a study against its risks, the patients need to be told about study procedures, treatment plans, side effects and the treatment options outside the study in a clear, concise and readily understandable way.

Box 1—ICD Working Group

Based on a growing awareness that patient informed consent documents (ICDs) can be a key factor in helping patients understand clinical trials and make an educated decision about participating, Pfizer Germany in 2008 set up an interdisciplinary working group for developing more patient-friendly ICDs. The working group consisted of clinical research, medical and patient relations experts from Pfizer Germany and representatives from local patient advocacy groups across several indications. The project proved to be a highly instructive experience for everybody involved: the patient representatives took home a better understanding of the tightly woven legal and regulatory framework around clinical trials while we at Pfizer learned about the practical and very personal implications of deciding about clinical trial participation. The group started out by putting together a 'patients' wish list' of desirable improvements in ICDs, revealing a need for better text organisation and design and simplified language. For the remainder of the four sessions, the group sat down for collaborative, hands-on editing of existing text material: sentences were shortened, abstract language reworded, complex issues explained in simple, accessible language, redundant information deleted and information missing from the patient's perspective added. The effort resulted in a patient-friendly core template for future use across studies conducted in Germany. In response to suggestions from the group, the new ICD format also includes a one-page summary-cum-table of contents and uses icons and coloured boxes for easy navigation. The collaborative editing experience also resulted in a set of rules for ICD authors to help them design patient-friendly ICDs. The approach taken at the time is also confirmed in a recent article by Jan Geißler, who reports similar experiences and conclusions in regard to informed consent from the perspective of patients [1].

1 My article will focus on ICDs for Phase II-IV treatment studies (excluding vaccines). I will therefore use the term 'patient' rather than 'participant' throughout this document.

2 The above list of questions emerged from the collaborative working group to improve informed consent documents Pfizer set up with patient representatives in 2008 [see Box 1].

3 These items are taken from a list of patient concerns in an article by Jan Geißler [1], page 5

Generating informed consent documents for multinational clinical trials in Germany

> **Investigators**

It is never an easy task to recruit suitable patients into clinical studies. In Germany, apart from other impediments to recruitment, many people are mistrustful of the pharmaceutical industry and clinical trials⁴. The investigator will therefore have to make extra efforts during the informed consent discussion to address these concerns. The ICD can be a tool to help the investigator reach out to potential trial participants, especially if it is:

- Designed to help get patients interested in the trial
- Comprehensive yet clearly organised to support the investigator in structuring the informed consent discussion

Ethics committees

As part of their role in protecting patient rights, ethics committees will carefully review the study ICDs submitted for compliance with legal requirements. In Germany, they will have a particularly keen eye on whether patients have been adequately informed of their rights with regard to data protection and mandatory patient insurance. Other items high on the ethics committees' priority list are that the ICD be as short as possible and that all medical terms be explained in lay language.

Stakeholders' wish list

From these stakeholder interests, the following core requirements for ICD documents can be deduced:

- Carefully structured, affording quick overview
- As comprehensive as necessary, but as short as possible
- Easy to understand, using adequately simple language
- Providing practical information relevant for the patients' daily routine
- Containing all information on legal rights

How do we go about satisfying this wish list? Typically, in international pharmaceutical companies like Pfizer, multinational clinical trial programmes are planned and developed centrally at global R&D or Clinical Research units for deployment in different countries worldwide. This involves the generation of one set of clinical trial documents, generally in English. These core documents, including a study-specific ICD core template, will be sent out for use in all of the countries participating in the clinical trial. The core template contains all the necessary study-specific information that should go out to the patients. However, to ensure that the stakeholders' needs outlined above will be catered to in this setting, the English core ICD template will need to undergo some further processing, which involves three steps: translation into German, localisation and customisation.

Translating the ICD

Typically, ICDs are not highly technical texts. They are therefore considered to be relatively easy to translate. Yet, a number of challenges are involved in translating ICDs from English into German.

Box 2—Assent forms

Assent forms are documents to provide information on a clinical trial to under-age patients. The language and contents of the document has to be written to be readily understood by the age group addressed. Since under-age patients cannot give legally binding consent, Assent forms cannot stand alone, they always need to be accompanied by a full consent form to be read and signed by the parents or legal representatives.

Language-related challenges

Unlike English, German has two forms of address—the polite, formal 'Sie' and the casual, non-formal 'Du'. This does not constitute a problem when translating ICDs for adult patients, where the formal address 'Sie' will be used by default. However, decision-making is necessary when translating what are called *Assent forms* targeting under-age patients between the ages of about 14 and 17 years (as pointed out by Marion Alzer, personal communication) [Box 2]. In Germany, young people typically start being addressed using the formal 'Sie' from the age of 16 onwards. Using the formal address with adolescents younger than 16 tends to make them feel uncomfortable, creating an unwanted language barrier. One way of solving this problem is to use the informal 'Du' in the document and add a comment for the 16-17 year olds, explaining why this choice was made.

The fact that English uses gender-neutral forms for terms like 'patient' while German does not, can make for another translation challenge in ICDs: When the English-language ICD for a trial on breast cancer speaks about 'patients with breast cancer', the reader will not know whether this refers to female patients only or to both male and female patients; the term covers both options. In fact, some breast cancer trials are done only in women, some will include both men and women. Since German does not have a gender-neutral term for 'patient', to pick an adequate translation the translator will have to find out whether the trial involves just women or both men and women: if the study is done in female patients only, the correct term would be 'Patientinnen mit Brustkrebs' [female patients with breast cancer]. If the study includes both men and women, the translation would be 'Patientinnen und Patienten mit Brustkrebs' [male and female patients with breast cancer]. This means that *implicit* information in the English text will have to be made *explicit* in the German text.⁵

4 Jan Geißler [1], page 6.

5 Even though the politically correct way in German would be to use both the female and the male form (Patientinnen und Patienten, as suggested in the text) in studies involving men and women, in practice, this approach is not very reader-friendly and is therefore often abandoned. For convenience sake, the male form is understood to include the female form. It is therefore quite acceptable in German to use the *male* form only ('Patienten') in studies that *involve both men and women*. It would *NOT* be acceptable, however, to use the *female form only* ('Patientinnen') in studies that also include male patients (such as breast cancer studies in men and women). Discussion about this convention, of course, is ongoing from a gender-equality point of view.

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While in English, medical terms such as pneumonia, appendicitis or colon cancer are readily understood by lay people, in German, the equivalent Latin- or Greek-based medical terms (Pneumonie, Appendizitis, Kolonkarzinom) are reserved for communication between medical professionals. These ‘hard words’ are considered ‘doctors’ speak’ and typically form a language barrier between the ‘educated’ doctor and the ‘uneducated’ patient. Most (but not all) of these Latin- or Greek-based medical terms also have a German-based equivalent (Lungenentzündung, Blinddarmentzündung, Darmkrebs), which should be used for German ICD translation [Box 3].

Culture-related challenges

Most culture-related challenges in ICD translation will come up due to differences in the health care systems in the source (English) and target (German) cultures. Examples include:

- Concomitant medications: Drugs mentioned in the source text are not available or come in different strengths, formulations or drug combinations in Germany.

Box 3—Medical terminology and target audience

In this article, we have defined the target audience of ICDs to be ‘patients’, who are assumed to be ‘lay people’. However, the seemingly homogenous target audience ‘patients’ can be very diverse. Let’s look at two different settings with regard to the ‘target audience’:

Patients with an acute, life-threatening infection.

These patients will neither have the time nor the opportunity to educate themselves about their disease. They are likely to have been rushed to the hospital with no access to the internet or other sources of information. This means that their state of knowledge about clinical trials as such and about their condition is limited: These patients are unlikely to be familiar with the medical terminology associated with their disease. In terms of ICD language, this means that extra care is needed to explain the disease-specific technical terms and procedures in lay language.

Patients with a chronic disease. Let’s imagine patients with a chronic disease such as metastatic cancer on the other hand. Most likely, they were diagnosed years ago. If their cancer stage is advanced, they will typically have gone through a series of therapies and medical procedures before. In the process of trying to cope with their disease, they will perhaps have turned to the internet, joined patient advocacy groups and read medical articles and books. So, these patients can be expected to have gained detailed, specific medical knowledge about their disease and the treatments available. In this setting, the use of disease-specific technical terms will be much more acceptable and even appropriate.

- Different roles of institutions, such as ethics committees: Because ethics committees in Germany cannot decide on the participation of study participants at individual study sites, the sentence in the original “study enrolment of patients with XYZ disease is at the discretion of the sponsor and Institutional Review Boards/Ethics Committees at participating study sites” needs to be culturally adapted.
- Terms such as ‘assisted living facility’ or ‘respite care’. These concepts may be difficult to translate because they are not institutionalised in the same way in the target culture.
- Different roles and functions of health care professions: For example, there is no equivalent in Germany for ‘nurse practitioner’ or ‘physician assistant’. Also, the role of the psychiatrist is different in Germany from for example in the US.
- Another translation challenge can come up with units: An LDL level of 3.35 mmol/L does not convey any meaningful information to a German patient unless the expression is converted to the culturally adequate German equivalent of 130 mg/dl. The expression ‘a quarter-sized red patch of skin’ (i.e. a patch of skin the size of a US 25-cent coin) finds its culturally suitable German translation in the idiomatic and equally graphic term ‘Zweimarkstück-großer Fleck’ (a skin patch the size of a 2 deutschmark coin).⁶

When the translator encounters these culture-related translation challenges, he or she will often have to consult the sponsor. Together, the translator—who is the expert on the cultural issues at hand—and the sponsor—the expert on the study specifics—will have to find appropriate solutions for the necessary cultural adaptation in the target text.

With all translation challenges resolved, the German translation is now ready to go through the next phase of the ICD production process—localisation.

Localising the ICD

The next step in the ICD generation process is what I call ‘localisation’, a term that originated in the computer industry. What do I mean by ‘localisation’ in the context of an ICD? Today, the requirements for adequately informing prospective clinical trial participants are firmly enshrined in international laws and regulations, including the World Medical Association Declaration of Helsinki, the ICH Guideline for Good Clinical Practice and European Directive 2001/20/EC. In addition, industry standards such as standard operating procedures (SOPs) and policies are in place to ensure implementation of these legal provisions and to safeguard patient rights. All of these legal and

⁶ Interestingly, the term ‘Zweimarkstück-groß’, being an idiomatic expression, still refers to the old currency deutschmark; a similar idiomatic expression using ‘Euro’ does not exist.

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> ethical aspects are fully covered in the core ICD template prepared by Pfizer's global Clinical Research Unit.

ICDs used in Germany additionally will need to satisfy the regulatory requirements laid down in the specific German laws and regulations such as the German Medicines Act, the German GCP Ordinance, the German Data Protection Act, and the German Infection Protection Act. Appropriate incorporation of these local legal aspects into the ICD has to be ensured during localisation.

Pursuant to the German Medicines Act, mandatory subject liability insurance has to be taken out by the sponsor of any clinical trial conducted in Germany. The law is very specific about the scope and nature of this insurance. Information about the insurance must be communicated to the patient in the ICD. The German Medicines Act also requires that "trial participants shall be informed of the purpose and scope of the recording and use of personal data, especially medical data". To satisfy this requirement, the law's relevant sections on the use of personal data (together with additional requirements laid down in the German Data Protection Act) are incorporated into the German consent form.

Very conveniently, recommended standard language for these legal aspects is available from the *Working Party of the German Ethics Committees*, a joint committee of ethics committee representatives. Wherever possible, this recommended wording from the ethics committees is used in our ICDs, not least because doing so is likely to ease the ethics committee review process and shorten application turnaround times.

Other German legal requirements affecting the generation of ICDs include those laid down in the Infection Protection Act, which requires certain infectious diseases or detected pathogens to be notified to the competent health authorities, among them HIV (anonymous notification) and hepatitis (notification by name). In studies where such notification is likely to arise, e.g. when the protocol includes testing for the relevant pathogens, the patient will have to be informed accordingly.

Customising the ICD

With the localisation step completed, we can move on to what I call the 'customisation' step. This is the final step in the ICD generation process. Its aim is to ensure that all the requirements on the ICD wish list outlined at the beginning of this article are satisfied. Thus, to ensure a clear structure, every ICD contains an upfront table of contents which includes a short summary of each ICD section. This helps patients navigate through the document and quickly find the decision-making criterion that is most important from *their* point of view. For a better overview, we make ample use of bulleted lists. We use coloured boxes and icons to highlight important information. The document

will be carefully edited for shortness, stripping it of any duplicate information and summarising details where this is adequate and possible.

In addition to using lay terms for any medical information, the whole document is screened for other technical terms that need to be explained or 'translated' into lay language. Such terms include 'study site', 'investigator', 'adverse events', 'Phase II', 'randomisation', 'double-blind', etc. Next, extra information will be added, e.g. about the approximate length of the study visits, hospital overnight stays and payment of travel expenses to address the patients' need for practical detail. Sometimes only minor changes are needed to improve clarity: while a study period of 77 weeks seems somewhat confusing, 1 ½ years is a duration any patient can relate to. Similarly, patients are likely to be at a loss (and reminded of those dreadful math lessons back in childhood) when they are asked to drink "2000 ml of liquid before the test"; asking patients to drink "2 litres of liquid", however, will be readily understood and easily followed.

After a thorough internal review and approval process, involving two colleagues independently checking the document for completeness, consistency, and clarity and for compliance with the protocol, relevant regulatory provisions and internal SOPs, the ICD is ready to go out to the ethics committee and, eventually, to the patient.

Summary

As a translator and medical writer, I deal with a great variety of fascinating texts, ranging from highly technical documents, such as autopsy reports, to glossy marketing brochures. Given a choice, my favourite is to write patient informed consent documents for clinical trials. Why? During our collaborative effort with patient representatives it became clear that a well-structured and comprehensible informed consent text truly supports patients in making a decision about their treatment options. So, if I use my best skills both as a translator *and* a writer—in-depth knowledge about language, culture and translation techniques, creativity and experience in text organisation—combined with my know-how about the clinical trials process, and put it into generating a patient-friendly ICD I can really make a difference in somebody's life. Isn't this a great reward for making 'just this extra bit of an effort'?

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Translation resources



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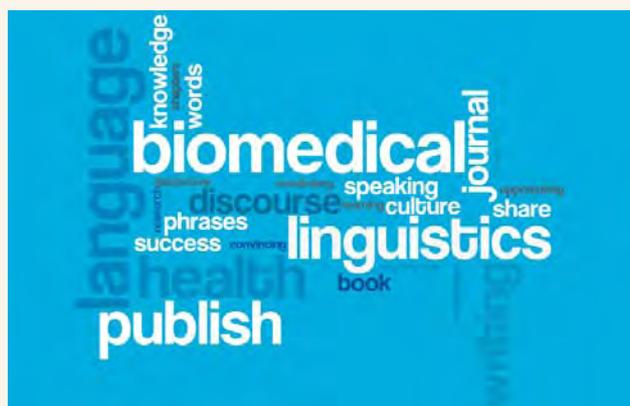
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