Volume 27 Number 3
September 2018

Medical Writing

Editing

Also in this issue...

- Anonymisation: A new challenge for medical writers
- Reports from the spring conference in Barcelona
- Updates on regulatory public disclosure

EMWA EUROPEAN MEDICAL WRITERS ASSOCIATION

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Medical Writing is the official journal of the European Medical Writers Association (EMWA). It is a quarterly journal that publishes articles on topics relevant to professional medical writers. Members of EMWA receive *Medical Writing* as part of their membership. For more information, contact mew@emwa.org.

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Medical Writing

Editing

Medical writing is an umbrella term that involves not only writing but also editing and translating medical texts between different languages. While some of us will work specifically as editors in medicine or science, editing skills are paramount to medical writers, translators, and communicators in general.

The success of the Writing Better Workbook published in the spring 2017 issue of *Medical Writing* (Volume 26, Issue 1 at http://journal.emwa.org/writing-better/) underscored the importance of improving both our writing and editing skills as medical writers. With this goal in mind, we put together this issue on editing including articles that cover the essential aspects of editing and practical tips to implement on a day-to-day basis. The first articles are organised in a workbook style including exercises on proofreading, macroediting, and editing for non-native speakers of English. The following offer practical tips on microediting, editing after translations, giving feedback to medical writers, and the implications of a certification in editing. We brought together experienced editors from different fields who contributed with state-of-the-art information on each of these topics.

Naila Zaman opens this issue with a step-by-step guide to become a bullseye proofreader with the ability to identify and remedy grammatical, typographical, and spelling errors in medical content. **Krithika Muthukumaran** puts emphasis on "How clear is the story?" to ensure clarity and flow while keeping in mind the intended aim of the article and readership making the story powerful and effective. EMWA's workshop leader **Kari Skinningsrud** covers the challenges and good practices when editing texts written by non-native speakers of English. In the following article, the highly experienced **Barbara Grossman** and **Marian Hodges** put together a structured and methodical approach to ensure both consistency and accuracy in delivering a high-quality product in their article "Microediting: Details matter." **Laura Collada Ali, Paz Gómez Polledo,** and **Claire Harmer** talk about "Revision: Parameters and practices within the translation industry" and how these practices are paramount and differ from merely editing in English. **Bridget Pfefferle** highlights the importance of giving feedback as an editor and practical insights to leverage this soft skill. Finally, **Lillian Sandø**, one of the few BELS-certified EMWA members, writes about her experience with the exam and the relevance of this certification for both medical writers and editors.

GUEST EDITOR

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We put together this issue on editing including articles that cover the essential aspects of editing and practical tips to implement on a day-to-day basis.

In a similar fashion to excelling at our writing skills, editing and its nuances should be at the core of our working habits as medical writers. Every article included in this issue tackles a different aspect of this practice. However, I would like to highlight one that, in my opinion, should be at the top and many times is underestimated: keeping our audience in mind at all times. In academia, most often we aim to just get our results out there, and that's why most academic papers are incredibly long, complex, and hard to read. One of the primary skills that we should train when transitioning from academia to medical writing is the ability to make complex content readable and tailored to our target audience, whoever that might be.

Finally, we nowadays have technological development on our side with tools like Grammarly (among others) that help us improve our writing skills and even check for plagiarism while we write or edit. Tools such as these are widely available online and facilitate writing and editing. However, we should not rely solely on them but use them as learning resources. Our writing and editing skills should become a habit to the point that we make use of our bullseye even when writing emails, putting together a presentation, or submitting our résumé for a job application.

A great medical writer never rests. Enjoy this issue!

President's Message

Dear EMWA Members,

In the apparently quiet time after the spring conference in Barcelona, much has been going on in the background of the association's life. Before moving to the details of our activities, I would like to mention that two veteran members of the Head Office, Candi Bond Gunning and Sophie Brocklehurst, ended their work for EMWA after the conference in Barcelona. They played an important role for our successful conferences in the past, and we will miss them at the registration desk in the future. On behalf of the Executive Committee, the past Presidents, and the EMWA volunteers, I would like to warmly thank Candi and Sophie for their valuable support and great collaboration, as well as our enjoyable time together.

Recently we had to say goodbye to another person, long-time member Nicky Dodsworth, who was very committed to EMWA; she enriched our educational programme with her knowledge and our hearts with her bright personality. In this MEW issue, we dedicate some space to remember her in a more personal way with comments from members who knew her well.

Turning now to the activities of the past 3 months, let me mention just a few items.

- We have been planning the autumn conference in Warsaw, assessing new workshops, working on our presence on the social media and in the web, streamlining the EMWA Newsblast, and enhancing the webinar programme. Right after the conference in Barcelona, a number of volunteers began planning the symposium and the expert seminars for the next spring conference. They have identified various relevant topics and are contacting potential speakers from regulatory authorities, industry, and international societies. The committees and groups involved have recently grown to ensure well-balanced expertise and task sharing.
- There have been some calls for volunteers over the last few months to seek support in various areas of EMWA: I was really pleased to see that members with varying levels of experience have shown interest. Bringing together volunteers with different backgrounds, levels of experience, and ideas in our sub-committees is a crucial way to enhance and tailor what we offer to our members.
- In line with this aim, I am currently exploring topics and needs that could be addressed by our experienced members, the holders of the Nick Thompson fellowship, and our past presidents. I strongly believe that EMWA should benefit from their expertise and knowledge of the association, as well as gather suggestions from them with regard to new initiatives and offerings for experienced members. Establishing working groups within EMWA can more effectively lead to informed discussions on specific topics and new initiatives.
- We are working in parallel on our relationships and collaborations with other international professional associations. The Joint Position Statement has been translated into two new languages (Russian and Farsi), an important step forward to further raise awareness about the role of professional medical writers. The role of EMWA within the medical communicators and medical writers community has been increasingly recognised over time; besides the Joint Position Statement, we have recently been in touch with other organisations with regard to other possible areas of cooperation and expert groups. I look forward to reporting on these exciting projects soon!
- The Ambassador programme is being carried on at a steady pace and we are increasing our network with universities, career events, and meetings for medical communicators.

Establishing working groups within EMWA can more effectively lead to informed discussions on specific topics and new initiatives.

As you see, there is much to do and support is continuously needed!

Let me conclude my message with a warm invitation to our autumn conference. The full conference programme is online and the registration is open. See you in Warsaw!

Tiziana von Bruchhausen
President@emwa.org

EMWA News

Membership announcement

SECTION EDITOR

Maria Almeida
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We recently announced with deepest sadness the loss of Nicky Dodsworth, a long-term EMWA supporter and workshop leader. Nicky enriched our educational programme with her knowledge and our hearts with her bright personality. We are thankful for her valuable contribution, the good memories, and the friendships that developed at EMWA. Nicky will be truly missed by her EMWA friends. Here are a few memories of Nicky from EMWA members:

Marian Hodges, chair, EMWA Professional Development Committee

"Very good workshop. Good energy, great interactivity." "Workshop was very well delivered, interesting, informative, and Nicky made the 'dry' nature of the subject of quality more exciting." These comments, typical of those from many participants in Nicky's workshop, demonstrate how very fortunate EMWA was to have her support for our education programme. She imaginatively and engagingly shared her expertise with fellow medical writers in her workshop on Quality Awareness in Clinical Study Report Development. This was a valuable part of the programme since she first presented it in 2010, and many EMWA colleagues have benefited from learning from her extensive knowledge and experience.

Sam Hamilton

Nicky gave me my first break in medical writing. She was my manager for several years in the "noughties", when we worked together in a large CRO; Nicky and I soon became firm friends. She was very funny and kind and we stayed in touch. After we parted ways at work, we looked forward to catching up in person at EMWA conferences – I often heard her from across the room before I saw her – laughing and charming those around her. She was a beautiful person, inside and out, with her mass of blond curls, bubbly persona, and her warm way with people. She was always so interested in my family – both my children were born when I worked for her, and she and my husband Paul got on famously. As well as her successful multidisciplinary clinical research career – most recently in QA – Nicky freely gave her time and expertise as a member of her local health authority's research ethics committee. She was an energetic "giver" in many other ways too in her local community, especially after her beloved twin boys, Sam and Tom – now in their mid twenties – left home. Her devoted husband, Steve, accompanied Nicky to the Cyprus conference, where Paul and I, along with Nicky's many other EMWA friends, enjoyed a lively evening in their company. Happy memories. Nicky was so full of life; she was taken far too soon from her family and friends. I, like so many others, will miss her so much.

Debbie Jordan

I am sure many people who have met Nicky will have the same first impression of her as I had – a bright bubbly person with a permanent smile on her face, an infectious laugh, and a mass of gorgeous blonde hair! She was always chatting and laughing and she would get on well with everyone and she always took the time to be friendly and to get to know the people around her. However, as well as being an incredibly nice person she was also extremely knowledgeable. She spent the early part of her career in QA as an auditor, before moving out for a while into the medical writing field, where she ended up heading up the medical writing group in a large CRO, working with all sorts of documents as well as handling many large submissions. She also spent a lot of time training and mentoring other writers, all of whom I am sure learnt a lot from her since she was a natural trainer with real empathy. However, her natural calling was QA so she returned to this field, gradually working her way up to become the Vice-President for QA, but she couldn't break her bonds with medical writing and was a regular EMWA trainer teaching on the QA aspects of clinical research.

On a personal note, Nicky took me on as a freelance writer when she was Head of Medical Writing at PRA and she provided me with a lot of work in my early years as a freelancer, both directly and through recommending me to her colleagues, for which I will always be grateful. However, what I remember most about those days is whenever I had to attend a meeting at the company main office she would always make time to come out and invite me into her office for a cup of coffee and a chat about all sorts of things – family, children, politics, life, and occasionally a bit about work too (and on several occasions she made me late for the meetings I was there to attend!). The last time I saw Nicky was at the railway station in Birmingham after the EMWA conference in spring 2017. All the workshop leaders had been given a large green umbrella as a thank-you present for running our workshops and I remember seeing Nicky coming along the crowded platform with a suitcase, a laptop bag and a handbag and trying to avoid hitting people with this large green umbrella that she had tucked under her arm. She caught my eye and turned round and smiled, side-swiping some poor man with this umbrella that had us both in stitches laughing (when he was out of earshot of course!). We had a lovely chat and catch-up while waiting for the train, and I feel very sad that I won't get to do so again. Our conferences in the future will certainly be poorer without her laugh, her smile, and her infectious personality.

EMWA webinars coming in the near future

EMWA's outreach for its freelance members: activities and resources

September 28 at 14:00 to 15:00 CET

Satyendra Shenoy

This webinar aims at informing attendees on facilities and resources available to EMWA members who are freelancers. This includes introduction to the Freelance Business Forum at the conferences, OOOO section of MEW, and online resources. Moreover, attendees will be provided a few pointers on how they can also contribute to EMWA.

Veterinary medical writing – same but different: Introduction to medical writing for veterinary medicinal products

October 30 at 14:00 to 15:00 CET

Sandra Götsch-Schmidt – DREHM Pharma GmbH

Have you ever considered writing on veterinary topics? This introduction webinar will point out the similarities and differences that you might face when writing about veterinary medicinal products.

Personal branding through social media for medical writers

December 6 at 12:00 CET

Evguenia Alechine

For many scientists and medical writers, personal branding and effective use of social media to promote your own business or freelance services is a still a 'black box.' Although most have a basic understanding of Facebook, Twitter, and LinkedIn, few understand how to leverage these technologies (and other up-and-coming networks) to positively impact their own business. This webinar will show medical writers the necessary tools and resources to feel comfortable, confident, and enthusiastic about personal branding.

EMWA's webinar series

Full details of EMWA's webinar programme are available at https://www.emwa.org/training/emwa-webinars-programme/. Webinars may be recorded or live. For live webinars, you only need to register and then connect to our webinars platform on the webinar date at the above address. A recording will be available shortly after the event in the Archive section. Nevertheless, we advise you to participate to allow you to ask questions and contribute the discussion. For recorded webinars, we encourage you to send us any questions by the date indicated so that they can be answered. For further information about webinars contact webinar@emwa.org.

New member benefit: Discount on PerfectIt licenses

A full list of EMWA member benefits is available at https://www.emwa.org/members/membership-benefits/.

The latest EMWA member benefit is 30% off a PerfectIt licence. PerfectIt helps deliver error-free documents. It improves consistency, ensures quality, saves time and helps to enforce style guides. PerfectIt is used by thousands of editors around the world because it lets editors control every change, giving you the assurance that documents are the best they can be. There's a 14-day free trial available from http:// www.intelligentediting.com.

EMWA members receive a 30% discount on a single license of PerfectIt. To claim the discount, logged-in EMWA members can use the special link in the EMWA Member Offers page. There you can also avail of a number of other discounts exclusive to EMWA members.

Joint Position Statement – Russian translation now available

EMWA is involved in the translation of the Joint Position Statement on the Role of Medical Writers (https://www.emwa.org/about-us/position-statements/joint-position-statement-for-professional-medical-writers/). This statement was prepared together with our colleagues at the American Medical Writers Association and the International Society for Medical Publication Professionals in order to set out ethical standards for medical writers in developing scientific and medical publications. We are now spreading the word among non-native English speakers in Europe and beyond.

The position statement has now been translated into Russian and can be accessed by clicking on the relevant language tabs from the English language Joint Position Statement page (https://www.emwa.org/about-us/position-statements/joint-position-statement-for-professional-medical-writers/russian/).

Updated NewsBlast instructions to contributors

Contributions to the NewsBlast should be sent to **pr@emwa.org** by the 22nd of each month so that it can be published in the following month. Updates should be concise (150-200 words) and can be included on one of the EMWA webpages.

The full archive of EMWA NewsBlasts can be accessed at https://www.emwa.org/about-us/emwa-news/.

Honing your proofreading skills

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Abstract
As part of their role, medical writers and editors are expected to be excellent proofreaders with the ability to identify and remedy mistakes such as grammatical, spelling or formatting errors. This article details the steps that can be taken with each proofread to assist you in becoming an efficient and adept proofreader. The accompanying exercises provide examples of common mistakes and inconsistencies you may come across when editing and proofreading scientific content.

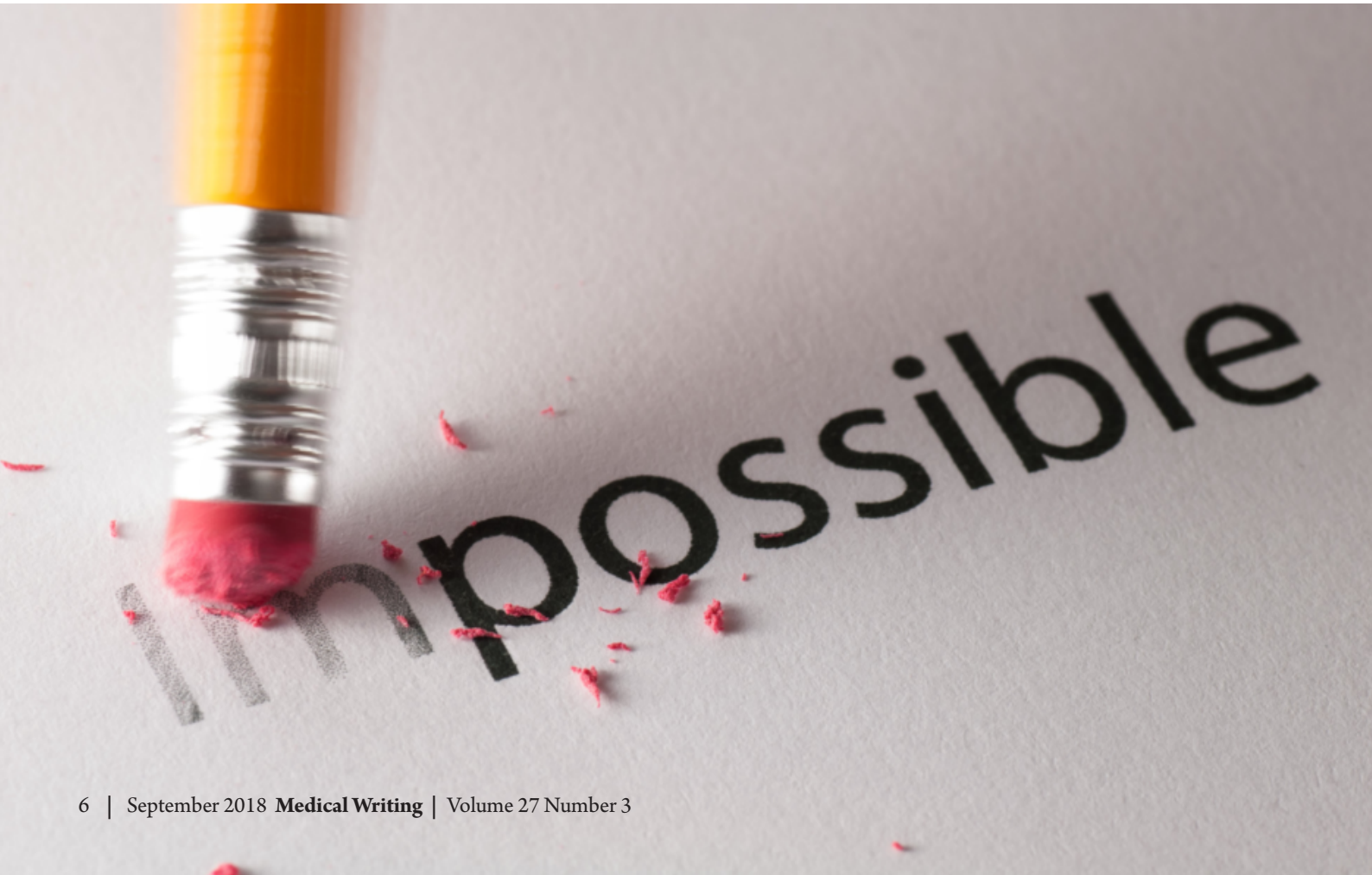
Medical writers and editors play an important role in the field of scientific publishing and communications. While the responsibilities between these can differ, all medical writers and editors have skills in common – for example, they must have a strong grasp of the English language and an eye for detail. A large part of many writing and editing roles involves the ability to proofread and edit text to a high standard. Whether you are editing a manuscript or abstract for a journal, a poster for a conference, or a sales aid aimed at healthcare professionals, being able to pick out and correct errors easily and efficiently is key. After all, a proofreader is the last line of defence against glaring spelling errors, inconsistencies and awkward grammar. A well-edited piece of content can, among many other factors, determine its success.

Online articles and books provide tips on the common errors to look out for while proofreading. While these are useful, particularly for new writers and editors who are just beginning their career, memorising lists may not be the most effective way to learn. This article is aimed at both new and experienced medical writers and editors alike, detailing the steps to take when proofreading to allow you to hone your skills and become an efficient proofreader.

Before proofreading
Prior to proofreading anything, there are steps that can be taken to ensure you are set up to maximise your efficiency and ability to spot and correct errors.

Limit distractions
Editing and proofreading requires high focus and concentration. Before beginning, ensure that you are in an environment that fits your style of working. This will vary between individuals; some may prefer to be in complete isolation, while others will thrive in a busy coffee shop or other areas with background noise.

Know your medium preference
Another important step before beginning is to know which medium – electronic or hard copy – you prefer and which you work best with. Some



people may prefer the more traditional style of using hard copies, as it is often easier to see errors in formatting (i.e. different font sizes or styles), colour differences, and crop and bleed marks. Others, however, will prefer proofreading digitally because of built-in features of software, such as spelling and grammar checkers and *Find & Replace* functions, which allow for swift correction of common errors. Using a digital format also aids in the detection of subtle differences in line and paragraph spacing that is not easily discerned through printed copy.

Although it will not always be possible to use the medium which you work best with, as different organisations and clients work differently, it is useful to have both. Once you have finished proofreading, I recommend doing a final check in both mediums – i.e. if you used a digital copy, print it out at the end to identify anything you might have missed; conversely, if you proofread a hard copy, open the digital version and check for errors such as line spacing and subtle font size differences that will have been difficult to notice from a printout.

Know the context

Are you proofreading a manuscript in which formal and technical language is more likely, or a conference poster aimed at healthcare professionals where the wording is more engaging and marketing terms may be used to sell the piece? Is the target audience only those who are native English speakers or is it also intended for non-native speakers? Before you begin, get as much information as possible on the context of the document you are checking. This will help you to make sure that the style and tone remains consistent throughout and is not inappropriate for the intended audience – for example, idioms should generally be avoided in texts where the audience may include non-native English speakers.

During proofreading

You are ready to proofread, but what can you do to assure yourself that nothing is missed?

Read aloud but also silently

Reading silently has the advantage of making it easier to check for issues with readability and sentence flow; however, silent reading may also encourage skimming of text and unintentionally skipping over small errors as your brain fills in the gaps. Reading aloud, on the other hand, forces you to read more slowly and without skimming text, allowing you to catch the errors you might have missed while doing so silently. But what about punctuation? As punctuation marks are silent, reading aloud will not help with finding any incorrect uses of full stops, commas, exclamation marks and so on.

There is therefore no *better* way to read a piece of text when proofreading. I recommend doing both to ensure you are able to identify as many errors as possible. Over time, you may find a preference for one over the other but, generally, it doesn't hurt to do both.

Read the sentence backwards and in isolation

As with small errors that can go unnoticed when reading silently, your brain will fill in the gaps from context when reading forwards and encountering misspelled words. While the sentence will not make sense if you read it backwards, it will help pick up spelling mistakes. Similarly, reading a sentence or paragraph in isolation will assist in detecting issues with readability or sentence structure. This can be done electronically by adding a return or paragraph break in between sentences or by increasing line spacing. If using a hard copy, a ruler or piece of paper to block out text is also effective.

Make notes or a checklist

As you go along, make notes or a checklist of anything you're not sure about or need to check later. This is especially useful if you are editing or proofreading to a specific style guide; moving back and forth between the style guide and the content can take you out of the focus of the latter, so it can often be more useful to note things down as you go along so that you remember to check thoroughly later. This will also prevent you from correcting something that doesn't need to be corrected – for example, when proofreading a manuscript, imagine that the author uses *qd* in both the Abstract and Introduction but in the Methods section switches to using *once daily* instead. Rather than correcting each time as you go along, you can note it down and check against the style guide later. It may very well state that *once daily* is the correct form to use, so correcting to *qd* throughout because it was used first would not be the correct approach.

Compare the content to a similar piece of work

When checking visual content – such as a conference poster or a galley proof – there can often be styling inconsistencies where it is not clear from the style guide which is correct; for example, the way the authors' names and affiliations are written, or the size of a logo. Where possible, compare it to a similar piece of work. For a conference poster, you can check against the poster for the same meeting that occurred in a previous year; for a galley proof, you can check it against a published article in the same journal.

Final checks

Once the bulk of the proofreading is out of the way, it is always good to do a final check of the work to uncover any errors that might have been missed.

> Prior to proofreading anything, there are steps that can be taken to ensure you are set up to maximise your efficiency and ability to spot and correct errors.

Check for weird fonts, colours and sizing

Do a quick scan of the work and double-check anything that *looks* odd or inconsistent. There may be subtle errors, such as black versus dark grey font colouring, that were not caught earlier.

Use digital tools

Features of digital software such as grammar and spelling checkers are useful tools as part of final proofreading checks; however, these are not perfect and should not be relied upon. They will not be able to discern between homophones (e.g. lesson vs lessen, peak vs peek, whether vs weather, etc.) and are not reliable when checking for grammatical errors. At this stage, if all the aforementioned steps have been followed, there should be very little – if anything at all – for these checkers to correct.

Take a break

Reading the same thing repeatedly will make the brain skip words and phrases, reducing your ability to identify errors. Taking a break and coming back to it with *fresh eyes* can be more effective. A day or more away is ideal though not always possible because of deadlines, so even as little as 30 minutes away can help – go for a walk in this time or read a book. The key is to take your

brain's focus away from the document. If using an electronic copy when proofreading, changing the look of the content (by amending font size, colour, and sentence or paragraph spacing) will also trick your brain into thinking it is looking at something unfamiliar when you come back to it. It may also be preferable to work in short blocks of time, as concentration and focus can wane over longer periods.

Summary

Proofreading is a learning process. Over time, as you gain experience with different types of content, you will be aware of the common errors to look out for and the techniques you can use to ensure you are proofreading to a high standard. The following exercises put this into practice, providing examples to test what you have learned in this article. I hope the processes and tips provided here will help you on your journey to becoming a more efficient and adept proofreader.

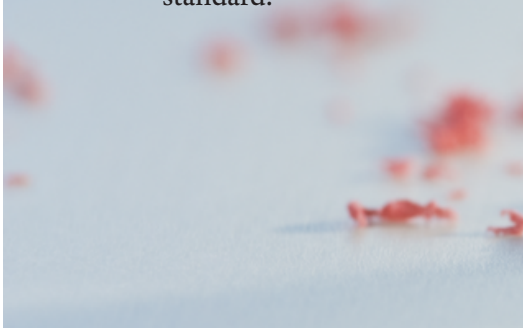
Conflicts of interest

The author declares no conflicts of interest.

Author information

Naila Zaman started her career as an Editorial Assistant for a scientific journals publisher before moving on to work in educational and healthcare publishing. With over 5 years of editing experience, Naila has participated in training colleagues on how to edit and proofread content for high accuracy and quality.

Over time, as you gain experience with different types of content, you will be aware of the common errors to look out for and the techniques you can use to ensure you are proofreading to a high standard.



Exercises

Exercise 1: Find the error in each sentence

Instructions: Circle the error in each sentence. There is one error per sentence.

1. These results indicate that Drug X is more effective then placebo in reducing symptoms in patients with diabetes.
2. We showed that this method is more percise than the current standard diagnostic tools.
3. Tools are available for physicians to assist them in the management of the patient and they're disease.

Exercise 2: Find the errors in each sentence

Instructions: Circle the errors in each sentence. There are multiple errors per sentence.

1. More than ≥50% of patients expereinced treatment-emergent adverse events, the most common of which was headache, nausea and dizziness.
2. Healthy males and women aged between 18 or 35 years with a body mass index of <30kg/m^2 and total body wait of 50 kg were enroled into the study.
3. The incident rate ration (IRR) for diarrhia was 0.91 (95% confidence interval [CL]: 0.21–3.22) for treatment with drug A, 0.90 (95 CI: 0.63–1.11) for drug b, and 2.85 (95% CI: 0.65-8.35) for drug C.

Exercise 3: Find the inconsistencies in the text

Instructions: The following paragraph pairs are taken from the same manuscript. Identify and circle the inconsistencies between each paragraph.

Manuscript 1:

Paragraph 1: This was a Phase 3 multicentre trial to determine the safety, efficacy and tolerability of Drug X in patients with chronic obstructive pulmonary disease. Patients aged 18-54 years were assessed prior to study start and at Month 48. The primary endpoint was the proportion of patients with reduced frequency of exacerbations with Drug X compared with placebo.

Paragraph 2: This phase III multicenter trial found that patients receiving treatment with drug X had a reduced frequency of exacerbations compared with patients who received only placebo. The primary end point was reached in all treatment groups, except for those in the 40–54 yrs age group.

Manuscript 2:

Paragraph 1: Overall, 200 patients were free from relapses at Month 12 after initiation of the study drug. This proportion was highest in the subgroup of patients that received twice-daily dosing (n=101; 82.5%) followed by patients receiving once-daily dosing (n=99; 73.3%). The mean relapse rate (standard deviation [SD]) decreased significantly from 1.35 (0.77) before study drug initiation to 0.23 (0.72) after 12 months of treatment, representing a reduction of 83% (p<0.0001).

Paragraph 2: The reduction in the number of relapses was significant in all treatment arms, with the highest reductions observed at month 12 in people who received the study drug b.i.d. (N= 101; 86.3%; P < 0.001).

Answer key

Exercise 1: The errors are underlined.

1. These results indicate that Drug X is more effective then placebo in reducing symptoms in patients with diabetes.
2. We showed that this method is more percise than the current standard diagnostic tools.
3. Tools are available for physicians to assist them in the management of the patient and they're disease.

Exercise 2: The errors are underlined.

1. More than ≥50% of patients expereinced treatment-emergent adverse events, the most common of which was headaches, nausea and dizziness. (5 errors)
2. Healthy males and women aged between 18 or 35 years with a body mass index of <30kg/m^2 and total body wait of 50 kg were enroled into the study. (5 errors)
3. The incident rate ration (IRR) for diarrhia was 0.91 (95% confidence interval [CL]: 0.21–3.22) for treatment with drug A, 0.90 (95 CI: 0.63–1.11) for drug b, and 2.85 (95% CI: 0.65-8.35) for drug C. (6 errors)

Exercise 3:

The inconsistencies between both paragraphs in each manuscript are detailed below.

Manuscript 1:

- Phase 3 vs phase III. The latter is in lower case and uses Roman numerals instead of Arabic numerals.
- Multicentre vs multicenter. "Center" is the US English spelling, while the first paragraph uses UK English spelling.
- Years vs yrs. The second paragraph uses the shorthand "yrs" when it was written out in full in the first paragraph.
- Hyphen vs en dash. In the age range in Paragraph 1, a hyphen is used but in Paragraph 2 an en dash is used instead.
- Endpoint vs end point. Paragraph 1 uses the correct spelling while the second paragraph adds an unnecessary space between the words.
- Drug X vs drug X. Generally, drug names will be in lower case unless the product is a brand.

Manuscript 2:

- Month 12 vs month 12. In the first paragraph, the first letter for month is capitalised as this is referring to a specific time point in the study. The second paragraph is in lower case, which is inconsistent but also incorrect.
- Twice-daily vs b.i.d. Although the meaning of these is the same, interchanging between them can be confusing for readers so it is preferable to use one style throughout.
- Patients vs people. The first paragraph uses patients, while the second refers to them as people. Although sometimes interchangeable depending on the context of the study, it is usually better to avoid switching between identifiers as this could be confusing to readers.
- Style of presenting n/N values. In the first paragraph, there are no spaces between the n and the equals sign and the value when referring to the number of patients, while the second paragraph has a space after the equals symbol. The way that this is written will depend on the style guide, but usually there are no spaces. In addition, a capital N is used to refer to the overall population whereas a lower case n denotes a subpopulation; therefore, in this instance, the "N=" in Paragraph 2 is incorrect as the number of patients is from a specific subgroup only and not the overall population.
- P value style. Similar to the above, there is no one correct way to present p values and styles will vary. However, in the absence of a style guide, the same style should be used consistently throughout the manuscript.

How clear is the story?

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Abstract
Editing in medical writing is an important task that requires good scientific background as well as soft skills like critical thinking and attention to detail. Other than correcting typographical and grammatical errors, a medical editor has to ensure clarity and flow of articles, keeping in mind the intended function of the article and readership. The given information should carry the story forward, have a good lede, be interesting, logical and complete. What is a lede? In journalism, lede refers to the opening sentence/paragraph of an article that is designed to capture the attention of the reader and create enough interest to continuing reading the full story. The sentences and paragraphs can also be rearranged for the story to be effective. It is vital to pay attention to the specialised terminology and check if adequate explanation is given when necessary. Finally, take a step back, have the audience in mind and look at the big picture.

Introduction
Medical writing involves science, critical thinking and creativity. Good writing involves clear and effective communication of information whilst keeping in mind the target audience and purpose of the article. The target audience could be regulators, patients, caregivers, general audience, or health professionals.[1] Once the writing is done, it is the editor's role to check whether the content is tailored to the target audience and recognise any errors or missing information. An editor has to do much more than just eliminating spelling and grammatical errors. Similar to the writer, the editor should also possess the ability to understand the purpose of the given article, the target audience, a thorough knowledge of the subject and scientific accuracy.

As an editor, first read the article entirely without making any corrections even when you notice any obvious error. Then take a step back and think if the article overall has a clear structure and meaning.

The beginning and the end
In academia, when we communicate, we are taught to start with the background information. However, when writing news articles and blog posts, we have to follow a classic newspaper style, also known as the inverted pyramid style. The most important point and its implications should be the opening paragraph. It draws attention to the article and creates enough interest in the reader to finish reading the article. The lede can be a summary of the main ideas, introduction of a character, a story, a quote, or what is new.

For example, in this blog post[2] I submitted last year, I start with a story in order to create curiosity and get the attention of the reader.

> *The neighbours describe how anxious they would get whenever they heard Mrs Amutha, a 70-year-old-lady, as she banged her head on the walls of her apartment and screamed. She suffered from severe headache and facial pain caused by advanced stages of oral cancer, and this is how she dealt with it. Unfortunately, Amutha suffering in pain would be the memory her family would have of her for years to come. This is the state for millions of patients and families across India, as less than 1% of the patients have access to prescription opioids to treat pain even in advanced stages of cancer.*
>
> *This is the reality I was aware of, growing up in Chennai, India. Through my mother, who is a palliative care physician, along with her colleagues and teachers, I have known of the various challenges faced by them with regards to increasing awareness about palliative care among the medical fraternity, availability of opioids for pain relief, and associated healthcare policies.*

As an editor, check to see if the lede is the first sentence/paragraph and not buried in the text.

The last paragraph is remembered most often and hence it is as important as the lede. Ensure it is impactful and contains the idea of the article.

For example, in this article titled "Why is it

taking so long to find a cure for Parkinson's disease", the concluding sentence summarises the key issues discussed.[3] *"Through continued collaboration, and concentration of energy and financial investment into the most promising research areas, there will ultimately be a time when Parkinson's will be a curable disease."*

Facts and references

Editors are responsible for checking the validity of any data presented and should keep in mind the importance of conveying the right information to the readers. Verify that the data are represented accurately and not hyped or understated. Check the facts and make sure they are referenced adequately. Ensure that any point of view and critique is not a personal attack, and instead well researched and written responsibly.

Clarity

Complex concepts do not mean complex sentences. When explaining scientific concepts, the sentences can be simple, interesting, and enjoyable to read. The objective of the writing is to convey information to the reader and not to confuse. Poor communication fails to translate the knowledge or create an impact thereby affecting patients, researchers and clinicians. For example, a study shows that lack of clarity in clinical practice guidelines documents often leads to non-adherence of the guidelines.[4]

Suggestions to improve clarity

- Remove vague words, unnecessary jargon, abbreviations, and clichés.

Example: In the future, with optical tagging or genetic markers, it might be possible to determine whether the source of the cells is within the striatum.

Suggestion: The term *might be possible* is vague, it creates doubt and uncertainty.

Example: Retinitis pigmentosa is the most common cause of inherited blindness, which is characterised by the progressive loss of photoreceptor cells.
Suggestion: Jargon need not be very complicated words, but they make research articles inaccessible to the general public or sometimes even to researchers who do not work in a specific field. In the above example, photoreceptor is a jargon.

Example: MicroRNAs (miRs) are small, regulatory RNAs that are expressed in animals and plants.
Suggestion: Here miR is an unnecessary abbreviation for microRNA, where RNA is already an abbreviation.

Example: Scientists have created a new substance long believed to the be the "holy grail" of chemistry.
Suggestion: "Holy grail" is commonly used to describe something that scientists hope to discover and it is a cliché that can be avoided.

- Use active voice as it is strong and improves clarity.

Example: Microglia responses to traumatic brain injury were analysed.

In active voice the sentence would be "The authors analysed microglia responses to traumatic brain injury".

However, in some cases, passive voice is acceptable. If you want to emphasise the experiment and not who performed the experiment, the above example need not be corrected.

- Use verbs instead of nouns.

We learn to use nouns instead of verbs in academia to sound more formal. But nouns slow down the sentence. Verbs carry the sentence forward, have more impact, and give sentences energy. With verbs, sentences are less complex and more engaging.

Example: This is the first study to examine the distribution of oligodendrocyte-lineage cells, and their proliferation and maturation after traumatic brain injury.
Suggestion: The above sentence contains the nouns *distribution*, *proliferation*, and *maturation* that could take verb form and be written as "This is the first study to examine oligodendrocyte-lineage cells and how they distribute, proliferate and mature after traumatic brain injury".

- Putting the subject close to the verb also helps simplify the sentence.

Example: Our results of attempting to force the brain into an anti-inflammatory state soon after traumatic brain injury (including sustained effects observed at 3 days after a single IL-4 injection) warrant further study of other IL-4 treatment regimes, and of long-term cellular and behavioural outcomes.

Following "results", we have to read through many words and a parenthetical interruption to learn that further study is warranted. This sentence was presented at the very end of a research paper after the methodology and results were already described. Describing future studies would be sufficient, thus removing all the words between "results" and "warrant" further study.

Flow enhances clarity

Article flow is achieved when you proceed logically from one idea to another. This happens both within the paragraph and between paragraphs. When you see that there is missing clarity, it could simply mean that the logic is missing. See if each sentence carries you to the next sentence, include transition sentences that help connect different ideas. One way to make it easier to explain complex science concepts is by using analogies. For example, when explaining the function of the mitochondria in layman's terms, it can be called as the power house of the cell. Words can also be used repetitively to bring clarity.

As an editor, ask yourself the following:[5]

- Does the first sentence of the paragraph describe the main idea?
- Do the following sentences expand on the

main idea and provide more information?
- Is it well researched and with references?
- Is the last sentence a summary of the main idea and/or does it lead on to the next paragraph?

Conclusion

Now go back to the introduction. Check to see whether the article has enough information to support the statements made in the introduction, whether the article is complete, whether there are any holes or unanswered questions, and whether the overall structure of the article makes sense and meets the guidelines.

Conflicts of interest

The author declares no conflict of interest related to this article.

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Exercise: Marco-editing

1. Question: In other words, the drug is able to halt disease progression.
Answer: The drug is able to halt disease progression.
Reason: "In other words" is a cliché, conveys no meaning and can be deleted.

2. Question: Heavy metals contamination of soil is a cause of serious concern due to the potential health impacts of consuming contaminated produce.
Answer: Heavy metals (copper, zinc, lead, manganese, nickel) contamination of soil is a cause of serious concern due to the potential health impacts of consuming contaminated produce.
Reason: Heavy metal is a jargon as all readers might not know what metals come under this classification and not all heavy metals are toxic. In which case the editor should ask the writer to include the heavy metals that are part of the study and commonly found to contaminate the soil.

3. Question: In order to show that the drug can halt disease progression, an environmental toxin rat model of Parkinson's disease was used.
Answer: We used an environment toxin rat model of Parkinson's disease to show that the drug can halt disease progression.
Reason: Changing the sentence from passive to active voice enhances the clarity and makes the statement more impactful.

4. Question: The highest percentage of astrocytes was seen in Group A (32%) followed by Group C (28%) and then Group B.
Answer: The highest percentage of astrocytes was seen in Group A (32%) followed by Group C (28%) and then Group B(?).
Reason: There is missing information and the data for Group B is not reported.

5. Question: Out of the 200 Trial A participants, 10 (10%) reported side effects.
Answer: Out of the 200 Trial A participants, 10 (5%) reported side effects.
Reason: There is an incorrect percentage calculation that needs to be rectified.

6. Question: The phospholipid bilayer allows for bidirectional flow of metabolites.
Answer: The cell membrane allows for bidirectional flow of metabolites.
Reason: The term phospholipid bilayer is jargon and it can be modified to cell membrane as it is simpler and still conveys most of the meaning.

7. Identify the lede: In India, more than 1 million new cases of cancer, most of them in advanced stages, is diagnosed every year. It is suggested that up to 80% of patients suffering from advanced cancer could live with pain. "Having morphine in the cupboard is not enough" says Dr M.R. Rajagopal, India's father of pain and palliative care.
Answer: "Having morphine in the cupboard is not enough" says Dr M.R. Rajagopal, India's father of pain and palliative care. In India, more than 1 million new cases of cancer, most of them in advanced stages, is diagnosed every year. It is suggested that up to 80% of patients suffering from advanced cancer could live with pain.
Reason: The lede was buried and the quote that highlights the root cause of the problem should be the opening sentence instead.

8. Check the flow of the paragraph: Parkinson's disease is the second most common progressive age-related neurodegenerative disorder. The symptoms include motor symptoms such as resting tremor, bradykinesia, and rigidity, as well as non-motor symptoms such as depression and anxiety. We still lack a disease modifying therapy. Parkinson's disease is characterised by the loss of dopaminergic neurons in the substantia nigra region of the brain and the development of neuronal Lewy bodies.
Answer: Parkinson's disease is the second most common progressive age-related neurodegenerative disorder. It is characterised by the loss of dopaminergic neurons in the substantia nigra region of the brain and development of neuronal Lewy bodies. The symptoms include motor symptoms such as resting tremor, bradykinesia, and rigidity, as well as non-motor symptoms such as depression and anxiety. We still lack a disease modifying therapy.
Reason: The paragraph was rearranged in such a way that following the introductory first sentence, there is explanation on what happens in the disease thereby leading to the symptoms. The last sentence is about the available treatment.

Clarity and Openness in Reporting: E3-based (CORE) Reference

An Open Access Resource to Support Authoring of Clinical Study Reports for Interventional Studies

DOWNLOAD THE LAUNCH PUBLICATION: http://dx.doi.org/10.1186/s41073-016-0009-4

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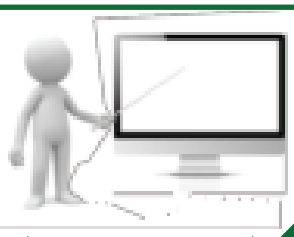
WRITE OR REVIEW CLINICAL STUDY REPORTS (CSRs)?

WRITE OR REVIEW STATISTICAL ANALYSIS PLANS (SAPs)?



YES

NEED HELP INTERPRETING ICH CSR AUTHORING REQUIREMENTS?

WHAT IS "RESPONSIBLE CLINICAL TRIAL DATA SHARING"?

NEED HELP UNDERSTANDING PUBLIC DISCLOSURE REQUIREMENTS FOR CSRs?

HOW DOES PUBLIC DISCLOSURE AFFECT CSRs AND PRESENTATION OF DATA?

SHARING KNOWLEDGE TO HELP YOU WRITE FIT-FOR-PURPOSE CSRs

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You should know about: http://www.core-reference.org

Please inform your senior colleagues

Consider CORE Reference a 'User Manual' that may be used in conjunction with company Standard Operating Procedures to support the authoring of Clinical Study Reports fit for today's modern drug development environment.

Editing for writers who have English as an additional language

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Abstract
Editors of English are typically met with expectations to make a quick fix of documents that need more radical changes than authors think. As editors, we should convey how we work to improve readability, and either adjust or gain acceptance for our approach. Next steps are to identify and discuss illogical, ambiguous content, check grammatical issues in the writer's first language that are different in English, and anything that deviates from clear, concise, consistent, well-formed prose, focused on the research question. A good way of communicating effectively with authors is to give reasons for suggested changes, and ideally, to name the problems.

In the past 6 years I have taught manuscript writing, to academic researchers with various language backgrounds,[1] with the intention to reduce the need for editing. My ideal job is to work with authors who have been through some of my training, so I can communicate more effectively with them about the radical changes that are often needed to create a good paper; i.e. clear, concise, and consistent (3 Cs), well-formed prose, focused on the research question (hereafter termed *purpose statement* because purpose is more often expressed through aims and hypotheses than research questions). *Language laundry* is a typical description of what Norwegian researchers want from editors of English. One job description I got was "*just check my use of definite articles*".

The articles *a/an/the* and subject/verb agreement
Use of these articles is often highlighted by journal editors and referees as needing attention in submitted manuscripts.[2] Many languages do not have equivalent constructions, and, in those that do, the articles are not necessarily used in the same way as in English.[3] I delete a lot of definite articles, usually because they're just superfluous, but sometimes because they're used wrongly. Consider the following sentence:
Our aim was to establish the association between X and Y.

From the context, it was clear that the intended meaning was to clarify whether X and Y were associated. The way it was written gave the impression that these variables were known to be associated, and that this particular study was designed to *establish* or perhaps *confirm* that knowledge.

As in Danish,[4] Norwegian has only one form of the verb for *is/are* (*er*) and *was/were* (*var*), so the singular and plural are the same. Subject/verb agreement is not an issue in these languages. For some Scandinavian authors this causes a lot of problems in English; one manuscript I worked on had subject/verb disagreement in almost every sentence (rare).

Critical reading to identify irrelevant, illogical, ambiguous content
Many supervisors tell their PhD candidates to look

English as an additional language
Science writers for whom English is an additional language are often termed non-native speakers, a negative term that describes them by something they are not. The more positive term *writers who have English as an additional language* is longer, but brevity is not always most important.

The author (second left) during a writing course in HELL (close to Trondheim, Norway); not as bad as its reputation.

at how papers in their field are written, and to learn writing by studying them. To prepare for my workshop on critical reading of scientific papers, participants are asked to find papers that are relevant for their own research, published by acknowledged authors in journals that are considered to be good in their field. They bring these *good* papers to the workshop, where we read them with the intention to misunderstand anything that can be misunderstood; the same way that I would read a paper that I am asked to edit, and the opposite way of how young researchers are often told to read. To get a snapshot of paper content, terminology and target readers, we start the session by looking at the journal title, article title,[5] keywords,[5] purpose statement and conclusion. Then we analyse abstracts sentence by sentence.

Backgrounds in abstracts have to be painfully short, so the main challenge for that subsection is to select interesting, relevant content. This real-life example *"There is much talk surrounding food fraud policy…"* is the opposite. The language could have been better, but since the content is too general to occupy that scarce space, I would suggest to either delete it or replace it with something substantial rather than try to revise it.

Objective, goal, aim, purpose

Some journals require that the abstract has subheadings such as Objective, Goal, Aim, and Purpose. If they do, and you're required to write complete sentences, use the journal's term to start your sentence because people have different ideas about what these words mean and whether they differ.[6] For example, if the journal uses the subheading *objective*, do not write *Our aim was …* or worse *The study's aim was*. The study itself should not be the subject of the sentence.

Every research project involves studying, assessing, evaluating or investigating, so avoid writing that the study purpose is to do one of these things. The purpose of research is not actually to do experiments or evaluate patients, but to find out something by doing those activities. In the purpose statement, describe the knowledge to be produced, not the actions involved.

The PICOT approach for formulating purpose statements

The PICOT approach recommends that the purpose statement specifies the following items (when relevant): target Population/or problem, the Intervention of interest, the Comparator, key Outcomes, and the Time frame over which the outcomes are assessed (the T can also refer to Type of study [design]).[7] Consider the following research question:

Is implantation of a multifocal-intraocular-lens in presbyopia patients with cataract or having refractive lens exchange effective to correct presbyopia?

The P is *"presbyopia patients with cataract"* and the O *"is corrected presbyopia"*; no information is given about the T and we cannot discriminate between the I and the C. This is an example of text that I would ask the writer about, because I assume that one of the interventions is of more interest than the other (and that it should be possible to discriminate between the I and the C). The description of patients is placed in the middle of the sentence (and is written in a non-parallel way),[8] giving the impression that it just refers to those who had the implant (misplaced modifier).[9] If the description of patients is placed in the beginning of the sentence, it refers to both procedures in a clearer way. If both interventions are of equal interest, consider:

Alternative 1: *In patients with presbyopia and cataract, can presbyopia be effectively corrected by a multifocal-intraocular-lens implant or by a refractive lens exchange?*

If the implant is more interesting than the lens exchange, consider:

Alternative 2: *In patients with presbyopia and cataract, does a multifocal-intraocular-lens implant correct presbyopia more effectively than a refractive lens exchange?*

Note that the revisions do not include the word *implantation*; a verb transformed into a noun (nominalisation). Nominalisations are highlighted as problematic/overused constructions in four of nine papers in the "Writing better workbook" published in *Medical Writing* in the first issue of 2017.[10]

A well-written purpose statement eases writing of the conclusion. Purpose statements and conclusions in the abstract must reflect those written in the main text. For my writing courses, participants are asked to find and check all of these statements in their chosen paper, and bring the one they like best to use in the course. There we check if that could also be improved.

Conflict of Interest between writer and reader?

A researcher recommended her colleagues publish in British journals because they allow more words than the American ones. When asked which ones she preferred to read, she quickly said "The American ones, they're shorter".

Wordy, unfocused introductions

A researcher in one of my workshops recommended her colleagues to publish in British journals because they allow

more words than the American ones. When I asked her which ones she preferred to read, she quickly said "*The American ones, they're shorter*". I thought it was a great way of expressing the *Conflict of Interest* between writer and reader. Researchers have so much they would like to share about their important project and what they have learned by reading piles of literature. Sadly, most readers of science papers just want to get to the main point/ what's new as quickly as possible.

A common error in introductions/ background sections, is to begin too broadly or too far off topic. Consider beginning with a startling statistic that illustrates the seriousness of the problem you will address, and get to the point as soon as possible. Do not provide dictionary definitions of terms that readers already know.[11] Authors should gradually guide readers' thoughts to the study aims, which are described in the last paragraph of the introduction. Ideas should be organised so that, immediately before reading the aim, the reader understands the relevance of the topic and anticipates which gap in knowledge has to be filled.[12] When I ask researchers what they find most challenging about writing, many say "*writing concisely*". If you, as an editor of English or co-author of an article, think that a text should be 25% shorter, convey that carefully to the author – the risk of offending is overwhelming. A good strategy for an editor is to give reasons for why they suggest changes, and ideally to name the problem – e.g. non-parallelism[8] or misplaced – ing forms.[13]

Dangling modifiers and -ing forms

A verb ending with *-ing* can be a present participle or a gerund; the gerund is a verb functioning as a noun.[13] For Norwegians, the -ing form seems to be perceived as a hallmark of English. Problems associated with the construction are usually about ambiguous subject referral (due to their location in sentences). If placed in the beginning of a sentence they may not refer to a subject at all (dangling modifier[14] [*dangling* because the clause *hangs loose*, not firmly attached to an appropriate subject]); if written/misplaced after a noun they are not supposed to refer to, they create uncertainty about what the subject is.

Here's an example of a dangling modifier (present participle in this case):

Using the survey data, the effects of education on job satisfaction were determined.

Who is using the data? Implied subject = we/researchers, grammatical subject = the effects. Corrected: Keeping the passive voice *The survey data were used to determine the effects of education on job satisfaction* or changing to the active voice *We used the survey data to…*

Consider this example: *This study suggests that it is possible to influence the self-efficacy of 12–13-year-old, socially withdrawn children with a school-based intervention using a solution-focused approach (SFA).*

It's not clear who was using a solution-focused approach, but it certainly wasn't the intervention (placement of *using* immediately after *intervention* implies referral to that word). The last example sentence has other problems as well, see Exercise 1.

Conflicts of interest

In addition to writing this article because of a personal need to formulate her own editing strategy, the author is interested in selling her writing courses.

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Every research project involves studying, assessing, evaluating or investigating, so avoid writing that the study purpose is to do one of these things.

Exercises

Be creative and use all your knowledge about English to improve the sentences below. Some tips are given under each sentence.

Exercise 1

Conclusion: This study suggests that it is possible to influence the self-efficacy of 12–13-year-old, socially withdrawn children with a school-based intervention using a solution-focused approach (SFA).

Problems: *The study itself as the sentence subject, misplaced present participle, illogical flow of information, weak verbs, multiple hedging*[4] *and wordiness.*

Exercise 2

Functioning as the exterior interface of the human body with the environment, skin acts as a physical barrier to prevent the invasion of foreign pathogens while providing a home to the commensal microbiota.

Problems: *Unclear subject, non-parallel, wordiness, superfluous definite article.*

Exercise 3

Objective: To explore Somalian new mothers' experiences with the Norwegian healthcare system and their experienced needs during the hospital stay and the postpartum period.

The journal did not require complete sentences in the abstract, so starting with *To* is fine.

Problems: *Repetitive, inappropriate verb choice, non-parallel.*

Answers to exercises

1. "Conclusion: Our results indicate that the school-based intervention, SFA (solution-focused approach), can improve the self-efficacy of 12–13-year-old socially withdrawn children."

The study itself is not the sentence subject and does not "*suggest*" anything; alternative beginnings are *The authors suggest* or *Our results indicate*. I prefer the latter because it emphasises that the conclusion builds directly on the results. The word *indicate* is stronger than *suggest*, but is modified sufficiently by *can improve* later in the sentence to keep the meaning. *Influence* is an unspecific word; we understand that it does not mean *aggravate*, but then we may as well write *improve*. An abbreviation would not normally be explained in a conclusion; it is included here just to make a point. Note that the abbreviation is written before the explanation. There is no formal rule about which to place first, abbreviations or explanations, but you have to adhere to style guides.[15] Two different signs are used correctly to describe the children's age "12–13-year-old": the en-dash and the hyphen.[16]

2. "Skin is the human body's exterior interface with the environment; a physical barrier that prevents invasion of foreign particles while providing a home for the commensal microbiota."
Notes: *Function* and *act* are synonyms in this context and there's no need to use both.

3. "Objective: To document Somalian new mothers' experiences and needs in Norway, in the hospital and postpartum at home."
Explore is a big word that is overused in my opinion (don't have a reference for that). I often suggest alternatives such as clarify, describe, document. *Healthcare system* does not add information (course participants agreed). Experienced needs are just needs. The term *postpartum period* is used in a confusing way (and there's no need for the word *period*); it seems to start after the mother has come home from the hospital (women who have given birth in Norway are discharged quickly, but not immediately). By adding *at home*, the sentence becomes parallel and clearer; the study documents the women's experiences in two locations.

Microediting – details matter

Quality, authority, and reputation: The value of microediting

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Abstract

Microediting aims to ensure consistency as well as accuracy within a document and across a document series. Also known as technical editing or mechanical editing, it is an important stage in editing, needed to gain and retain a reader's interest and respect: to assure them that you are giving them a high-quality product. Microediting can involve a large number of wide-ranging tasks, from language editing to formatting and checking the accuracy of data or hyperlinks. We suggest a structured and methodical approach that keeps the reader in mind.

Move over microediting with your fine detail – macroediting comes first.

We know this. And as passionate as we are about microediting, we appreciate that text needs to make sense and be relevant to the reader before we concentrate on the detail such as formatting, consistent spelling, and use of hyphens. What's the point of working on the finer points of text that may well be moved, or even removed, before it's finalised?

The editor's first priority is to make the text clear and enticing so that the reader wants to … read on.

But it's not just unclear and over-wordy text that can discourage readers. Lack of attention to detail can drive them to distraction and make them doubt the quality and authority of what they are reading. Missing out the microediting stage is dangerous: the message of the text may be lost as readers move on quickly to a more authoritative source; bear in mind that a *reader* such as a journal editor or regulator may be making decisions that are crucial for you or your company.

What is microediting?

Microediting is also known as technical editing or sometimes as mechanical editing. For the purposes of this article, we'll use the term microediting, which we consider to be where

you're getting down to the detail, such as looking at the presentation of numbers – a vast and controversial field that could occupy pages and pages of this issue of *Medical Writing*.

The purpose of microediting is to ensure consistency as well as accuracy within a document and across a series of documents. (We use the term document here, but the principles of microediting will also apply to text in digital media such as websites.) When microediting, the editor will be looking out for things such as:

- Adherence to format requirements, as in a journal article
- Formatting, such as heading levels, tables and figures, and page layout
- Use of bold, underline, and italics
- Language, including grammar, spelling, and punctuation
- Hyphenation
- Capitalisation
- Bulleted lists
- Brackets
- Abbreviations
- Reference style
- Units
- … and, of course, numbers!

For digital products, the editor may need to check that all hyperlinks are in the correct style (and that they work!) or the coding that dictates how content is displayed.

Where does microediting fit in the process – when to do it?

As we noted earlier, we think it is more efficient to focus on microediting *after* macroediting. However, that doesn't mean it should be an afterthought. Indeed, we suggest that microediting be considered when planning the editorial process. Asking all contributing authors to adhere to a guide on style essentials should reduce the amount of editorial work needed later. Providing a robust, easy to use template will also help maintain consistency.

Who microedits?

Everyone involved in authoring and editing should be aware of the factors involved in microediting: for example, authors should ensure abbreviations are defined and that they have only one meaning, references are complete, and tables and figures are referenced in the text. However, it's likely to be a medical editor rather than an author who does the full microedit on completed text to spot and correct the inconsistencies, omissions, and errors.

You will probably love microediting if you get enraged by a supermarket sign telling you the check-out lane is for people with *10 items or less*, the greengrocer offering *potato's for sale*, or the missing superscript linking to a footnote in a scientific paper. If you prefer to see the big picture, and enjoy rewriting and restructuring text, macroediting may be your thing. But all medical writers should be aware of the aims and tasks of microediting and its role in document quality.

How to microedit?

Remind yourself about the reader

- Who is the document for?
- What do they want to know?
- What is the message?
- How is the product going to be presented?

The answers to these questions are essential in macroediting, but need to be borne in mind in microediting too. For example, they may influence your decisions on how much to use abbreviations, whether UK or US English is more appropriate, or even what font size would be best.

Know what is required

The tasks covered by microediting to achieve consistency and accuracy are many and varied. What is required will, to some extent, be dictated by the nature and aim of the product being edited. Is consistency across a multi-author work or set of conference proceedings essential? Do you need to check against sources, or has that already been done in the macroediting or in another quality control procedure? Are there tasks you need to do that are specific to the medium of the product, such as checking hyperlinks or the animations in a slide set?

It helps to have a standard operating procedure or list of what tasks need to be done.

Work in style

Use a style guide. That way, you only have to decide once on a particular style issue, making the editing process more efficient.

Most companies have a style guide, but – as you'll be well aware if you work for a contract research organisation or are freelance – they are not all the same. Many aspects of style are subjective. Organisations and individuals have their own preferences, and opinions on whether to use words or numerals for numbers up to nine (or 10 or 12) can be very strongly held. You may disagree with the style guide. Our advice is to live with it unless it introduces an inaccuracy or will offend or confuse the target audience.

If there is no style guide, note decisions you make as you edit so that you can be consistent.

Be methodical

There are several things that can help you take a structured and methodical approach to microediting and enable the job to be done efficiently (see Figure 1).

Rather than trying to check everything as you work through a document, batch up tasks and work in a systematic way: do sequential checks, one task at a time. For example:

- Check the whole document for heading levels.
- Next, check the whole document for abbreviations.
- Finally, run a spelling and grammar check on the complete document.

Checklists can serve both as a reminder of what needs doing and a record of what has been done.

Technology can be your friend, provided you use it wisely. Use the spelling and grammar checker in Word, but think about what you are doing: Take care. For example, do you really want to change every instance of "…ize" to "…ise" and end up with "the sise of the group was 35"? You can also use the more advanced features of Word or specialist software.

Taking a methodical approach requires concentration. Find yourself somewhere to work where you can focus without distractions, such as the sound of emails arriving or other interruptions.

Use common sense

The job of the editor is to achieve consistency, adhere to the style guide, aim for perfection. Right? Yes … and no.

Although we highly recommend that you use a style guide, we also caution about becoming a slave to it. Use common sense and think about the reader. For example, the style guide may specify to use numerals rather than words for all numbers and to minimise the use of hyphens, but what's easier to understand:

- We held 1 1 day meeting.
- We held 1 1-day meeting.
- We held one 1 day meeting.
- We held one 1-day meeting.

Consider your reader again when using an abbreviation: it may be widely understood by

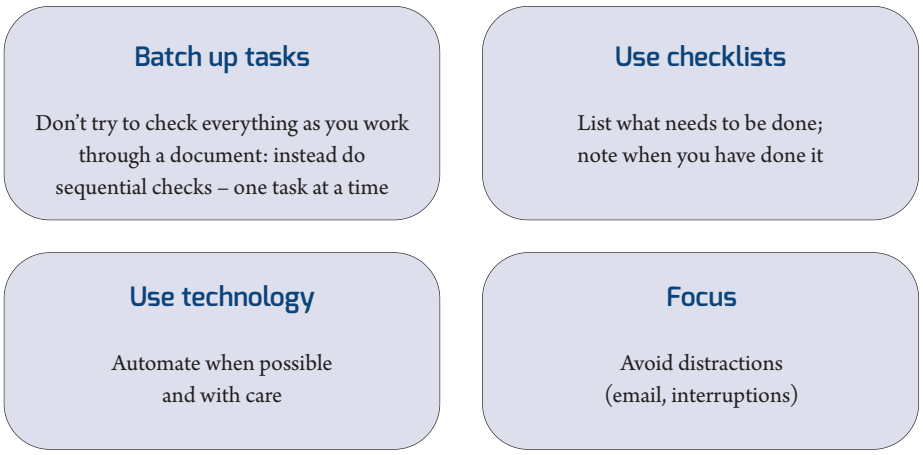

Figure 1. Efficient microediting

specialists but not be familiar to generalists or the public. Take care also with an abbreviation that could have more than one meaning in your document. So, use your judgement and be prepared to explain your decision to the author.

We suggest that it's important to remember that there's invariably more than one way (or even more than *1* way!) of editing a text and someone is sure to disagree with whichever way you choose. So, be flexible, be open-minded, and remember that the English language is constantly evolving. Years ago, we were told that *ongoing* was an Americanism not fit for the pages of a respectable UK journal. Who would give it a second thought now? Be prepared to move with the times.

And perfection? Don't waste time preparing a gold standard document if bronze is acceptable for your reader. The incremental step to reach *perfection* has cost implications, in both time and financial terms. Editorial resources need to be used cost-effectively. Remember that once you have used up your budget, the money has gone.

Want to know more?

In this article, we've aimed to give you an introduction to what microediting is and what is involved in doing it. There is much more to microediting than we can cover in this article. Look out for the *Language and Writing* workshops at EMWA conferences.

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Resources

Language and Writing workshops at EMWA conferences.

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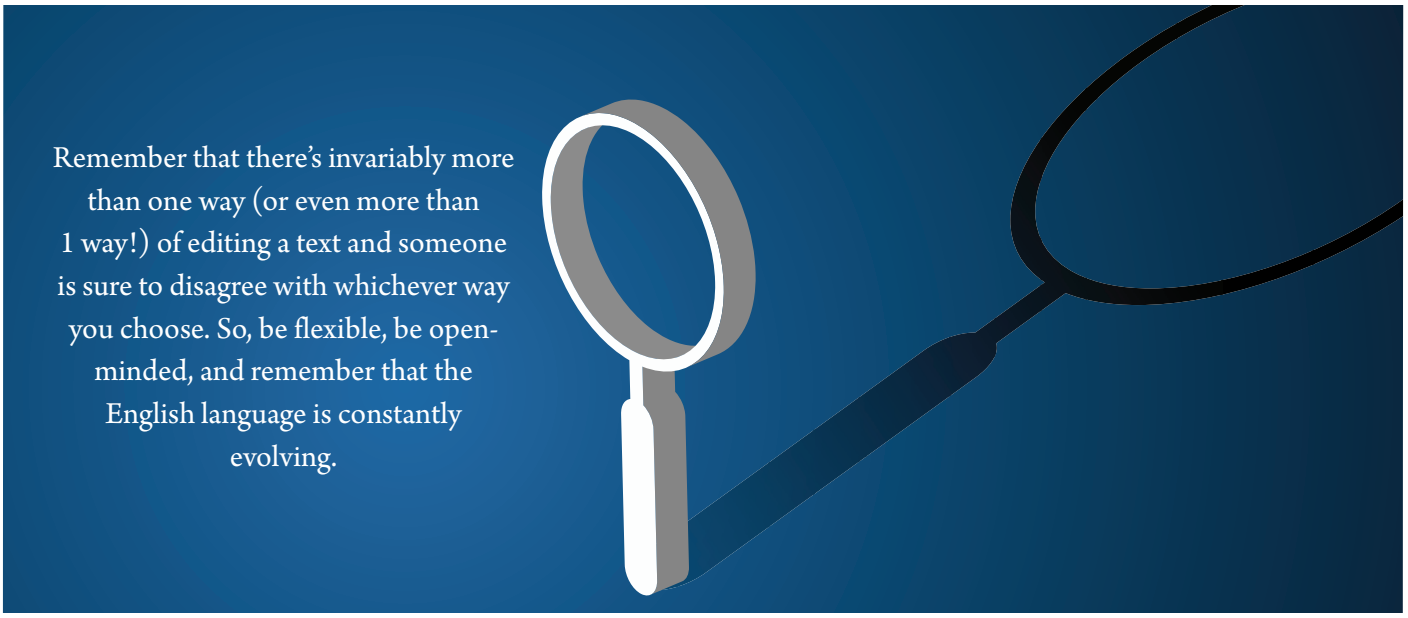

Revision: Parameters and practices within the translation industry

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Abstract
In this article we look at what it means to revise a translation, the parameters that should be taken into account, and the various challenges posed by the process. We also explore how the quality of a translation affects the revision stage, and various approaches that can be used to revise a text with the aim of delivering a usable piece.

Usually, when a translator has finished working on a given text, it means that he or she has both translated and revised the text. Revising a translation is essentially a very careful reading exercise: the text is read to spot problematic word choices, sentences, or paragraphs, and to correct or improve it if necessary.[1]

Much of what is done when revising is identical to what is done when editing. Nevertheless, revisers will often come across unidiomatic wording as a result of interference from the source language – a problem which editors will not normally encounter unless the writer is not a native speaker of the language. Revisers must also find and correct mistranslations and unneeded additions.[1]

With the increasingly widespread use of translation memories (databases that store segments of text that have been translated as translation units, in order to help translators in their future work by providing a repository of already translated text),[2] revising translations done by others is becoming more commonplace than it used to be – particularly when working for translation agencies. Many translators use memories that contain translations done by a large number of other colleagues. When material from these translation memories is imported into the translation on which a translator is currently working, he or she must decide to what degree the imported wording is usable in the current context.[1] It may be necessary to make changes for a variety of reasons:

- the meaning of the imported text is different;
- the imported text is stylistically inconsistent with the translator's own wording;
- there is a lack of cohesion between an imported sentence and the preceding or next sentence;
- different imported sentences are not consistent with each other in terms of terminology.

While the above considerations are important even when importing material from a memory that only contains the translator's own translations, the revision burden is greater when importing translated segments written by others, since there is far less certainty about the readability of work done by the others.[1]

Why revising translations is necessary

There are several possible reasons why someone other than the translator should check a text, and perhaps make changes, before it is sent off to readers:

- While translating a foreign text into the target language, it is extremely easy to write sentences that are structured in a way that will lead readers to misunderstand them or find them difficult to understand.
- It is also rather easy, while translating, to forget about future readers and write something which is not suited to them or the intended use of the translation – which may differ from the intended use of the source text.
- A text may fail to conform to society's linguistic rules, or the prevailing ideas about the proper way to translate for a particular genre.
- Finally, what the author or translator has written may conflict with the publisher's goals.

To deal with these problems, revisers and editors amend texts in two ways: they correct and they improve. Revising is not a matter of a vague "looking over". There are specific things the editor or reviser needs to look for – these will be analysed later on in this article.

Quality in translation

In ISO 8402 from 1994, the International Organization for Standardization defines quality in general as "the totality of characteristics of an entity that bear on its ability to satisfy stated and implied needs".[1] Thus, quality is always related to needs, which also means that there is no such thing as absolute quality. Different translations will have different quality criteria because the texts have different needs. In one translation, readability may need to be improved to a very high level, while in another a lower degree of readability will be enough. Sometimes, some documents obey two different degrees of quality: information quality (when the document will be used in-house by a small number of people for information only and then discarded) and publication quality (when the document will be read by a large number of outside readers over a period of time).[3]

Different concepts of quality

There are several broad concepts of quality that are currently used in the world of translation, and these lead to different "philosophies" of revision.[1]

- **Quality means satisfying clients.** This may lead a reviser to pay most attention to finding errors such as not respecting client-related terminology.
- **Quality means that a translation is fit for purpose.** The translation is, in the reviser's view, suited to the people who will be reading it and the purpose for which they will be reading it. This concept is endorsed by ISO EN 15038 "Translation services – Service requirements", which state that "The reviser shall examine the translation for its suitability for purpose".
- **Quality means doing what is necessary to protect the target language.** This view will typically be found in language communities where translators want to counter the effects

of a formerly or currently dominating foreign language. This is rather common in English to Spanish translations of medical texts, for example.

What are the specific things the editor or reviser needs to look for?

Due mainly to the time constraints imposed by deadlines for each revision, an experienced reviser will become accustomed over time to not thinking about what kind of errors to look for and in what order of priority, but instinctively tries to identify them simultaneously, covering all kinds of translation errors, while comparing the target text with the source text sentence by sentence, paragraph by paragraph. Also, revisers instinctively act as proofreaders would, checking spelling, punctuation, words and phrases which are in bold, underlined, or italicised, and presentation. Even if a full revision is not possible due to time constraints, especially if the client asks for specific house style and glossaries to be checked, an experienced reviser's eye may also catch consistency and content errors.

Things that can go wrong when translating would entail a long list, but Brian Mossop has been able to elaborate, in his book *Revising and Editing for Translators* (2001),[1] a reasonably short list of translation error types. He sums up 12 revision parameters, divided into four groups, which identify and classify these errors:

- Transfer: accuracy and completeness
- Content: logic and facts
- Language: smoothness, tailoring, sub-language, idiom, and mechanics
- Presentation: layout, typography, and organisation[1]

Mossop states that, "obviously [a reviser is] not going to go through each sentence twelve times".[1] In our experience, an experienced reviser actually checks those 12 parameters simultaneously by instinct when going through each sentence.

Mossop's model for translation revision is very useful for revisers, regardless of their level of experience, but also for translators, because questions asked in each of the four groups of parameters help to produce a better translation.[1]

Accuracy, completeness, and logic are the main parameters to check. Among them, accuracy is the most important feature of a translation. It requires a correct understanding of the source text and the ability to ensure that the translation expresses that understanding. The reviser has to guarantee that the translation conveys the message of the source passages – even if it is not a close translation and doesn't reproduce the original vocabulary and sentence structures. He or she must check that the source has been correctly understood and expressed in sentences that are not linguistically ambiguous, since ambiguity may lead readers to interpret the wording in the wrong way. Also, if numbers are central to the message of a text, it is a good idea to do a separate check for their accurate reproduction.

Regarding completeness, revisers have to ensure that translations render the entire message of the source text (but not necessarily its wording) with no additions and no subtractions – the so-called NANS principle. The most common completeness error is unintentional omissions, but the translator may also have unwittingly added ideas that are not present, even implicitly, in the source.

A translation has to be logical: it must make sense to the reader in its context. If it doesn't, maybe the source text is illogical and the translator didn't check the meaning with the client. Sometimes the logical connections between sentences in source texts may be very unclear because they are a collage of sentences from a variety of materials. In other cases, it is the translator who has introduced an inaccuracy or contradiction, maybe due to mistranslation or bad interpretation. We agree with Mossop that readers may not find much difference between content errors (in facts and logic) and transfer errors (in accuracy and completeness) if they compare a translation to its source, but they may appreciate them differently.[1] For example, if transfer errors make sense, these may pass unnoticed. By contrast, content errors, in particular logical error in facts, will immediately be spotted by experienced reviewers or subject-matter experts, and this will make them doubt the competence of the author or translator of the text.

Degrees of revision

There is no set definition of revision within the translation industry. This is primarily because the discipline of translation studies is relatively new, so there is a lack of terminology that is used consistently and by everyone – some terms are used interchangeably by some revisers, and various terms overlap (e.g., editing, proofreading, revising, reviewing, and rereading). Also, the term "revision" is used in different ways by different disciplines. For example, in publishing, revising often refers to amending a previously published work before printing another edition of it, which is very different to the way "revision" would be viewed by translators.[4]

Similarly, there are no set terms to denote the degrees or levels of revision. We, the authors of this article, use the following levels, all of which can be used as part of a *bilingual revision* (comparing the entire source text with the translation) or a *monolingual revision* (revising the translation as a text that stands alone, only consulting the source text when the translated version cannot be understood).

Full revision

This is where a translation is revised, ideally using the 12 parameters set out by Brian Mossop.[1] If the translation is particularly poor, this may involve re-writing parts of the translation, although this should always be discussed with the client beforehand.

General revision

We use the term *general revision* for a project where we decide to revise a handful of the 12 parameters. As an example, a client might state that he or she wants to ensure that spelling and punctuation are correct, and would like all medical terminology to be checked, but don't want to lose the author's voice in the revision process. In this case, we would make sure that we don't re-write any parts of the text.

Partial revision (a "good enough" approach)

This is the most difficult kind of revision. We normally use this approach when the budget and/or deadline are limited, and explain to the client that we will not be able to improve the translation to the extent we would like, asking them what they would like us to focus on. Some examples include correcting spelling and punctuation, improving coherence, readability, and phrasing (ensuring that it doesn't "sound" like a translation), and checking the accuracy of terminology. We would only focus on one or possibly two of these areas. The "good enough" approach allows us to focus on delivering a translation that the client is happy with, without

spending unpaid time on making extra corrections. In *Revising and Editing for Translators*, Brian Mossop emphasises the importance of reminding yourself: "Do not ask whether a sentence *can* be improved but whether it *needs* to be improved."[1] This is something we often need to remind ourselves of, particularly as linguists, because refraining from improving the writing quality can sometimes be a challenge!

Scan check (quality control)

This is generally carried out as part of a bilingual revision, flicking between the source text and the translation to check the following: a. spelling, b. completeness (ensuring that all the text is there), c. that the layout of the translation mirrors the source, d. that any visuals such as tables and graphs have been reproduced correctly, and e. that any numbers in the translation match the source.

How to determine the degree of revision required

One thing we have learnt through editing and revising translations is to always ask the client: Who is the translated text aimed at? (e.g., international clients, members of the public, healthcare professionals). We would say that this, together with the client's budget and deadline, are the main points to take into account when determining the degree of revision required. In general, we would inform the client of the kind of revision we think is needed, ask them whether they agree with our suggestion, then take it from there.

The views in this article (particularly regarding the different levels of revision) are held by the authors but are not necessarily shared by all translators. Degrees of revision are very much subjective.

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…readers may not find much difference between content errors (in facts and logic) and transfer errors (in accuracy and completeness) if they compare a translation to its source, but they may appreciate them differently. For example, if transfer errors make sense, these may pass unnoticed.

How to soften the red pen's blow: Tips for editing a colleague's work

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Abstract
Applying the dreaded red editing pen to a colleague's work can be nerve-racking for professional writers. But there are some concrete steps every writer can take that will improve his or her ability to communicate the type of clear, constructive feedback any co-worker will appreciate. Here I discuss five of these steps: be clear, use the author's preferred way to receive feedback, provide examples, take your time, and praise effort.

All professional writers know that the job description often includes fielding editing requests from colleagues – as well as friends, family, and the occasional neighbour. While you're probably happy to assist and wish to provide genuinely helpful recommendations, you may also be worried you'll bruise the author's ego.

But if the idea of taking the dreaded red pen to a supervisor's or a colleague's work fills you with anxiety, at least you can take comfort in the fact that you're not alone: according to a 2014 assessment conducted by Harvard Business Review, most people actually prefer receiving feedback to giving it.[1]

So, when the next edit request drops into your e-mail inbox, first take a deep breath and know that the odds are the author truly wants your feedback, not just a rubber stamp of approval. Second, try out the following tips to make the editing process smoother for both of you (see also Table 1).

1. Be clear
Sure, you could strike out a whole paragraph with a big red cross and move on down the page. You may know why some text isn't necessary, or why it could even be detrimental to the piece overall, but will the author? If you want to provide feedback that your colleagues will value, it's important to take a minute to provide clear reasoning for your edits when you can.

For example, if you reword a section of text from passive to active voice, make a note specifically describing this and why you've done it. If you're editing a digital document, you can also provide a link to relevant editorial preferences or a website on grammar, such as Purdue University's Online Writing Lab.[2]

2. Use the author's preferred means for feedback
You may have heard there are three different learning styles: visual, auditory, and tactile (or kinaesthetic).[3] But according to a 2004 study, there are a lot more than that – at least 71![4] Don't worry, there's no need to memorise them all. Use this much easier shortcut: ask the author how he or she prefers to receive edits, and then accommodate.

For instance, does your co-worker swear by tracked changes? Or would she prefer you sit down over coffee to watch you mark up the document with a red pen? Does your supervisor want an intensive re-write of his presentation, or is he just looking for your cursory thoughts on the tone? Save your time and energy – and theirs – and get these questions answered before you begin to edit.

3. Provide examples
In most professional writing environments, and perhaps especially in medical writing, you're very rarely inventing the wheel. There's a good chance you have old journals, presentations, research, websites, regulatory documents, etc., that you can reference for examples on everything from a strong introduction to a well-structured bibliography.

4. Take your time
Tempting as it may be to push these edits further and further down your to-do list (after all, this isn't even your project!), if you want to be a team player you've got to make it a priority.

You also don't want to rush the process. This

tip applies to your own writing too. You might think you work well, or even better than usual, under pressure from a fast-approaching deadline, but that's a bit of a myth. In fact, a 2001 study found people working to tight timelines actually make more mistakes than people who have more time.[5]

5. Praise the effort

Recent research tells us that while seasoned professionals (like you!) are more open to negative feedback, novices prefer positive responses.[6] So if you're editing for someone who is new to writing, you might try the "sandwich method": compliment, feedback, compliment.[7]

But medical writers beware: The feedback sandwich could backfire and cause you to appear condescending, especially if you're working with someone who has more experience in the field.

If you do choose to provide praise in addition to suggestions for improvement, be sure to be transparent and focus that praise specifically on effort versus innate talent. This is particularly important if you want to help improve your colleague's writing in the future. Studies conducted by Stanford psychologist Carol Dweck showed that when praised for effort – even when that effort resulted in a failure – students became more resilient and determined, whereas students who received praise based solely on talent or ability became more risk averse and sensitive to setbacks.[8]

So, as you edit, be sure to keep an eye out for which aspects of the piece work well (for instance, a conclusion that ties back to the introduction) and how the author can use those strengths to improve other areas (such as a weak introduction).

Finally, after you put the cap on your red pen or hit "save" for the last time, be sure to either write a positive note to go along with your feedback or share your praise face to face.

Conflicts of interest

The author declares no conflicts of interest.

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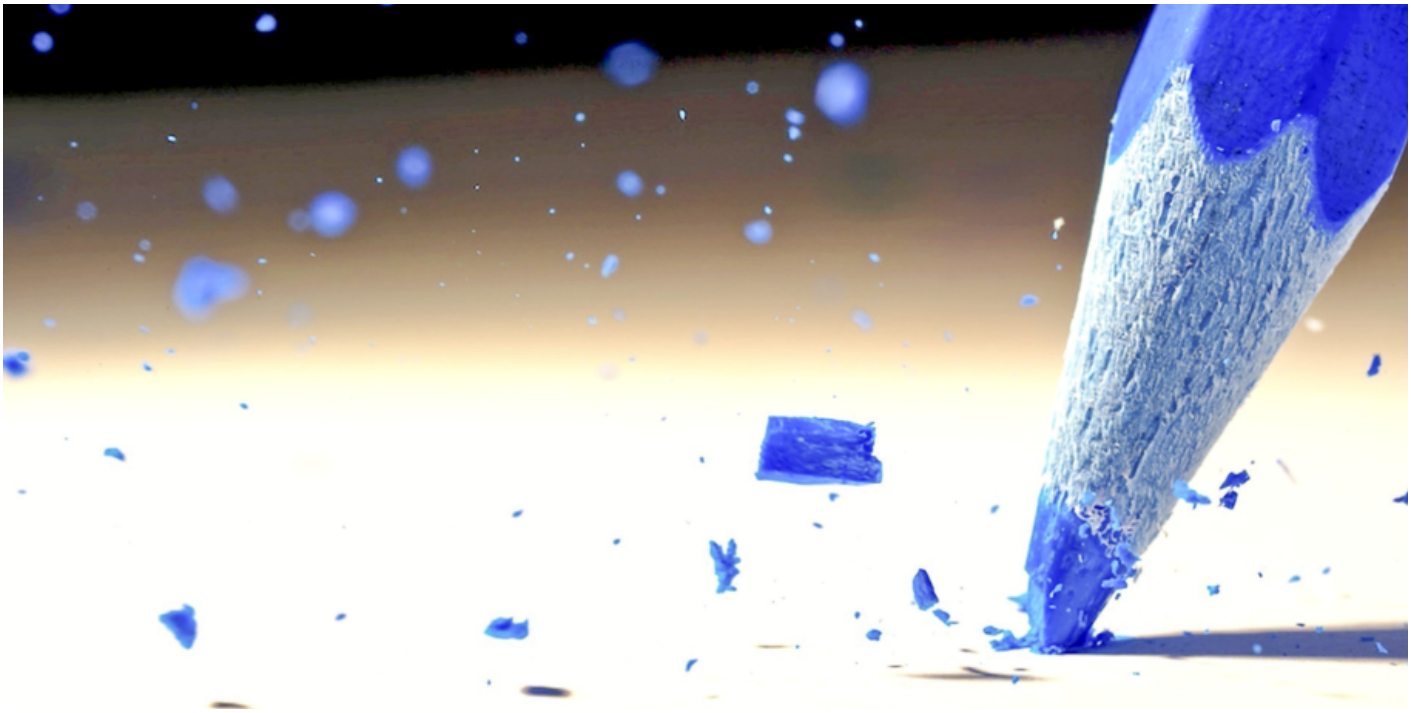
Table 1. Five tips for providing edits

Tip	Example
Be clear.	Be specific with notes about why you made the changes you did. Provide links to editorial guidelines or other resources as applicable.
Use the author's preferred means for feedback.	If the author is an auditory learner, they might prefer to have a phone call or in-person meeting to go over your edits.
Provide examples.	If the author struggles with passive versus active voice, provide a few examples from other articles.
Take your time.	Estimate how much time it will take you to make the edits, and then plan extra time before making deadline commitments to authors.
Praise the effort.	For less-experienced authors, point out what he or she did well – but try to focus on specifics. Praising talent alone isn't as motivating as praising persistence, effort, and growth. For more seasoned authors, you might consider skipping praise altogether as it can be seen as condescending.

Go certified – get ready for the BELS exam



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Abstract
If you are a manuscript editor, you can earn a certification through the Board of Editors in the Life Sciences (BELS), attesting your editorial proficiency. Such objective evidence is desirable for many writers and editors in the life sciences – especially for those of us who don't have a degree in linguistics or communication, or who like taking on a personal challenge, or who just love taking home a trophy. In this article, I describe seven steps that I think are essential to preparing for – and passing – the BELS certification exam.

How do you like the idea of benchmarking your editing skills? Of having a certification that demonstrates your competence to prospective clients or employers? Of taking on a personal challenge, perhaps, proving to yourself that you're really as good an editor as you think you are? That idea could become reality through the Board of Editors in the Life Sciences (BELS)

The US-based board works to maintain and promote a standard of editorial proficiency in the life sciences, offering certification exams across the world – in Europe usually once a year. For the past two years, the European BELS exam was held in conjunction with the EMWA spring conference. Attending the conference in Birmingham last year, I jumped at the chance of sitting the exam, finally ticking it off my bucket list.[1] I found the effort worthwhile – a thrill, actually – and I recommend it to anyone who is serious about editing.

When *Medical Writing* invited me to write an article on how to prepare for the exam, though, my first thought was, "well, that will hardly be a feature-length article – a tweet would be more apt." I didn't prepare much in the lead-up to the exam, apart from testing myself on the 22 sample test questions provided in the BELS Certification Study Guide.[2] According to this guide, "your daily work as an editor is the best preparation". This was indeed true for me, meaning that I had, in fact, subconsciously prepared for the exam for years. I had prepared for it since the day I took my first course in writing and editing. I had prepared for it since the day I started obsessing about good writing, gathering and reading books about it, reading anything I could find about it. I had prepared for it since the day I got serious about science writing and editing. Reflecting on this perennial preparation, I have formulated "The 7 Steps" to getting ready for the exam.
See fact box about BELS

1. Be eligible
First things first – or actually, the last thing first … because when you get to this part, you ought to have all the other parts down pat already. Before you can register for the exam, you need to apply to BELS and be deemed eligible. This means having a bachelor's degree or equivalent and at least 2 years of experience as a manuscript editor in the life sciences, or a PhD and at least 1 year of experience. Along with your diploma, your application to BELS must include letters from employers or clients describing and verifying

your work as a manuscript editor. BELS defines the latter as someone concerned not only with the form but also the intellectual content of a manuscript.[2]

Is a medical writer a manuscript editor in the life sciences? My manager wrote the following in support of my application to BELS:

> *All documents are created as a team effort with the medical writer as the lead writer, editor, and project manager. The job, therefore, contains both original writing based on data and input from other contributors as well as editing and critical revision of text written by the other contributors. The medical writer is responsible for the totality of the document, ensuring consistency, a clear story flow, precise communication of key messages and compliance with guidelines and style guides… [The medical writer] therefore fully meets the BELS definition of an editor.*

The medical writer therefore fully meets the BELS definition of an editor.

2. Obsess and read about good writing

Some time ago, one of my colleagues – a brand new medical writer – asked if I would give him feedback on a quality check he had done for me; it was his first "real" task at the company. In one of his comments to the document, he had written "Let me know if this is too much and I need to control my OCD". He had indeed done a very good, thorough job – getting down to the "incredibly nitty-gritty", as he put it. But what struck me and delighted me more than his eagle eye was the obsession with good writing that I sensed between the lines of his comments. I sensed his thirst for learning all the tricks of his new trade. So, I lent him my copy of *The Elements of Style* by Strunk and White,[3] which I thought might be right up his alley. Scarcely an hour later, he stopped by my office to return the book, beaming. After reading White's witty introduction – that timeless piece of beauty – he was sold on the book and had promptly ordered his own copy.

My new colleague half-jokingly wondered if he needed to curb his "OCD" when checking my document, but I thought his degree of obsession was perfectly healthy for a professional wordsmith. To excel at something, I think you *need* to obsess about it – in a healthy way, though, not compulsively. When you obsess about something, you naturally want to find out all you can about it; it's almost as if "it" finds you. When you obsess about good writing – a necessity for a good editor – certain texts will find you, just as Strunk and White's legendary little book[3] found my colleague.

To my mind, an essential and early step in preparing to become a certified editor is to kindle your obsession and seek out your favourite "writing bibles", your sources of inspiration and guidance. Note the plural – sources – because you need different perspectives to avoid becoming too prescriptivist. In the BELS Certification Study Guide,[2] you will find a list of useful reference books, including *The Elements of Style*.[3] Joining some kind of language forum, for example a LinkedIn group such as Grammar Geeks, can also be helpful.

3. Know your bones

Apart from teaching you about good writing, obsessing and reading about it will familiarise you with the conventions and terms of grammar and syntax that an editor is expected to know. Just as a car mechanic knows the names of car parts, or a pharmacist the names of drugs, or an orthopaedic surgeon the names of bones. To be sure, you can be an excellent writer without knowing the names of common syntactic problems. But to be a certified editor, a text surgeon, so to speak, you should know your "bones".

Among other things, the BELS exam will test your ability to recognise, for instance, a restrictive clause, a prepositional phrase, or a dangling modifier. It will test your ability to diagnose problems of grammar, punctuation, and syntax. So knowing your bones will help you cruise through the "editing 101" questions of the exam, leaving you more time for the meatier, far more intricate questions. A text surgeon, of course, must not only identify the bones but also fix any fractures, including complex ones.

A note on language: The BELS exam tests your proficiency in standard American English. So if your preferred brand of English is British, Australian, or something else, make sure you can easily circumnavigate the different variants. As a manuscript editor in the life sciences, you probably need to handle British and American English at any rate.

A text surgeon must not only identify the 'bones' but also fix any fractures, including complex ones.

4. Beware who does what to whom

Although it covers some typical style problems dealt with in copyediting, the bulk of the BELS exam is devoted to substantive editing. A typical question or set of questions relates to a technically dense passage that contains grammatical and syntactic problems. You are then asked which one of the multiple edits best solves the problem while retaining the author's original intention. And this is where it can get really tricky, especially when only tiny nuances separate the multiple-choice answers

As I see it, most of these problems have one thing in common: ambiguity around "who is doing what to whom". Not in a human relationships kind of way (my exam, at least, was devoid of any sauciness or savagery), but in terms of

Fact box

What is BELS?

- The Board of Editors in the Life Sciences (BELS) was founded in 1991 to evaluate the proficiency of manuscript editors in the life sciences and to award credentials similar to those obtainable in other professions.
- BELS offers certification exams worldwide. The exam is a three-hour multiple-choice test of scientific editing in standard American English.
- Editors who pass the exam may use the credentials "ELS" (Editor in the Life Sciences) after their names.
- BELS has more than 1,000 board-certified editors in more than 20 countries.
- Find out more at the BELS website (bels.org)

what is the subject and what is the object in a sentence

For an editor, this may be simple enough to work out in a simple sentence. But in a garbled sentence, especially one full of complex scientific information, identifying the subject(s) and object(s) will certainly spice up the editor's job. If you misinterpret the author's intention, you're in danger of warping or omitting important information from your revision. And that's the kind of "danger" that lurks in the multiple choices of the BELS exam.

How to arm yourself for that challenge? I think I can only echo the advice that "your daily work as an editor is the best preparation".[2] Untangling a garbled passage will always be challenging, but the more you do it, the better you become at deciphering the author's meaning. Something that honed my editing skills was working with journal manuscripts written by scientists with low English proficiency, which required heavy editing and much detective work. In your real job as an editor, of course, you would clarify any doubts and ambiguities with the writer. When sitting the BELS exam, you can only rely on your discipline of mind, your sense of language, and your command of syntax.

> Most of these problems have one thing in common: ambiguity around who is doing what to whom.

In my book, the ultimate purpose of syntax and grammar is to make it crystal clear who does what to whom. Life, you might argue, is also all about who is doing what to whom. Can we deduce from these two notions that the ultimate purpose of life is editing? I hope you say "no", because the BELS exam will also test your sense of logic.

5. Brush up on the science basics

BELS is not just about editing, it is about scientific editing, specifically in the life sciences. The certification exam therefore covers a few science basics. It will test your knowledge of scientific terms and units of measurement, your skill in interpreting numbers and graphs, and your ability to do simple maths. For instance, some questions require you to calculate percentages, or at least make quick, educated guestimates – a bit like those found in numerical aptitude tests.

> If your mathematical muscles have softened from lack of exercise, consider toning up with some numerical reasoning tests.

None of it is "rocket science", and anyone with a background in any life science should be able to answer these questions. But as in an aptitude test, you will be under time pressure. So, you need to keep your wits about you, pay attention to details, and stick to your sense of logic. If your mathematical muscles have softened from lack of exercise, consider toning them up with some numerical reasoning tests. On the internet, you can find many free aptitude tests as well as test books for purchase.

I would also recommend brushing up your basic undergraduate knowledge of different units of measurement, including units of radioactivity, electricity, heat, and light. Look over the SI base units and derived units, along with common non-SI units. If you have binned your old school books, don't worry – use Wikipedia.

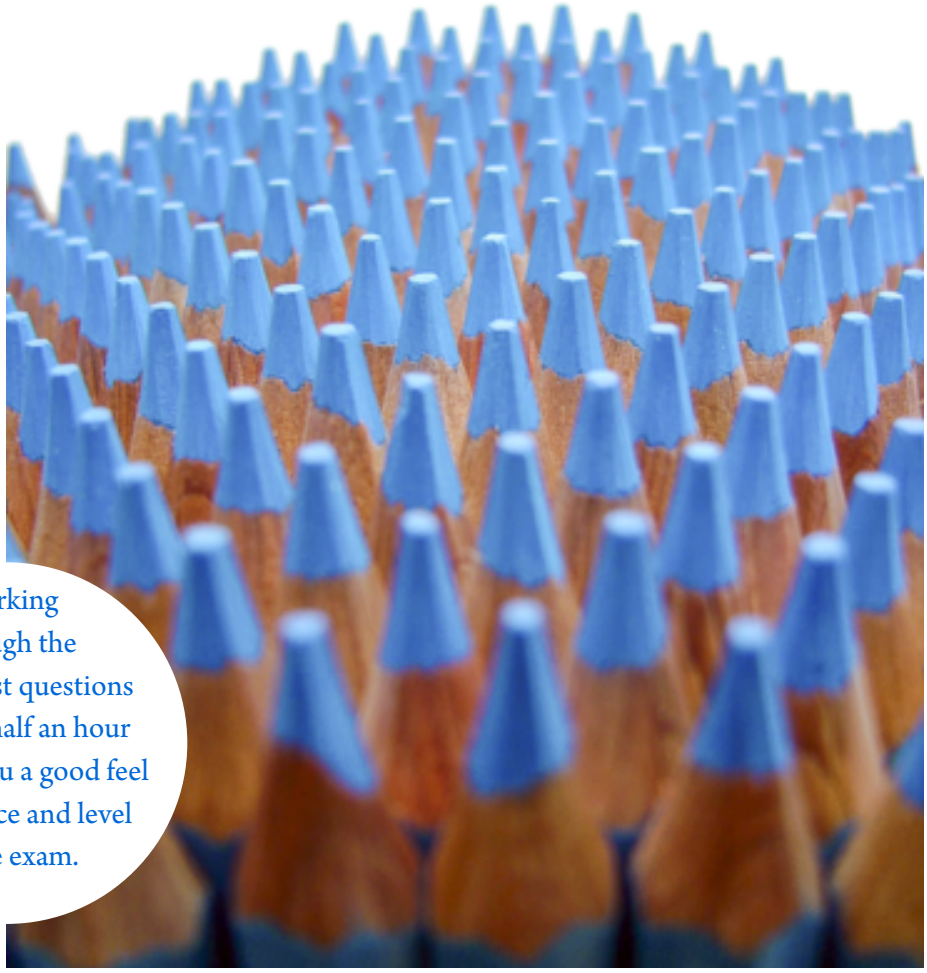
Also, revisit common types of

graphs. If it's been a while since you dabbled in logarithmic plot types, re-acquaint yourself with them. Again, consult your favourite scientific oracle, whether it's a textbook, Wikipedia, or some other online source.

The scientific material in the exam questions may come from any life science field, from botany to biomedicine. You don't need to be a subject matter expert to solve the editorial challenges, but a good, broad foundation in science will help. The more familiar you are with the scientific terms and concepts in any text to be edited, the quicker you can get to the heart of the syntactic, logical, or numerical problem.

6. Heed the publishing principles

If you have been around academic publishing for a while, the exam questions on bibliographic references should give you no trouble at all, as long as you keep your editorial eagle eye wide open. In my experience, those questions were fun little "spot the difference" games, with differences and errors in citation style rather than differences between two pictures.



Working through the sample test questions in about half an hour will give you a good feel for the pace and level of the exam.

Other questions will test your knowledge of publishing conventions, including use of copyrighted material, author-editor interactions, and ethical principles in scientific publishing. Some experience with publishing in a scientific journal, either as an author or an editor, along with your good sense will make these questions manageable. If you are not so familiar with publishing principles, I suggest looking up the editorial policy of one or more major journals and study topics such as copyright and licensing, conflict of interest, prior publication, confidentiality, and research integrity.

7. Try out the sample test

And now to the second most fun part: the BELS Certification Study Guide[2] has 22 sample test questions, which I think represent the exam fairly well. The sample questions amount to about a fifth of the number given in the actual exam, so working through them in about half an hour will give you a good feel for the pace and level of the exam.

If you get most of the sample questions right, consider yourself ready to sit the exam – which is, of course, the most fun part. Compared with the sample test, the exam is more of everything: more of the easy stuff, more of the tricky stuff, more verve, more nerves, more at stake, sweeter reward. Happy prepping, happy testing, and good luck!

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Disclaimers

The opinions expressed in this article are the author's own and are not necessarily shared by her employer, BELS, or EMWA.

Conflicts of interest

The author is a supporting member of BELS but is not in any way promoting the organisation nor the exam.

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Anonymisation: A new challenge for medical writers

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Abstract
In its commitment to transparency, the EMA implemented Policy/0043 and Policy/0070 to make data accessible to all; however, this has given rise to the need for anonymisation of personal data in clinical reports. The analysis of the 64 submission packages containing anonymised data submitted to the EMA as of March 2018 shows that the most frequent technique to anonymise data is redaction. This is typically performed after reports are submitted to the competent authorities. The study report team, through a strong cross-functional strategy, can reduce the anonymisation required after submission of the document by proactively reducing the use of unnecessary identifiers in the initial report drafts. Therefore, the challenge for medical writers is to become involved in the anonymisation strategy and the creation of a data anonymisation plan for the clinical documents from their initial stages, focusing on the balance between scientific value and risk of re-identification.

Introduction
In its commitment to openness and transparency, the EMA initially implemented Policy/0043[1] followed by Policy/0070[2] on the publication of clinical data for medicinal products for human use. The primary objective of Policy/0070[2] is to make data accessible to all; however, the implementation guidance for these policies[3] has given rise to the need for **anonymisation** of **personal data** in clinical reports, which per Policy/0070 includes clinical overviews, clinical summaries, and clinical study reports including appendices 16.1.1 (Protocols and Protocol Amendments), 16.1.2 (Sample Case Report Form), and 16.1.9 (Documentation of Statistical Methods).

Personal data protection is a fundamental right in many countries. In the European Union, this right is protected by European legislation[4-7] and agency directives.[2,3,8] Policy/0070 is fully compliant with the applicable regulations (in particular Regulation 45/20016 and Directive 95/46/EC7). Applicants/Marketing Authorisation Holders are required to submit clinical reports that have been rendered anonymous, meaning that, data must be written in a form that does not identify individuals. The anonymisation strategy should represent the best balance between data utility (maximal retention of scientifically useful information) and an acceptably low risk of re-identification.

Clinical reports contain **direct identifiers** and indirect or **quasi-identifiers.**[9] Direct identifiers are elements that permit direct recognition or communication with the corresponding individuals, such as name, email, phone number, or subject identifier. Quasi-identifiers are variables representing an individual's background information that can indirectly identify that individual (e.g., geographical location, dates, or demographic data).

The purpose of this analysis was to determine the most frequently used anonymisation techniques for direct and quasi-identifiers. In addition, we consider how medical writers can positively impact the anonymisation process by initiating anonymisation at the time of writing clinical reports. The goal is to reduce required anonymisation efforts after publishing, thus aligning with the EMA requirement to publish clinical data without jeopardising personal data protection.

Methods

The EMA clinical data website (https://clinicaldata.ema.europa.eu/web/cdp/home) was accessed under the academic and other non-commercial research purposes 'terms of use'. An advanced search for clinical reports published between October 2016 (the first date that the anonymisation reports were available in the database) and March 29, 2018, was performed.

A total of 86 entries listed by product name were obtained. The search results were exported into an Excel file. If there was more than one entry for the same product name, only the entry with the submission package containing the highest number of documents (including clinical overviews, clinical summaries, clinical reports, and anonymisation reports) was selected for analysis – for example, there were two entries for Humira (product name), one including eight documents and one including 10 documents; only the entry that included 10 documents was selected for analysis. Each of the selected entries (77 in total) was accessed and the anonymisation report was downloaded and reviewed. To determine the individual anonymisation techniques and identifiers used in each submission package, direct identifiers, quasi-identifiers, and the techniques used for anonymising them were recorded in the Excel export file. To create summaries of the anonymisation techniques by submission package and by type of identifier, the anonymisation techniques identified in the anonymisation reports were classified into the following categories:

Most of the submission packages that were anonymised (57 [89%]) used redaction only as the anonymisation technique for direct identifiers and quasi-identifiers.

- **Redaction**: included the terms "redaction" and "masking"
- Preserving **pseudonymisation**: included preserving anonymisation only
- **Randomisation**: included use of random offset dates and use of random values within the study inclusion criteria
- **Generalisation**: included generalisation of age (in years) to 5-, 10-, and 20-year intervals and generalisation of medical history terms to high level term, high level group, or system organ class
- **Suppression**: included suppression and replacement with alternate text used in the anonymisation

The number and frequency of submission packages were calculated by anonymisation technique category (or combination of categories). For the submission packages that used a combination of categories, the number and frequency of packages by type of identifier and by anonymisation technique category were also calculated. The Excel file was also used to perform specific subanalyses by type of drug (orphan drugs, generic and biosimilar medicines) using the same approach.

A glossary of anonymisation-related terms used in this article is presented in Table 1. All terms included in the glossary are written in bold font on their first use in this article.

Results

As of March 2018, applicants/Marketing Authorisation Holders have published anonymised clinical reports for 77 medicines on the EMA website, including orphan drugs, generic and biosimilar medicines, as well as medicines for use in children.

Thirteen (17%) of the 77 submission packages were not anonymised. Twelve were not anonymised because only the clinical overview was published, and the other because no documents were included in the package. These were excluded from the analysis, leaving 64 submission packages in our analysis.

Table 1. Glossary of terms

Anonymisation	The process of rendering data into a form that does not identify individuals and where identification is not likely to take place.
Direct identifiers	Elements that permit direct recognition or communication with the corresponding individuals (e.g. name, email, phone number, or subject identifier).
Generalisation	Consists of generalising or diluting the attributes of data subjects by modifying the respective scale or order of magnitude (i.e. a region rather than a city, a month rather than a week).
Personal data	Any information relating to an identified or identifiable natural person ('data subject'); an identifiable person is one who can be identified, directly or indirectly, particularly by reference to an identification number or to one or more factors specific to their physical, physiological, mental, economic, cultural or social identity (Article 2[a] of Regulation [EC] No 45/2001).
Pseudonymisation	Consists of replacing one attribute (typically a unique attribute) in a record with another. The natural person is still likely to be identified indirectly. Pseudonymisation reduces the risk of association of a dataset with the original identity of a data subject.
Quasi-identifiers	Variables representing an individual's background information that can indirectly identify individuals such as their date of birth, date of death, or date of clinic visit, residence postal code, sex and ethnicity. Quasi-identifiers also include demographics and socioeconomic information.
Randomisation	A family of techniques that alters the veracity of the data to remove the strong link between the data and the individual.
Redaction	Masking the data and text to be removed, often using a black box.
Suppression	The original value is replaced with alternate text. There are several ways that the replacement text can be selected, depending on the type of personal data and the readability in the anonymised reports.
Transformation	A process that reduces the risk of identifying a data subject by altering personally identifiable information in a dataset.

Table 2: Summary of the anonymisation techniques used for direct identifiers in the seven submission packages using a combination of techniques

Direct identifiers associated with trial individuals	Preserving pseudonymisation N=7 n (%)	Suppression N=7 n (%)	Redaction N=7 n (%)
Subject ID	7 (100.0)	–	
Screening number	2 (28.6)	–	2 (28.6)[a]
Accession number	2 (28.6)	–	1 (14.3)[a]
Manufacturer control number	2 (28.6)	–	1 (14.3)[a]
Patient ID	1 (14.3)	–	1 (14.3)[a]
Treatment ID	1 (14.3)	–	1 (14.3)[a]
Initials	1 (14.3)	–	1 (14.3)[a]
Sample ID	1 (14.3)	–	1 (14.3)[a]
Lot number	1 (14.3)	–	1 (14.3)[a]
Data clarification form ID	1 (14.3)	–	1 (14.3)[a]
Ticket number	1 (14.3)	–	1 (14.3)[a]
Sample reference number	1 (14.3)	–	–
Barcode	1 (14.3)	–	–
Custom ID	1 (14.3)	–	–
Kit number	1 (14.3)	–	–
Pharmacogenomic ID	1 (14.3)	–	–
Photos of trial individuals	1 (14.3)	–	–
Experiment number[b]	–	1 (14.3)	–
Oceans ID[c]	–	1 (14.3)	–
Direct identifiers associated with staff information			
Non-investigator staff names[d]	–	7 (100.0)	–
Sponsor and staff contact details[d]	–	7 (100.0)	–
Site ID[e]	–	5 (71.4)	–
Contract research organisation[f]	–	–	–
Signature	–	–	7 (100.0)

Abbreviations: ID, identifier.

a Redaction was used when the direct identifier was embedded in an image.

b Direct identifier was assigned to a subject sample in testing for the investigational product binding in an investigational product antibody assay.

c Oceans ID was a direct identifier assigned to a subject specifically in the event of development of progression of progressive multifocal leukoencephalopathy due to the investigational product.

d Suppression was used unless the information was associated with a subject ID, in which case this information was treated as a quasi-identifier associated with the subject ID.

e Site ID was considered a direct identifier when it was in the presence of staff but not in the presence of a trial individual. In one of the packages, the site ID was associated with a subject ID; the information was treated as a quasi-identifier associated with the subject ID.

f Suppression was used where the contract research organisation was named in the context of a staff member.

Anonymisation techniques for direct identifiers

Most of the submission packages that were anonymised (57 [89%]) used redaction only as the anonymisation technique for direct identifiers. The remaining seven (11%) submission packages used combinations of redaction and preserving pseudonymisation (six packages [9%]); or redaction, preserving pseudonymisation, and suppression (one package [2%]) for direct identifiers associated with trial individuals.

All seven submission packages used the combination of redaction and suppression for direct identifiers associated with staff information. The sponsor name was always retained, and the coordinating or site investigator names were retained unless they were directly associated with a subject.

Table 2 shows the anonymisation techniques used for each identifier for submission packages that used a combination of techniques.

Anonymisation techniques for quasi-identifiers

Most of the submission packages that were anonymised (57 [89%]) used redaction only as the anonymisation technique for quasi-identifiers. The remaining submission packages used a combination of redaction, suppression, generalisation, and randomisation (six packages [9%]); or redaction and randomisation (one package [2%]) for quasi-identifiers associated with trial individuals.

Table 3 shows the anonymisation techniques used for each quasi-identifier for submission packages that used a combination of techniques.

The study report team, led by a medical writer with a solid knowledge of EMA Policies 00431 and 00702 and the policies' implications for data protection, can reduce the anonymisation required after submission of the document by proactively reducing the use of unnecessary identifiers in the initial report drafts.

Table 3: Summary of the anonymisation techniques used for quasi-identifiers in the seven submission packages using a combination of techniques

Quasi-identifiers	Generalisation N=7 n (%)	Suppression N=7 n (%)	Randomisation N=7 n (%)	Redaction[a] N=7 n (%)
Age	6 (85.7)	3 (42.9)	5 (71.4)[b]	–
Race	–	4 (57.1)	–	–
Ethnicity	–	2 (28.6)	–	–
Height	–	2 (28.6)	–	–
Weight	–	2 (28.6)	–	–
Body mass index	–	2 (28.6)	–	–
Lean body mass	–	2 (28.6)	–	–
Body surface area	–	2 (28.6)	–	–
Waist	–	1 (14.3)	–	–
Drinking habits	–	3(42.9)	–	–
Smoking habits	–	3(42.9)	–	–
Family circumstances	–	1 (14.3)	–	–
Social circumstances	–	1 (14.3)	–	–
Medical history	6 (85.7)	6 (85.7)	–	–
Family medical history	–	2 (28.6)	–	–
Psychiatric hospitalisation	–	1 (14.3)	–	–
Dates	3 (42.9)	5 (71.4)	6 (85.7)[c]	–
Site ID	–	1 (14.3)	4 (57.1)[d]	–
Name	–	1 (14.3)	–	–
Staff name	–	1 (14.3)	–	–
Country	–	4 (57.1)	–	–
State	–	2 (28.6)	–	–
City	–	1 (14.3)	–	–
Region	–	1 (14.3)	–	–
Company/contract research organisation addresses	–	–	–	1 (14.3)
Organisation	–	2 (28.6)	–	–

Abbreviations: ID, identifier

a In three packages quasi-identifiers were redacted when these were embedded in images and could not be otherwise transformed. In three packages narratives were redacted; in three packages, listings were also redacted. The specific quasi-identifiers redacted in these packages were not specified.

b Age was supressed and replaced with a random value within the age range of the study population.

c The clinical dates were 'PhUSE offset' in five of the six packages; in one package calendar dates were adjusted based on an offset date.

d Site ID was supressed and replaced with a site ID chosen at random from the study.

The disadvantage of using redaction as an anonymisation technique, as opposed to techniques such as generalisation or randomisation, is that clinically relevant data that may be important in the context of the disease is lost in the redaction process.

Generalisation was used to transform age and medical history terms. The original age was replaced with a random age selected within an interval (5-, 10-, or 20-year intervals). The original medical term was replaced with a string of text corresponding to the high-level term, high-level group, or system organ class. The level of generalisation was dependent on the risk of re-identification for the individual subject (e.g., a subject could have his/her age generalised to a 10-year interval while another subject with lower risk could have his/her age generalised to a 5-year interval).

Randomisation was commonly used for dates and ages. Dates were replaced with a new date generated using a random offset for each individual and this offset was applied to all dates in the study for that individual. The most common algorithm used to offset dates was the PhUSE offset[10] (six of the seven submission packages that applied randomisation used this algorithm). Age was replaced with a random value within the age range of the study population.

Suppression was used for other quasi-identifiers such as race, ethnicity, weight, height, and body mass index. The alternate text used to replace the original value was dependent on the type of personal data and the readability in the anonymised reports; e.g., in some instances the alternate text was longer than the original text and tables could be difficult to read.

According to the anonymisation reports analysed, more than one anonymisation technique could be used for a given quasi-identifier; e.g., generalisation to a specific year interval or replacement with a random value within the inclusion criteria could be used for age, depending on the risk of re-identification.

Anonymisation techniques by type of drug

Of the 77 submission packages identified, 14 corresponded to orphan drugs, 14 to generics, and two to biosimilar medicines. The remaining 47 submission packages were not classified in any of these categories.

Of the 12 submission packages that were not anonymised because only the clinical overview was published, seven corresponded to generics. The remaining five submission packages were not classified as orphan drugs or biosimilar medicines. The submission package for which no anonymisation technique was used (because no documents were included in the package) was for

an orphan drug. These submission packages were excluded from the analysis.

Anonymisation techniques for direct identifiers by type of drug

All of the generic and biosimilar medicines submission packages that were anonymised used only redaction as the anonymisation technique for direct identifiers. A total of 10 (77%) of the 13 orphan drug submission packages that were anonymised used only redaction as the anonymisation technique for direct identifiers.

Three (23%) of the orphan drug submission packages that were anonymised used redaction together with other techniques; these equate to almost half (43%) of the seven submission packages overall that used redaction together with another anonymisation techniques.

Of the three orphan drug submission packages that were anonymised using redaction together with other techniques, two used a combination of redaction and preserving pseudonymisation; and one used redaction, preserving pseudonymisation, and suppression for direct identifiers associated with trial individuals. All three anonymised orphan drug submission packages used redaction and suppression for direct identifiers corresponding to staff information.

Anonymisation techniques for quasi-identifiers by type of drug

All of the generic and biosimilar packages used only redaction as the anonymisation technique for quasi-identifiers, except for one generic package that used redaction in combination with randomisation (calendar dates were adjusted based on an offset date).

A total of 10 of the 13 (77%) orphan drug packages used only redaction as the anonymisation technique for direct identifiers.

Three (21%) orphan drug submission packages used redaction together with other anonymisation techniques (a combination of redaction, suppression, generalisation, and randomisation). These three orphan drug submission packages equate to almost half (43%) of the seven submission packages overall that used redaction together with other anonymisation techniques.

Discussion

The results of this analysis show that the most frequently used approach to anonymise data in reports submitted to the EMA is redaction of identifiable personal data that has been included in the original document. The use of other anonymisation techniques, such as **transformation** or generalisation of identifiers, is generally limited, and most frequent in orphan drug reports.

In addition, our analysis shows that anonymisation is typically performed after reports are submitted to the competent authorities. Therefore, redaction is the most suitable method of anonymisation because it is performed retrospectively. These findings are supported by Kumar and Sareen[11], who suggested several reasons for using redaction only: (1) most of the documents are anonymised retrospectively, (2) most of the automated anonymisation tools are proficient only in performing redaction, and (3) application of other techniques in addition to redaction makes the process more time consuming.

The disadvantage of using redaction as an anonymisation technique, as opposed to techniques such as generalisation or randomisation, is that clinically relevant data that may be important in the context of the disease is lost in the redaction process. For example, using age ranges instead of redaction allows determination of whether specific findings are only related to specific age population groups (such as paediatric or geriatric subjects).

Another technique that is used to preserve data utility is pseudonymisation of subject identifiers. However, pseudonymisation is not considered an anonymisation technique because it allows for a subject to be tracked throughout a report. Although it reduces the risk of association of a dataset with the original identity of a subject, it is still possible to track the subject's data across different data sets.[12,13]

The study report team, led by a medical writer with a solid knowledge of EMA Policies 0043[1] and 0070[2] and the policies' implications for data protection, can reduce the anonymisation required after submission of the document by proactively reducing the use of unnecessary identifiers in the initial report drafts. This requires the development of a strong cross-functional strategy on data anonymisation (a data anonymisation plan) involving key contributors such as the medical writer, the medical monitor, the clinical data manager, the biostatistician, and the regulatory affairs representative.

The data anonymisation plan may involve several different strategies to reduce the risk of re-

identification while maintaining data utility. These may include the use of age ranges and pseudonymising as previously discussed. Other strategies are to avoid the use of subject identifiers in the body of the report; generalise from country to region; avoid the use of gender-related words; and present relative days (e.g., day since drug administration) rather than the actual dates.

Therefore, the challenge for medical writers is to become involved in the anonymisation strategy and the creation of a data anonymisation plan for the clinical documents from their initial stages, focusing on the balance between scientific value and risk of re-identification, especially for studies involving small populations and on rare diseases.

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Conflicts of interest

The authors are employed by PPD.

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Reports from the spring conference in Barcelona

SECTION EDITOR

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We invited EMWA members to report on the medical device symposium and selected Expert Seminars during the spring conference in Barcelona, held in May 2018. We hope that this initiative will help to keep EMWA members up to date with our fast changing profession. Thank you to all the contributors.

6th EMWA symposium: Medical devices and technologies

Historically, medical devices were mostly limited to surgical tools, such as those for bloodletting and removing kidney stones. However, as modern medicine developed, doctors became equipped with more and more tools and treatment options. Today, medical devices span a wide spectrum of items from correction glasses, dental fixtures to insulin pumps and pacemakers. In fact, there are over 500,000 types of devices registered on the European market, with total annual sales reaching 110 billion euros.

To ensure patient safety, certification and registration of medical devices is tightly regulated. Similar to pharmaceutical products, the effectiveness and safety of a medical device must be properly documented before receiving approval for regulatory authorities. However, shorter developmental timelines and relatively short presence on the market poses several challenges for providing timely and accurate documentation. To harmonise the requirements and procedures for registration in the EU, new directives for medical devices and *in vitro* diagnostic medical devices have been introduced.

The objective of EMWA's 6th Symposium was to familiarise medical writers with the field of medical writing for medical devices and what changes lie ahead. Experts in the field, representatives of regulatory authorities, and manufacturers were invited to give participants a broad overview of the field, the required types of documentation and showed opportunities for medical writers to become involved.

Introduction to medical devices

Speaker: **Claudia Frumento (International Communication in Medicine and Technology)**
Written by: Gabriela Plucinska, PhD, communication and graphic design, Utrecht, The Netherlands

Medical writers may find themselves intimidated when faced with requests for preparing documentation for a medical device approval and certification. Claudia Frumento shared her experience. From the start, she emphasised that writing about medical devices requires not only comprehensive knowledge of the human anatomy, but also an understanding of physics and engineering related to the functionality of the product. This technical information is collected in the form of a product dossier, which contains all the data related to manufacturing and intended product use. This dossier is required to release a medical device to the market, as well as data confirming the device's safety. The type of documentation required for certification of a particular device is based on the European risk classification, which reflects the risk that the use of the device poses for the patient.

The EU has recently tightened control over high risk devices by introducing new regulations and adopting the certification process to meet higher transparency standards. Frumento emphasised that while new guidelines may extend overall approval time and prove challenging to adapt for smaller companies, at the same time they open unique opportunities for medical writers. As many of the policies are still being established, writers can become involved in the legislation process and, working alongside the authorities, help shape the field and set future standards.

Writing for pharma versus medical devices – similarities and differences

Speaker: **Gillian Pritchard (Sylexis Ltd.)**
Written by: Gabriela Plucinska, PhD, communication and graphic design, Utrecht, The Netherlands

Medical writers associated with the pharmaceutical industry typically prepare a wide variety of documents, clinical study reports, pharmacovigilance documents, publications, lay summaries, and consent forms. This spectrum of documentation requires medical writers to develop an array of unique skills, which include: knowledge of clinical study design, ability to follow guidelines, language and communication skills, systematic approach to writing projects, and project management skills necessary for working with multiple partners and managing client expectations. As Gillian Pritchard took to the stage, she pointed out the high relevance of those skills when transitioning to writing about medical devices.

This is also reflected by the types of documents submitted for certification of a high risk medical device, which mirror the requirements for approval of new medications and treatments. Starting from articles about *in vitro* and animal studies, clinical investigation plans and clinical investigation reports, medical writers will find themselves working with familiar types of documents and templates that are similar to those required in pharma. In the certification process all of those documents are assembled into a clinical evaluation report (CER): a summary of the all available clinical information about the device. This information should be regularly updated.

The post-market surveillance (PMS) report may prove the most difficult to prepare for medical writers, Pritchard reflected. This is due to the fact that at the moment, some companies have not consistently gathered information about

a product once it was marketed. In such cases writers would first need to gather sufficient information about the product from literature searches, use the data that the company already has and then perform gap analyses.

From a legislative perspective – new requirements for medical devices registration

Speaker: **Paul Piscoi**
(European Commission)
Written by: Gabriela Plucinska, PhD, communication and graphic design, Utrecht, The Netherlands

Medical devices are typically present on the market for 18–24 months before improved versions become available. Such a fast turnover poses several challenges for regulatory authorities that are responsible for controlling safety. New EU regulations (2017/745 on medical devices [MDR][1] and 2017/746 on *in vitro* diagnostic medical devices (IVDs)) are implemented to improve coordination mechanisms and risk management associated with use of medical devices. Specifically, medical devices will be subjected to higher scrutiny, including creating a clearer and more transparent certification process. This is accompanied by establishment of expert panels, reference laboratories, and development of an EU wide medical devices database – Eudamed – expected to go live in March 2020.

Paul Piscoi from the European Commission explained that among the most important changes are the enhanced criteria for the conformity assessment. This assessment will be in part based on the CER, which for the high risk medical devices should contain data sourced from the clinical investigations conducted with a specific product. Evidence based on a similar certified device will be considered admissible, provided manufacturers demonstrate equivalence and have sufficient access to the technical and clinical documentation. To allow companies adequate time to adjust to the new regulations, hire appropriate staff, and apply for re-certification, the legislators introduced a transition period until 2020 for medical devices and 2022 for IVDs. During this time, certain clauses of the previous directives will remain in force.

As new regulations are starting to take effect and guidance documents are drafted, the European Commission is engaging in consultations with the public and stakeholders. Mr Piscoi encouraged EMWA to participate in this EU call and join the forefront of the upcoming changes.[2]

MDR and MEDDEV – What notified bodies are looking for in Clinical Evaluation Reports (CER)

Speaker: **Itoro Udofia**
(UL International UK Ltd.)
Written by: Malgorzata Paradowska, MPH, Proper Medical Writing, Warsaw, Poland

New MDR[1] forces notified bodies to focus more on solid information regarding device safety and performance under its normal intended use, which "shall be based on clinical data providing sufficient clinical evidence" to support compliance with essential requirements. The level of scrutiny will depend on the product risk, classification and novelty.

Technical documentation houses proof of compliance with essential requirements, and clinical evaluation is a key element. The sources of data for clinical evaluation are: clinical investigations, peer-reviewed scientific literature, and PMS regarding the device itself or an equivalent one. However, the clinical evaluation process does not end on finalising the CER before marketing. (Note: MEDDEV Guidance[3] was described as very supportive while writing CERs, but it does not cover all requirements from MDR.) A proactive PMS plan must also be provided. Apart from CERs, the following documentation will be scrutinised by notified bodies: risk management documentation; PMS plan and report; periodic safety update report (PSUR); post-market clinical follow-up (PMCF) plan and report; and summary of safety and clinical performance (SSCP, which will be available publicly on Eudamed). All these documents must be interlinked and constantly updated.

Notified bodies are expected to write Clinical Evaluation Assessment Reports (CEARs), which are based on the CER itself (including methodology, authors' qualifications, frequency of updates, demonstration of equivalence, conclusion on clinical benefit/risk analysis) and also, the following associated documents: device description and intended purpose; pre-clinical evaluation data; risk management documentation; clinical investigation plans, results, and justifications; PMS/PMCF plans and justifications; and conformance to the relevant essential requirements.

"The bars have been raised", Udofia said. Professional medical writers will be extremely helpful in preparing high quality medical device documentation. Such medical writers need to: understand the product and its description, impact and relevant clinical data; apply up-to-date regulations; and write for the target audience, including notified bodies, competent authorities and expert panels.

Patients as users: Apps, technologies, security, potential failures

Speaker: **Kyle J. Rose**
(International Diabetes Federation, IDF)
Written by: Malgorzata Paradowska, MPH, Proper Medical Writing, Warsaw, Poland

People living with diabetes often struggle to balance their blood glucose concentrations as it is a tedious and challenging process. They make approximately 50 disease-related decisions every day. New mobile applications are specially designed to support diabetes patients. The most effective are able to provide a consumer-friendly user experiences and increasingly meet patients' expectations of reducing the disease burden.

As certain diabetes apps affect disease management, these ones should be considered medical devices and thus be treated in a proper regulatory manner. The following groups of health apps, relevant to diabetes patients, were discussed:

1. **Logbook trackers.** Apps documenting daily events: blood sugar levels, exercise and medications
2. **Nutrition and exercise**. Apps that encourage people to be active, take care of nutrition and

facilitate carbohydrate counting.

3. **Motivation, education and coaching** programmes.
4. **Middleware & eHealthcare Solutions (EHS)**. Apps that serve as a medium to communicate with medical devices and health systems.
5. **Device manufacturer software**. Software made for devices such as insulin pumps, continuous glucose monitoring (CGM), and traditional blood glucose meters (BGM).
6. **DIY (do-it-yourself) apps** created by patients such as the NightScout Foundation for remote glucose monitoring.

For more information on diabetic software, please see the International Diabetes Federation (IDF) position paper[4] and a monograph on the digitalisation of healthcare.[5]

Rose presented directions for medical writers involved in the development of diabetic medical devices. Medical writers have the power to influence patients with diabetes through the written word, which can be accessed also via medical apps. Their message should present accurate information about the condition, dispel outdated stereotypes, and also be adjusted to the phase of the disease. Medical writers should use inspiring and motivational communication, and not always focus so much on complications (the diabetes "monster" can be scary at times). It is important to write a balanced argument to make the text realistic. In addition, any description on the use of a medical device should be supported by real-life examples. "Good communication and understanding patient expectations can help create medical devices people will love", Rose concluded.

Systematic reviews in medical devices

Speaker: **Ivan Krstic**
(RELX Group, EMBASE/Elsevier)
Written by: Małgorzata Paradowska, MPH, Proper Medical Writing, Warsaw, Poland

EMBASE is a commercially available tool for peer-reviewed scientific literature searching that is recommended by the EMA, Cochrane Collaboration, WHO, and other institutions. The European Commission recommends using EMBASE when performing literature searches for CERs.[3]

Although the Medline database is a good starting point, it is insufficient for systematic searching, as it has incomplete coverage of European journals. Therefore, other supportive data sources are recommended when conducting systematic reviews, including EMBASE and the Cochrane Central Database. The literature review should be performed by "applying objective, non-biased, systematic" searches and use PICO methodology, which splits the clinical question into four concepts: Patient, Intervention, Control, and Outcome.[3] The process of conducting a systematic review is described in detail in the Cochrane handbook.[6]

EMBASE ensures comprehensiveness by including Medline content and an additional ~3,000 non-US journals (mainly European journals, but also ones from Asia and the rest of the world). EMBASE content comes from peer-reviewed journals and conference abstracts. Indexing is based on the Emtree taxonomy, which focuses on drugs, diseases, and devices. Two search forms are available for medical devices: 1. a *medical device search form* that limits the search according to manufacturer or trade names, among others; and 2. a *PICO search form*.

For each of the PICO components, the most specific Emtree term should be used first, and then supplemented with as many synonyms as possible. The taxonomy synonyms (including trade names) are automatically proposed by EMBASE. The system records the search term and all synonyms, allowing the full search strategy to be documented. Results can be easily exported and packed into a reference management system. Furthermore, regular updates can be received automatically by setting up e-mail alerts for any relevant query. Furthermore, regular updates can be received automatically by setting up e-mail alerts for any relevant query.

From bench to publication – A case example takes us through the life-cycle of a medical device

Speaker: **Dipl.-Ing. Myriam Stieler**
(Director Medical Affairs at Biotronik)
Written by: Mariella Franker, PhD, Franker Medical Communications, Beinsdorp, The Netherlands

Myriam Stieler's case example of a new bioresorbable scaffold nicely illustrates the development of a medical device throughout its life cycle. The first step to develop a novel product is defining key design requirements. The introduction of the permanent stent – and subsequently the drug-eluting stent – greatly improved treatment of coronary artery disease. However, other complications, such as restenosis and stent thrombosis, arose. Biotronik defined a solution: a stent that removes the blockage and then completely disappears. They developed a bioresorbable magnesium-based prototype. First, extensive testing in pre-clinical bench tests was done e.g. to assess the stent backbone flexibility. Subsequently, safety studies in animals were performed to assess restenosis rate and thrombogenicity. As pre-clinical data cannot be directly translated to humans, a clinical trial in humans was thereafter performed to assess safety.

The first-in-human trial PROGESS and later the BIOSOLVE studies were to investigate safety and efficacy in humans. After the BIOSOLVE-I study, application for CE mark was rejected

because of the small sample size and lack of statistical analysis (which was not required by the old regulations). These issues were addressed in BIOSOLVE-II. Data from this trial showed that the stent dissolved too quickly after implantation, causing restenosis. Essential changes were made to increase the half-life of the stent in the body. The results of the following trial were greatly improved and CE mark was finally obtained in 2016. Pivotal and post-market studies are currently ongoing (BIOSOLVE-III and IV). Publishing validated data, both before and after the product is released to market, is essential to monitor performance of the device and for future developments.

"Ideally, you move through each developmental phase only once. In reality, several iterations and improvements are required at every stage before you come to the final product.", Dipl.-Ing. Stieler noted.

New focus on clinical evidence: the added value of a publication strategy plan

Speaker: **Patrice Becker, MSc, MBA (Global Director Scientific Communications at Sofradim/Medtronic)**
Written by: Mariella Franker, PhD, Franker Medical Communications, Beinsdorp, The Netherlands

The new MDR 2017/745 increasingly requires peer-reviewed clinical evidence when applying for approval or re-approval of a medical device.[1] Clinical evidence must be obtained before and after a product enters the market: pre-clinical, clinical pre-approval and clinical post-approval studies. It is important to have a publication and communication strategy in place that covers the entire life cycle of a product. Such a strategy will aid manufacturers to be prepared for the new requirements either for market approval and post-market evidence generation.

A publication strategy "tells the story" of an invention and communicates important scientific data to the right audience at the right time. For example, publishing in peer-reviewed journals during the early phases of the product life cycle will support early awareness of key opinion leaders and promotes the information dissemination of the product after approval. Of course, there are also challenges to face. The limited sample size of studies with medical devices, and the transferability of animal study data to humans are constant areas of debate. In addition, the objectiveness of publications about industry sponsored studies that originate solely from company authors may be challenged by authorities.

In post-market phase, medical writers will have a big role to play in supporting authors with the different types of clinical publications. During the panel discussion, Patrice Becker and Itoro Udofia (Notified Body, Underwriters Laboratories) discussed that clinical evidence will become the new standard for medical devices. Becker emphasised that experts from many different areas, such as medical affairs, clinical, regulatory, marketing, R&D, and medical writers, must work together to create an effective publication strategy.

"[In the future] Medical affairs will have a preponderant role in evidence generation.," said Becker.

Get your money's worth – Interesting opportunities for medical writers in market access

Speaker: **Oleg Borisenko, MD, PhD (Director at European MedTech and IVD Reimbursement Consulting Ltd.)**
Written by: Mariella Franker, PhD, Franker Medical Communications, Beinsdorp, The Netherlands

Reimbursal and funding are essential steps for market access and the success of a product. A value dossier contains all relevant data of a product, such as indication of the epidemiology and burden of disease, current treatment modalities and their limitations, systematic literature review for the procedure in scope, health economic analysis etc. Excerpts are often used for reimbursement and health technology assessment (HTA) submissions. Concepts of reimbursement and funding are complex and significant differences exist between countries. Nevertheless, there are clear opportunities for medical writers when it comes to creating the value dossier and other reimbursement and HTA submission documents. Oleg Borisenko provided some useful and practical tips for writers who want to move into this field. He recommends: 1. seek collaboration with existing agencies and group your knowledge of different country systems, 2. take advantage of existing submission templates, and 3. increase your language skills to cater to demand in different countries.

"It is a complex world, but one that can provide a lot of opportunities [for medical writers] as well", Dr Borisenko noted.

The key concepts in market access are reimbursements, funding and the HTA. Reimbursement is a system that provides payment for a procedure or technology. While in most EU countries, reimbursement is based on cost data, some countries demand evidence of efficacy, safety and sometimes cost-effectiveness (Austria, France, Belgium, Netherlands). Funding is the willingness to pay for a procedure and can be influenced by multiple stakeholders. Funding is decided at hospital level in some countries, contrary to pharma, different types of medical technologies compete for the same hospital budget. The key objective of the HTA is to advise policymakers. It includes systematic literature review of efficacy and safety of the product and a health economic analysis. HTA is typically performed by governmental or independent organizations and can have a large impact on reimbursement and funding policies.

Conclusion

New EU regulations are introducing higher scrutiny standards to the field of medical devices. With requirements for more clinical data and close monitoring of device use come unique opportunities for medical writers in the field.

Speakers at the symposium highlighted the relevance of the transferable skills of medical writers including knowledge and understanding of regulatory procedures and objective writing. Thanks to those skills writers familiar with writing for pharmaceutical industry will easily adapt to medical devices field. At the same time this is a chance to expand writers portfolio by writing new types of documents, such as systematic reviews, market approval documentation and post-market surveillance reports.

Broad range of required documentation gives writers an opportunity to find the niche for themselves, whether it is with standard regulatory writing, scientific publications or patient oriented documents. Finally, as manufacturers take advantage of modern digital technologies writers can take roles of complex science translators to broad public.

In summary, medical writers willing to join the medical device field will find themselves working with familiar scientific concepts, while preparing new types of documentation and expanding their expertise to physics and engineering. Furthermore, as new regulations are taking effect writers will be working on the forefront of establishing new standards in the field.

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EMWA social events programme

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(with contributions from some of the team at Trilogy Writing & Consulting – Rachel Beeby, Elizabeth Millar, Jeffrey Fielhauer, Laia Pedro-Roig, and Bryan Greene)

The social programme for the 46th EMWA conference in Barcelona offered a diverse range of options for exploring the city, culture and cuisine of Barcelona. These included the annual dinner, a Spanish Cuisine cookery class, and both Gothic and Modernist walking tours.

The annual dinner, "Dinner with Friends", took place at Mussol Caspe, where delegates enjoyed a traditional Catalan meal. There were 10 small tapas courses including Montseny sausages (butifarra), coca bread with tomato, garden vegetables, and much more. Dishes were prepared with fresh regional ingredients, and accompanied by Catalan wine. Each course was served with a break in between, which allowed for a leisurely meal and an opportunity to catch up and to make new friends. The evening reflected some true elements of Spanish character: sociability and sharing!

The hands-on Spanish cuisine cooking class provided the opportunity to acquire new cookery skills in making gazpacho and also paella.

Delegates found the walking tours through Barcelona very informative, including immersion in Spanish history from excellent tour guides. Particular highlights were seeing the ruins, walls and graves from an ancient Roman settlement the the older parts of Barcelona. Other highlights were the Mercat de la Boqueria market just off the main street of Las Ramblas, which had a variety of exotic fruit, chocolate and nougat. Las Ramblas was a diverse and vibrant street with lots of hustle and bustle, yet not far from this was the gothic quarter, the oldest part of the city, where there were small, quiet courtyards surrounded by tall buildings. Another stop was at the Sagrada Familia, the Roman Catholic church designed by Catalan architect, Antoni Gaudi. Here, the architecture amazed with so much detail. Incredibly, the designing and building of this church began over 100 years ago and is still ongoing. All in all, a memorable experience!

Expert Seminar: Use of clinical study reports for Cochrane Reviews

Written by: Marisa Granados, email: mgranados85@gmail.com

Background

Systematic reviews have traditionally been based on randomised controlled trial (RCT) reports, but clinical study reports (CSRs) are now becoming more widely available for use. Dr Sera Tort, Clinical Editor at the Cochrane Editorial Unit in London, explained why this is important, and how Cochrane is working to include CSRs in Cochrane Reviews, if needed.

Cochrane is a non-for-profit global network that summarises research results to make scientific evidence readily available. Its main output, Cochrane Reviews, are recognised internationally as the gold standard for high quality, trusted information.

Key takeaways

- Over-reliance on RCTs for systematic reviews can sometimes be problematic. RCTs suggesting a beneficial effect tend to be published more easily than similar trials showing negative results. In this context, a systematic review including only published studies could identify a false beneficial effect or miss an important adverse effect.
- CSRs are very detailed documents that describe the methods and results of clinical trials and are used by regulatory agencies to assess the safety and efficacy of drugs. CSRs have typically been confidential, but this is now changing. Cochrane is developing a set of guidelines about when to use CSRs in Cochrane Reviews, which will be released soon.
- Currently, the Cochrane Library (cochranelibrary.com) is about to launch an enhanced online platform to improve user experience and functionality, which will be available in English and in Spanish.

Comments and discussions

Much of the discussion session focused on the use of CSRs and the role that regulatory medical writers can play in Cochrane Reviews. Particularly, are currently available CSRs being used in reviews, and if so, should the writers be acknowledged?

Although some CSRs are already available through the EMA website, most Cochrane Reviews don't use them for now. As Dr Tort explained, the guidelines Cochrane is preparing will help identify the criteria for including CSRs in Cochrane Reviews. Future development will include methods and tools for extraction and analysis.

Expert seminar: Medical journalism – one small step for the medical writer

Written by: Adrian Tilly, adrian@azurhealthscience.com

Do you ever dream of writing for a larger audience? At the recent Expert Seminar Series on Medical Journalism, the combined experiences of Sabine Louët (media entrepreneur/founder, SciencePOD), Brian Trench (senior lecturer, Dublin City University) and Danny Buckland (award winning freelance health writer, UK) presented valuable insights, with wit and warmth, for any medical writer with a journalistic itch that just won't go away. For those wanting to make the leap, here's the low-down from their advice:

- **In dreams begin responsibilities:** Whether you want to write to better inform the public, or to hold those in power to account, journalism is assumed to be unbiased. This brings its own obligation for accuracy and fidelity in reporting. Thankfully, such skills are not anathema to the medical writer.
- **Don't believe the hype:** The public is not as interested in the science *per se* as in its future application. However, journalism often goes from scientific discovery to application without drawing breath. Therefore, be realistic about timescales, risks and benefits; think of your reader with the condition.
- **Anatomy of a story:** The public has an increasing appetite for science-related stories, but how do you get *your* story read? Firstly, it needs to be relevant (topical) and of human interest (ask yourself: who cares?). Hooking the reader with the headline is paramount, followed by content that is clear and engaging backed up by meaningful statistics, but

Expert seminar: Data privacy and uility-led-anonymisation

EU General Data Protection Regulation (GDPR) and EMA Policy 0070 – linkage and overlaps

Written by: Stephen Jackson, PhD, Voisin Consulting Life Sciences (VCLS), jackson@voisinconsulting.com

Keeping up with new regulatory requirements and legislations is complex and time consuming for medical writers – but there are some changes that can't be missed! The new EU General Data Protection Regulation 2016/679 (GDPR), effective from May 25, 2018, aims to harmonise the data protection laws across all member states to maintain standards of privacy and safeguard EU citizens against data breaches in our evolving electronic world. Individuals, organisations, or companies that are either "controllers" or "processors" of personal data from the EU have obligations under the GDPR, and non-compliance will incur significant financial penalties.

EMA Policy 0070 enables academics and researchers to access clinical trial data that could enhance scientific knowledge and quality of research within the pharmaceutical industry. Whilst the GDPR endeavours to protect by

design (i.e., built-in systems or technology designed to ensure compliance) and by default (i.e. minimisation of data collection and processing), Policy 0070 requires clinical reports that are disclosed in a public portal (https://clinicaldata.ema.europa.eu) to also be compliant with data protection legislation. The use of proactive pseudo- and anonymisation techniques by medical writers can help prevent re-identification of subjects and retain the utility of clinical data. During the seminar, case studies, including the right of data subjects to be forgotten, clinical reports submitted to national competent authorities under the decentralised procedure, and use of post-mortem data, were used to highlight the overlap between the GDPR and Policy 0070, and the complexities facing medical writers. With this important legislation in mind, finding the right balance between data protection, transparency, and scientific utility is paramount to gaining public trust.

Chair:

Sam Hamilton, PhD[1]

Presenters:

Elizabeth Youngkin, JD, LLM, CIPP-E[2]
Raquel Billiones, PhD[3]

Affiliations:

1. Sam Hamilton Medical Writing Services Limited, Newcastle Upon Tyne, UK
2. Certified privacy law professional for Europe, North Carolina, USA
3. Clinipace AG, Zurich, Switzerland

lacking boredom-inducing detail. Simple!

- **Work smarter, not harder:** Use today's technology to find stories (what's #trending), as well as getting on an editor's good side (provide images and video alongside your story).
- **How to win friends and influence people:** Journalism gives a voice to more people than just the "author"; convincing peers to comment on the work of colleagues gives third party credentials to your story. Therefore, honing your powers of persuasion will be time well spent.

Finally, **persevere:** Remember J.K. Rowling was turned down by numerous publishers.

Expert seminar: Orphan drugs and rare disorders

Written by: Marisa Granados, mgranados85@gmail.com

Rare diseases are uncommon and in Europe, are considered as such if less than one in 2,000 people is affected. Typically, these diseases are genetic and left untreated, are fatal.

Drugs for rare diseases are called "orphan" because few companies are willing to invest in them, and not without cause. Orphan drug development is fraught with obstacles. For one thing, finding enough patients willing to participate in clinical trials is difficult. Furthermore, the lack of literature on the subject means there is no knowledge about the appropriate treatments, dosage, duration or endpoints to measure effectiveness.

Orphan drug legislation approved in Europe in 2000 provided commercial incentives for companies to pursue the development of these drugs. This led to an increase in orphan drug approval and, by 2021, sales are expected to take up 21% of the market.

This expert seminar series focused on the particularities of medical writing in the field of rare diseases, the increasingly active role of patients, and the regulatory requirements of orphan drug applications.

Medical writing for orphan diseases: What you need to know

Background

Medical writers in the field of orphan drugs face unique challenges related to the small number of patients and the limited knowledge and awareness of rare diseases. Dr Carl Bjartmar, Chief Medical Officer at Wilson Therapeutics AB, outlined the most important points that medical writers in this subject should keep in mind.

Key takeaways

Medical writers play a key role in providing the quality information needed to support orphan drug development, as follows:

- **Publication planning**

The clinical trial programme is small in orphan drug development, so there may be less opportunities to publish data. Researchers might want to consider publishing clinical data sparingly. Raising disease awareness may also be needed, requiring publishing review papers. Also, journal selection can be complex as there may be few specific journals and general medical journals are often reluctant to publish an article on a rare disease. Other considerations include a small author pool and limited expert peer reviewers.

- **Communicating clinical trial data**

Certain aspects of the study design like a small sample size, may need to be justified and endpoints will probably also need to be explained.

- **Regulatory writing**

The writer needs to have an understanding of the marketing authorisation processes, as well as regional differences in incentives, and the implications of potential fast-track designation.

The rare disease patient – a medical writer's unlikely ally

Background

Patient engagement is particularly important in the field of rare diseases, where knowledge is scarce. Patients are experts on their condition and their expertise is critical to help define research needs and strategies and to identify patient-relevant outcome results. In this talk, Dr Elisa Ferrer, Patient Engagement Senior Manager at EURORDIS (Rare Diseases Europe), provided key insights on how medical writers can involve patients with rare diseases in regulatory document development, and why they should.

Key takeaways

- The role of patients in research and drug development is increasing. This not only helps patients feel valued and acknowledged, but there are also clear benefits gained by their participation at every step of the drug development process. PSC Patients Europe, for example, is an organisation that provides patient-led lay summaries of scientific papers. Their initiative has resulted in these papers being translated into 27 languages, dramatically increasing their reach.
- One fruitful way to increase patient engagement is to reach out to disease-specific patient organisations. Another way is to collaborate with community advisory boards, which are groups of volunteer patients who offer their expertise to sponsors of clinical research data.
- When pursuing patient collaboration, consider following guidelines like the EURORDIS Charter for Clinical Trials. Patient organisations should be informed of all aspects of the clinical protocol before collaborating, and study results should be published, even if they are negative or inconclusive.
- Finally, as valuable as their knowledge from the inside is, not all patients are trained in drug development. Therefore, there should be documents to support trained and non-trained patient engagement. EURORDIS Open Academy offers a summer and a winter school, where training and mentorship are available for patients.

Three stages to orphan designation

The three main stages to obtaining an orphan designation are submission and validation, evaluation, and decision. Dr Elisabeth Penninga, Chief Medical Officer at Danish Medicines Agency and Member of the Committee for Orphan Medicinal Products (COMP) at EMA, provided a step-by-step guide to the process as well as valuable advice for successful applications.

Background

Applications for orphan designation are evaluated by the COMP, which is part of EMA. Receiving the orphan drug status carries with it a number of advantages, including protocol assistance, scientific advice and access to a

centralised procedure, which guarantees equal access for the drug in the EU.

Key takeaways

The application for Orphan Designation can be made at any point in the drug development process. It consists of three main stages:

- **Submission**

The application should be made using the template available on the EMA homepage. It requires a detailed description of the condition to be treated as well as the medical product to be tested. Often the most challenging part is justifying medical plausibility, i.e. that the product has effect and significant benefit in treating the condition. Significant benefit must be claimed for all products marketed for the same indication. It is highly recommended to take advantage of the pre-submission meeting to resolve any questions before submission. Applicants may also request scientific advice, which is not legally binding but can be very helpful.

- **Validation and Evaluation**

The purpose of validation is to check that sufficient data has been submitted for assessment. After validation, the committee will evaluate the application.

- **Decision**

Sixty days after submission the committee will communicate its decision. It can be positive, negative, or there may be further questions before a final decision can be made. In this case, the Company will be invited for an oral explanation, after which the final decision is made. If it is negative, there is an option to appeal.

Questions and comments

Three topics dominated the discussion session that followed: scientific advice, issues related to international trials, and the problem of the small patient numbers.

Regarding scientific advice, what sorts of obligations are tied to it? Are sessions limited to the questions the applicants have or can they expect more input from the advisers?

According to Dr Penninga, although scientific advice is not legally binding, if, while reviewing the application, the committee notices that the advice was not followed, it may raise questions.

It is important to give good reasons and proper argumentation for not following the advice.

The process of scientific advice should be thought of as a collaboration. Applicants lead the session with their questions, but if the advisers have interesting ideas of their own to share, they will.

We have seen the process for orphan designation in the context of the EU, but does it work the same way when global trials are involved?

The answer is, in short, yes. The clinical trials can be conducted internationally, but most often, European patients must be represented as well; at least this will ease the process. There are guidelines for this situation (available on the EMA homepage).

How can the shortage of patients be overcome?

Dr Bjartmar suggested using adaptive techniques, statistical methods, and merging phases of clinical trials to account for small sample size. Dr Ferrer agreed and noted that patients are also positive about finding new strategies for small population studies. Also, another alternative is to use historical controls whenever possible. "This is a well-known issue in rare diseases," said Dr Penninga, and suggested asking for scientific advice and protocol assistance to find solid ways to overcome it.

Expert seminar: The new EU RMP guidance and template in daily pharmacovigilance practice

Written by: Diana Radovan, PhD
diana.radovan@trilogywriting.com

Regulatory background:
The session addressed the major revision (Revision 2) of the Guidance on EU risk management plans (RMPs): the Good Pharmacovigilance (PV) Practice Module V (published by the EMA in March 2017) and the related RMP template update, as well as their impact on the daily lives of PV medical writers.

Speakers:
The speakers were *Val Simmons*, MBBS FFPM, and *Sven Schirp*. Val Simmons, the European Qualified Person for PV (QPPV) at Eli Lilly, has more than 30 years experience in pharmacovigilance and has been a member of various working groups, including the European Federation of Pharmaceutical Industries and Associations PV Expert Committee. Sven Schirp, the Head of Global Pharmacovigilance Writing at Boehringer Ingelheim, has been active in PV since 2009 and presented on risk-benefit at the 3rd EMWA Symposium in 2015. The ESS PV session was moderated by Tiziana von Bruchhausen, PhD, EMWA President, Chair of the EMWA PV Special Interest Group, and Senior Global PV Writer at Boehringer Ingelheim.

Key takeaways:
Val Simmons, having been closely involved in the RMP Revision 2, explained that the industry needed more focused RMPs. Before the revision, RMPs sometimes included a high number of safety concerns (i.e., important identified risks, important potential risks, and missing information) and ran over 1,000 pages, "the RMP had lost its way." The concept of an important risk has not changed with the revision, but has been revisited and explained in line with ICH principles. The revised guidance clarifies the focus of RMPs with regard to safety concerns, strengthening a risk-proportionate approach. To illustrate these principles, Val presented the following explanation (kindly provided by the QPPV of Astra-Zeneca):

- **signals:** petty thieves who want to be criminal, although very few succeed
- **adverse drug reactions (ADRs):** adequate evidence to be sentenced for causal relationship, sometimes only based on circumstantial evidence
- **risks:** the damage (broken window or nose) caused by the ADR
- **important risks:** more severe vandalism, where probation and/or a rehabilitation programme is deemed necessary

Val gave several examples to illustrate the differences among the concepts above. If the clinical outcome (the risk, e.g., infection caused by the ADR neutropenia) is a clinically relevant change severe enough to impact the benefit-risk, then this risk is important. Val also provided tips for the practical implementation of these principles in RMPs and shared the following rules of thumb:

- discussing the benefit-risk impact in the RMP (Module SVII.3), clarifies whether a risk is important
- either a safety concern is important enough to conduct additional risk management activities, or it is not important enough to be included in the RMP.

Sven Schirp – who has broad experience with RMPs and their assessment – discussed the impact of Revision 2 on the RMP global management: the more stringent approach in the definition of safety concerns may lead to differences in the list of safety concerns between EU RMPs and global periodic safety update reports (PSURs).

Regarding the practical implementation of the revised format, Sven analysed the impact on the PV writer throughout the RMP sections in the Revision 2 template, discussing which new information or data needed to be provided or revised. Sven's rule of thumb for PV writers was to advise their teams to use common sense while updating RMPs, for example, not to generate new data for products that have been on the market for a long time only for the sake of the revised template. He advised writers to provide transparent justifications for empty sections and to cross-reference to previous procedures, to help the assessor understand how sections were populated.

Sven also advised RMP authoring teams to carefully consider the potential impact on other documents when introducing changes in the RMP. If safety concerns are removed, added, or reclassified in the EU RMP based on the Revision 2 guidance, this will impact RMPs submitted to other countries and the benefit-risk profile in the PSUR, which is a global document.

Comments and discussions:
Val and Sven gave interactive presentations, sharing their opinions and providing practical tips for PV writers. The participants asked various questions on the implementation of the revised guidance. One participant expressed feeling motivated to return to his desk and apply the tips he'd learnt.

The key message of the session was that converting an RMP to Revision 2 format is not a simple matter of condensing and copy/pasting; the need for a critical review of the safety profile of the product offers the opportunity to remove safety concerns as appropriate. However, the impact of the changes in the list of safety concerns needs to be carefully discussed within the authoring teams. A deep understanding of the principles and requirements of Revision 2 is essential to re-focus the RMP and to effectively plan risk minimisation measures. PV writers should properly train RMP authors at the RMP kick-off meeting.

The session was well received. Conference participants could further talk with the speakers during an informal PV lunch roundtable discussion.

News from the EMA

The articles included in this section are a selection from the European Medicines Agency's News and Press Release archive from April 2018 to June 2018. More information can be found on the agency's website: www.ema.europa.eu

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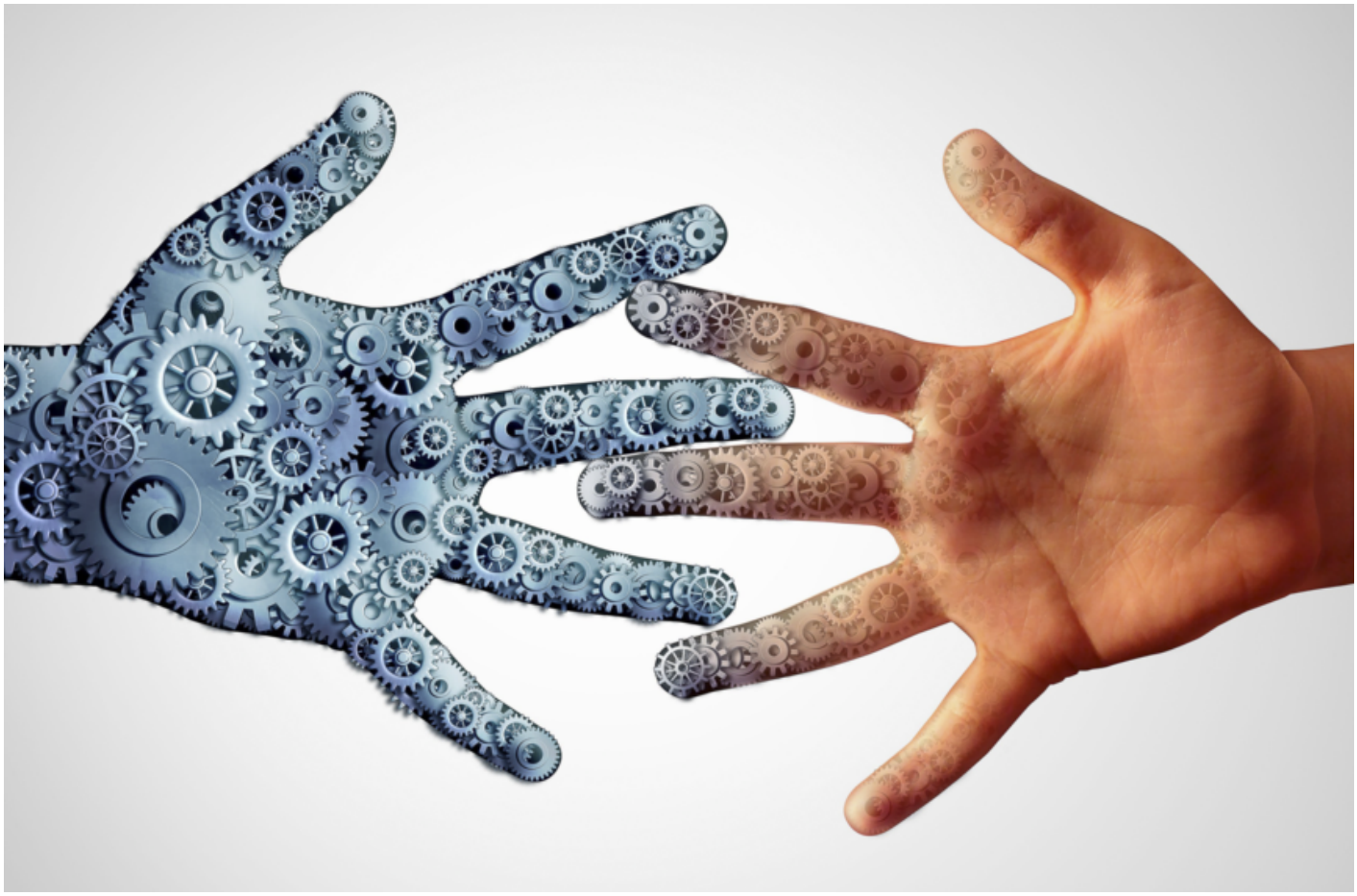
Increasing oversight of API manufacturing through international collaboration

April 12, 2018 – The European Medicines Agency's (EMA) and its European and international partners have successfully strengthened their interactions to improve the oversight of active pharmaceutical ingredient (API) manufacturers worldwide, as highlighted in the International API inspection programme report for 2011-2016, published today. APIs are the substances responsible for the activity of a medicine.

This international collaboration allows EMA, several European Union (EU) national authorities (France, Denmark, Ireland, Italy, and the United Kingdom), the European Directorate for the Quality of Medicines (EDQM), the United States Food and Drug Administration (FDA), Australia's Therapeutic Goods Administration (TGA), Health Canada, the Japanese Ministry of Health, Labour and Welfare (MHLW) and Pharmaceuticals and Medical Devices Agency (PMDA), and the World Health Organization (WHO) to share information on good manufacturing practice (GMP) inspections of manufacturers of APIs that are located outside the participating countries.

Nowadays, many pharmaceutical companies outsource the production of APIs to contract manufacturers located all over the world. This has led to an increased need for inspections, to ensure adequate oversight of these facilities. The overall objective of this initiative is to ensure more sites are monitored by making best use of inspection resources worldwide through increased co-operation, mutual reliance between participating regulatory bodies, reducing duplication of inspections and increasing inspection coverage.

The initiative started with a pilot in 2008–2010, and became a full programme in January 2011. The report published today gives an overview of the activities carried out by European authorities, the FDA, TGA, and WHO between 2011 and 2016. Over 6 years, 1,333 inspections were carried out at 458 manufacturing sites of common interest. These sites were located in 18 different countries, most of them in India (49%) and China (36%). The participating authorities have concluded that this programme is beneficial and agreed to continue their collaboration.



Two years of PRIME

May 7, 2018 – In the 2 years since its launch, the PRIority Medicines scheme (PRIME) of the EMA has succeeded in driving innovation and improved the efficiency of the development process in therapeutic areas with the most pressing unmet medical needs. The goal is to support and optimise medicine development, so that patients whose diseases cannot be treated or who need better treatment options have access to new medicines that enable them to live healthier lives.

Since the launch of PRIME in March 2016, EMA has received and assessed a total of 177 requests for eligibility to the scheme. Of these, 36 (21%) have been accepted. The agency has received requests across a wide range of therapeutic areas; oncology and haematology medicines make up the largest share, but there have also been notable submissions for medicines that cover indications in infectious diseases, neurology and psychiatric disorders.

An overview of the 36 medicines accepted for PRIME shows the focus of the scheme on therapeutic areas where the availability of new medicines could be particularly beneficial: 83% concern rare diseases and 44% are intended to treat paediatric patients. 40% of the medicines admitted into PRIME are advanced therapy medicinal products (ATMPs), which have the potential to reshape the treatment of a wide range of conditions. A large proportion of these medicines are being developed by small and medium-sized enterprises (SMEs), who often lack experience in the regulatory approval process. 22 (61%) of the medicines accepted for PRIME have received scientific advice from the Agency

Two years on, the agency has already received the first three marketing authorisation applications for medicines that were accepted for PRIME. They are all currently are under evaluation with the first opinion expected later in 2018.

A key feature of the PRIME scheme is "kick-off" meetings – a unique type of meeting for medicines that are eligible for PRIME. The aim of the meetings is to agree on next steps on how best to address any identified issues and/or to identify issues to be discussed normally in the context of scientific advice. These multidisciplinary meetings bring together the rapporteur for the medicine as well as the chairs and experts of relevant EMA committees to ensure that all aspects of a medicine's life cycle are discussed early, including risk management issues.

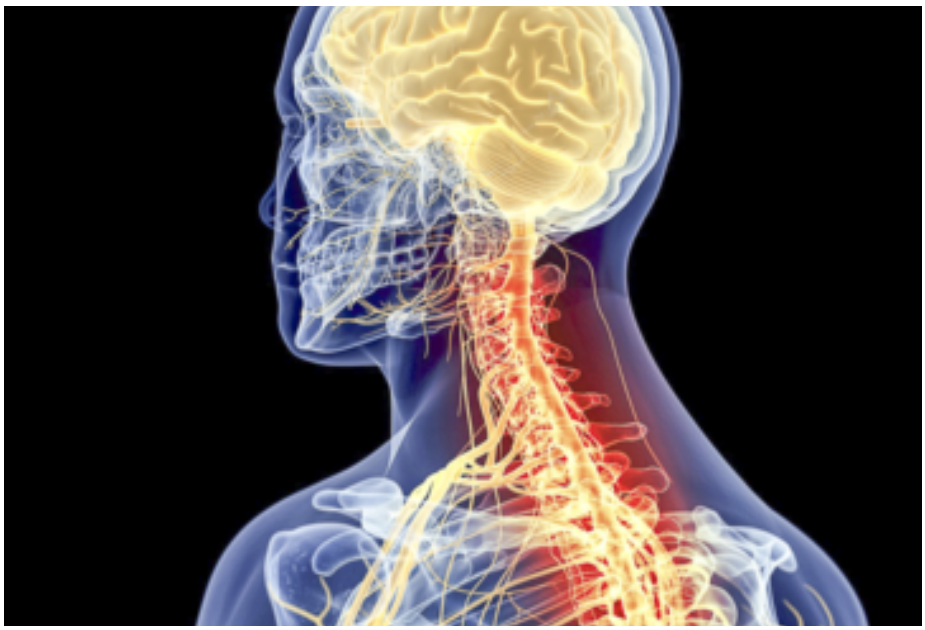
EMA has published new guidance for applicants on interactions in the context of PRIME which covers the preparation and conduct of kick-off meetings, questions and answers and the template for applicants' requests.

Multiple sclerosis medicine Zinbryta no longer authorised as its risks outweigh its benefits

May 18, 2018 – The EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has confirmed that the multiple sclerosis medicine Zinbryta (daclizumab beta) poses a risk of serious and potentially fatal immune reactions affecting the brain, liver, and other organs. Patients could be at risk from the start of treatment and for several months after stopping treatment, and it is not possible to predict which patients will be affected.

Zinbryta was authorised in 2016 for treating relapsing forms of multiple sclerosis. To date over 10,000 patients have been treated with Zinbryta worldwide, of which the majority of EU patients were in Germany.

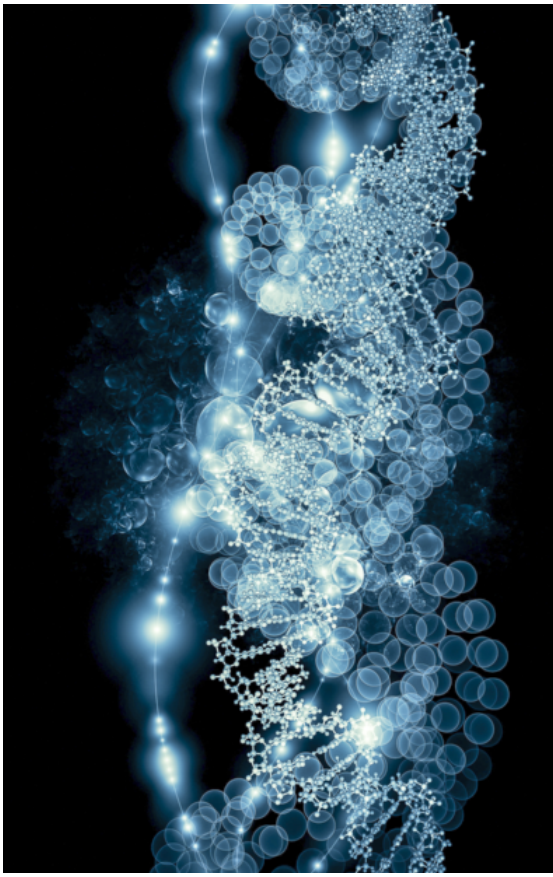
The review of Zinbryta was initiated following a request from the European Commission on February 26, 2018. On March 6, 2018, while the review was ongoing, EMA's PRAC recommended suspension of the marketing authorisation of Zinbryta and a recall of the product. The European Commission issued a legally binding decision to suspend the marketing authorisation on March 8, 2018. On March 27, 2018, the European Commission withdrew the marketing



authorisation of the medicine at the request of the marketing authorisation holder (MAH) Biogen Idec Ltd.

Zinbryta is no longer authorised in the EU. Healthcare professionals are expected to continue monitoring patients who have been treated with Zinbryta, in line with recommendations issued in March 2018.

Antisense oligonucleotide to treat a rare hereditary disease



June 1, 2018 – The EMA's Committee for Medicinal Products for Human Use (CHMP) has recommended granting a marketing authorisation in the EU for Tegsedi (inotersen), a medicine for treatment of stage 1 or stage 2 polyneuropathy (a condition in which the peripheral nerves are damaged) in patients with hereditary transthyretin amyloidosis (hATTR). Latter is a rare disease estimated to be diagnosed in approximately three cases per 10 million people in Europe yearly.

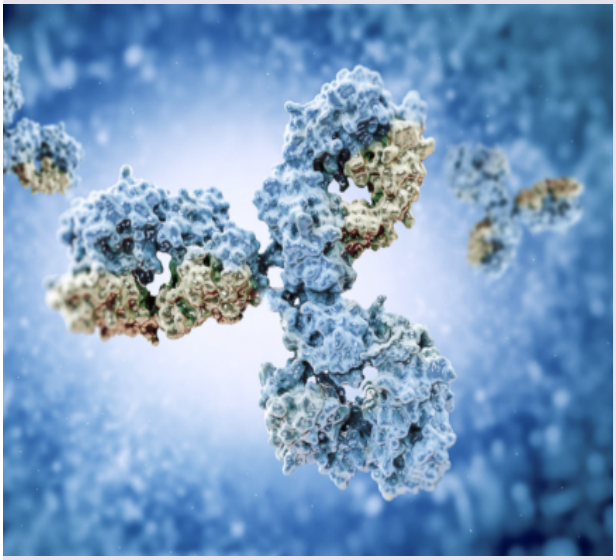
In patients with hATTR, a blood protein called transthyretin is defective and breaks easily. The broken protein forms a fibrous substance called amyloid that builds up in the peripheral nervous system and multiple organs, such as the gastrointestinal tract, kidney and heart, where it interferes with their normal functions.

Tegsedi is an "antisense oligonucleotide", a very short piece of synthetic DNA designed to attach to the genetic material of the cells responsible for producing the transthyretin protein. This is expected to decrease transthyretin production, thereby reducing the formation of amyloids and relieving the symptoms of hATTR.

The effects of Tegsedi were evaluated in a study involving hATTR patients with stage 1 or stage 2 polyneuropathy, but not stage 3. The study showed clinically relevant effects on the neurological manifestations of the disease and on patients' quality of life.

Tegsedi was designated as an orphan medicine in 2014. Current therapeutic options for hATTR are liver transplant, treatment with tafamidis and off-label use of a non-steroidal anti-inflammatory drug (NSAID). All of these have considerable limitations for patients with stage 2 and stage 3 polyneuropathy, meaning there is a clear unmet medical need. Therefore, the CHMP considered that Tegsedi is of major interest for public health and agreed to the applicant's request for an accelerated assessment of this medicine.

Aimovig: First monoclonal antibody therapy for prevention of migraine recommended for marketing authorisation



June 1, 2018 – The EMA's CHMP has recommended granting a marketing authorisation for Aimovig (erenumab), the first human monoclonal antibody therapy for prevention of migraine. Aimovig belongs to a new class of medicines that work by blocking the activity of calcitonin gene-related peptide (CGRP), a molecule that is involved in migraine attacks.

It is estimated that approximately 15% of the European population suffers from migraine. Patients experience recurrent episodes of intense, throbbing headache, most often only on one side of the head. Sometimes, the pain is preceded by visual or sensory disturbances known as an "aura". Many people also experience nausea, vomiting and increased sensitivity to light or sound. Migraine can substantially impair a patient's ability to function physically, at work or school, and socially.

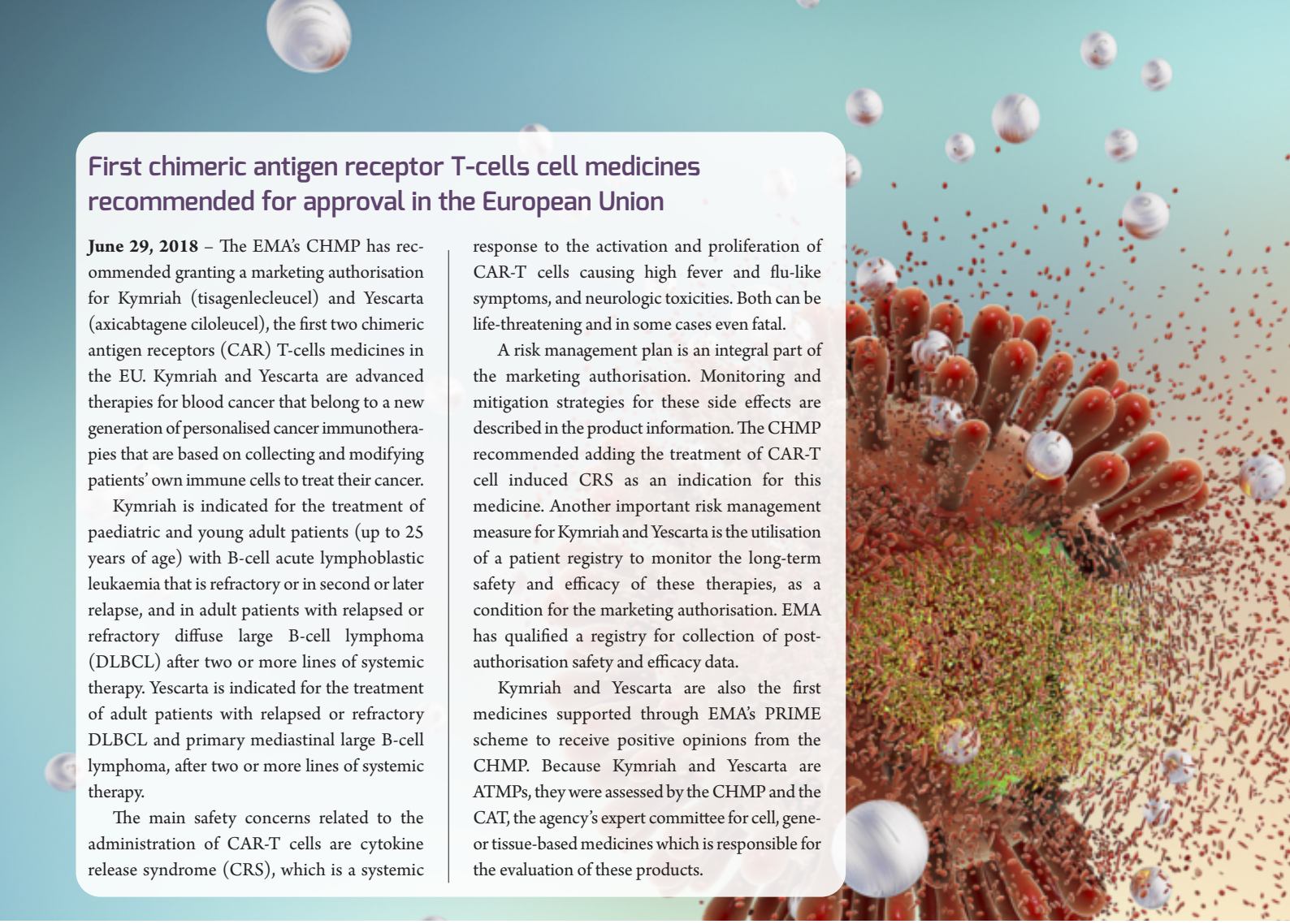
The exact cause of migraine is unknown, but it is believed to be a neurovascular disorder with disease mechanisms both within the brain and the blood vessels of the head. It is most frequent in women and has a strong genetic component.

There is no cure for migraine, but there are a number of treatments available both to tackle the symptoms and reduce the frequency of migraine days. However, existing prophylactic treatments are frequently associated with variable efficacy and poor safety and tolerability. There is therefore an unmet medical need for new treatment options.

The benefits and safety of Aimovig were studied in two pivotal trials involving 667 patients with chronic migraine and 955 with episodic migraine. After 3 months of treatment, patients with chronic migraine showed a reduction of 2.5 monthly migraine days on average compared to placebo. For patients with episodic migraine the reduction was either 1.3 or 1.8 days, depending on the dose taken. The most common adverse events observed were injection site reactions, constipation, muscle spasms and pruritus.

Aimovig should only be taken by patients who have at least 4 migraine days a month. It is a solution for injection that is administered once a month. Patients can inject themselves after appropriate training.

The opinion adopted by the CHMP is an intermediary step on Aimovig's path to patient access. The CHMP opinion will now be sent to the European Commission for the adoption of a decision on an EU-wide marketing authorisation.



First chimeric antigen receptor T-cells cell medicines recommended for approval in the European Union

June 29, 2018 – The EMA's CHMP has recommended granting a marketing authorisation for Kymriah (tisagenlecleucel) and Yescarta (axicabtagene ciloleucel), the first two chimeric antigen receptors (CAR) T-cells medicines in the EU. Kymriah and Yescarta are advanced therapies for blood cancer that belong to a new generation of personalised cancer immunotherapies that are based on collecting and modifying patients' own immune cells to treat their cancer.

Kymriah is indicated for the treatment of paediatric and young adult patients (up to 25 years of age) with B-cell acute lymphoblastic leukaemia that is refractory or in second or later relapse, and in adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy. Yescarta is indicated for the treatment of adult patients with relapsed or refractory DLBCL and primary mediastinal large B-cell lymphoma, after two or more lines of systemic therapy.

The main safety concerns related to the administration of CAR-T cells are cytokine release syndrome (CRS), which is a systemic response to the activation and proliferation of CAR-T cells causing high fever and flu-like symptoms, and neurologic toxicities. Both can be life-threatening and in some cases even fatal.

A risk management plan is an integral part of the marketing authorisation. Monitoring and mitigation strategies for these side effects are described in the product information. The CHMP recommended adding the treatment of CAR-T cell induced CRS as an indication for this medicine. Another important risk management measure for Kymriah and Yescarta is the utilisation of a patient registry to monitor the long-term safety and efficacy of these therapies, as a condition for the marketing authorisation. EMA has qualified a registry for collection of post-authorisation safety and efficacy data.

Kymriah and Yescarta are also the first medicines supported through EMA's PRIME scheme to receive positive opinions from the CHMP. Because Kymriah and Yescarta are ATMPs, they were assessed by the CHMP and the CAT, the agency's expert committee for cell, gene- or tissue-based medicines which is responsible for the evaluation of these products.

Hydroxyethyl starch solutions to remain on the market conditionally

June 29, 2018 – Hydroxyethyl starch (HES) solutions for infusion are used to replace plasma volume following acute blood loss, where treatment with alternative products known as 'crystalloids' alone is not considered sufficient. HES belong to the class of medicines known as 'colloids' and are blood volume expanders to prevent a dangerous drop in blood pressure following acute bleeding.

In the EU, HES solutions for infusion have been approved via national procedures and are available in the Member States under various trade names. In January 2018, EMA's safety committee PRAC recommended suspending the marketing authorisations of these medicines because they continued to be used in critically ill patients and patients with sepsis despite restrictions introduced in 2013 due to the risk of kidney injury and death in these patients.

The CMDh, which is a medicines regulatory body representing Iceland, Liechtenstein and Norway, has now decided that HES solutions for infusion should remain on the market provided that a combination of additional measures to protect patients is implemented. The CMDh agreed with the PRAC's assessment, however, the CMDh gave further consideration to the place of HES in the clinical practice of some countries, noted that previous risk minimisation measures had some effect, and considered that a combination of new risk minimisation measures would effectively ensure that HES solutions are not used in patients at risk.

The new measures are:

- Implementation of a controlled access programme by MAHs to ensure that only accredited hospitals will be supplied with these medicines. The accreditation would require that relevant healthcare professionals receive training on the safe use of HES solutions for infusion.
- Warnings in the medicines' packaging and at the top of the summaries of product characteristics (SmPCs) reminding healthcare professionals that these medicines must not be used in patients with sepsis or kidney impairment or in critically ill patients.
- Writing directly to healthcare professionals to ensure that they are fully aware of the conditions of use of the medicines and the groups of patients that must not receive them due to an increased risk of kidney injury and death.

The CMDh also requested MAHs to conduct studies to check that only patients who should be treated with these medicines are receiving them. This is in addition to ongoing studies on the benefits and risks of HES solutions in patients with trauma and those undergoing elective surgery.

The CMDh position was adopted by majority vote and the matter will now be sent to the European Commission, which will take an EU-wide legally binding decision.

Profile

SECTION EDITOR

Simon Page
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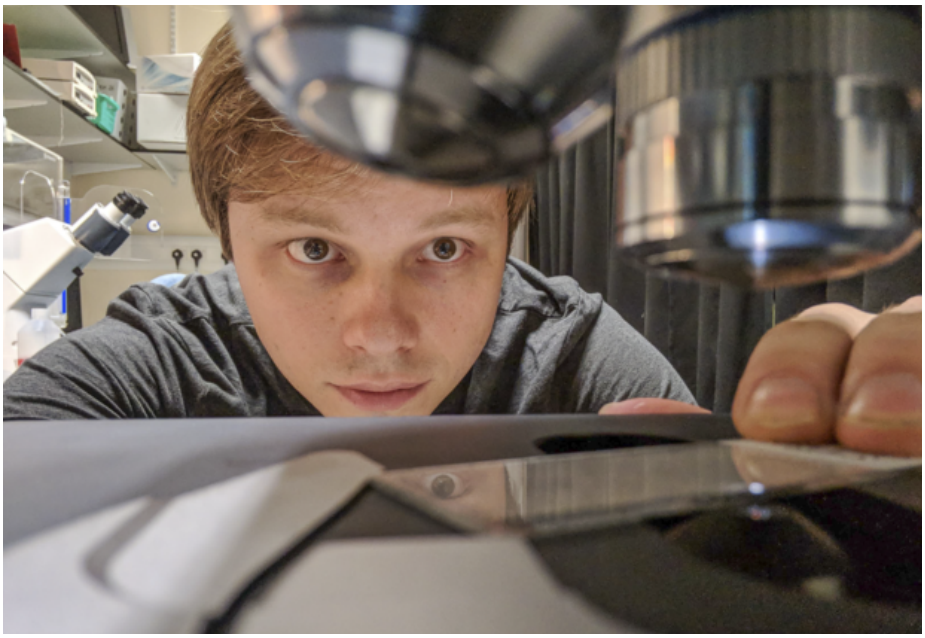
An interview with Richard Wheeler

Principal investigator in parasite cell biology at Oxford University and expert in the tropical parasites *Leishmania* and *Trypanosoma*

You step out of the plane and into a blast of baking heat and the taste of dust. The relative cool of the airport provides a brief moment of calm, before you clamber into a sweltering taxi, which is quickly surrounded by a crush of cars and lorries, their horns adding to the clamour of street merchants shouting from corrugated iron shacks. Your car inches through the crawling traffic, the road flanked by an ever changing mix of tumbledown buildings and modern tower blocks, before eventually escaping to an arcadian green university campus. This is the University of Ghana, in Accra, and you've come here to meet Dr Richard Wheeler, research fellow at Oxford University and published expert in tropical diseases.



MEW: Hi Dr Wheeler, thanks for agreeing to be interviewed by us. Firstly, I'd love to know a little about your research career to date: when it started, how it developed, and where it's taken you.

RW: My parents were always worried I would become a scientist. The signs were there from a young age when, one morning, they walked into the back garden to discover a six-year-old Richard measuring the size of a fungus fairy ring on the lawn. I have always had a fascination for how things work, and at school I loved the subjects that allowed you to explore this. Science was my strongest suit and so, supported by some fantastic teachers, I continued my education at the University of Cambridge, reading Natural Sciences. This modular science course (relatively unusual at the time, but becoming more common) allowed me to explore the interfaces between biochemistry and physics.

My first experience of parasite cell biology was pure coincidence. I was looking for lab work experience during my undergraduate degree and was lucky enough to get a place at Oxford University in the laboratory of Keith Gull, a world expert in *Trypanosoma* parasites.

That work experience has turned into a full-blown academic research position! My research focuses on two poorly known unicellular parasites: *Leishmania* and *Trypanosoma*, which both cause deadly tropical diseases. They are a little like malaria parasites, in that they're unicellular nucleated cells with a devastating effect on human life – taken together, they are responsible for around one hundred thousand deaths per year – but they are from a totally different branch of the tree of life to malaria parasites, and are as different from malaria as a human is from a tree.

MEW: OK, so Cambridge, Oxford, and now … Ghana? What led you here to the west coast of Africa?

RW: *Trypanosoma* and *Leishmania* parasites affect the tropical and subtropical parts of the world, particularly Sub-Saharan Africa, India, and Brazil/Central America. I wanted to make the most of this link. The connection with Ghana comes specifically from *Trypanosoma brucei* which causes sleeping sickness in people and nagana in animals across huge areas of Sub-Saharan Africa.

About 8 years ago I was given the opportunity to help run a roving science course, teaching parasite biochemistry to some of the brightest young students in Africa. It absolutely grabbed my attention – to see the people and places directly impacted by these diseases, and then teach local scientists how to combat them – so I jumped at the chance.

It is impossible to describe quite how much I learnt from my first long drive through Africa

Dr Wheeler teaching graduate students in the West African Centre for Cell Biology of Infectious Pathogens at the University of Ghana

(5 hours through the middle of Tanzania from Dar es Salaam to Morogoro), and since then I've been out to Africa to run many similar courses, most recently at the University of Ghana. I have always found teaching a vital way to look to the future, and helping people carry out research into these diseases situated in the places it impacts is truly inspirational.

MEW: And – speaking of teaching – what can you teach us about these diseases?

RW: *Trypanosoma* and *Leishmania* cause several neglected tropical diseases, including sleeping sickness, Chagas disease, leishmaniasis, and nagana. However, there are many surprising gaps in knowledge about how they act as a parasite. For example, it was only discovered in the last couple of years that *Trypanosoma* parasites don't just swim in the blood but also often hide in the skin.

My research focuses on understanding the fundamental biology of how these parasite cells work, and what that might mean for the disease. The parasites are single cells which are highly organised, and the textbook view of a eukaryotic cell (a bag of cytoplasm full of organelles with a nucleus in the middle) is an extreme over-simplification. My work is aimed at understanding how the organisation of the cell is controlled and adapted for different stages of the cell's life cycle.

As well as combating tropical diseases, understanding parasites can also help us to understand human biology. For example, a defining part of the parasite cell is the flagellum (or "cilium"). This is the 'tail' part that the cells use to swim, or to move material around them (see bottom right opposite). However, flagella are extremely important in people too – they're what keep our airways clear of debris and what keep our sperm swimming! – so an improved understanding of parasite biology may help to improve human health in a number of ways.

MEW: Is there any tool or technique that has been particularly important to your research career?

RW: The key inspiration for my research career has been microscopy. The first time I used a research-grade fluorescence microscope was exhilarating. The realisation that I could look into a cell that is 100 times narrower than a human hair, at individual molecules even, was incredible. And not only that it's possible, but that it's beautiful too.

Much of my current work revolves around microscopes as a measurement tool, and I use advanced image analysis to extract the data. This plays to my strength as a visual thinker, and my hobbies (design and photography) often merge into my work.

Images can be seriously big data: One of the projects I am co-running involves images of 5 million cells and tens of terabytes of image data! This "big data" project is called TrypTag (http://tryptag.org/). We are using high-throughput genetic modification tools to go through all 8,000 genes of the *Trypanosoma* genome, modifying each one in turn so that the protein is fused to a green fluorescent protein–like fluorescent marker. We then look where each individual protein is located within the cell. This type of sub-cellular map of proteins has only previously been done in yeast and (to some extent) human cells, so this will be the first time that it has been achieved in a pathogen, and the first time in such a highly structured cell where protein localisation is so strongly indicative of likely function.

MEW: You obviously chose to work in academia over industry. Why was this, and what would you advise as being the main pros and cons of each career path?

RW: My choice of an academic career was driven by the appeal of intellectual freedom: To drive my own research and address the questions I want to answer. However, having never worked in industry it is hard to know how true this is! Moreover, it is somewhat naïve to view academic research as true intellectual freedom; while you can choose what research to do, it must still generate results that people view as important, in order to secure funding from agencies who view your output as worthwhile. I can imagine that working in the biotechnology industry, particularly smaller companies, could be very similar – perhaps substituting "shareholders" for the academic field and "venture capital" for funding agencies.

I do think that the perceived separation of academia and industry is somewhat artificial, especially as funding agencies are increasingly focused on research that is "translational" or has good "pathways to impact" or other such jargon. Personally, I find this attitude frustrating, as it results in the government being the sole arbiter of which research has the clearest useful applications, leading to a risk that basic science (so called "blue skies research") will suffer. A common joke goes that, in this funding climate, Einstein wouldn't get funding to work on relativity, as he would have had to invent GPS first.

Interestingly, some academic research is now pushing to be more "industry-like". I spent over a year working in the Dresden Max Planck Institute for Molecular Cell Biology and Genetics, which runs an unusual research institute management structure with extremely large and well-funded core facilities (alongside traditional "research groups"). This was a very different way for me to do science, and is a structure that is clearly inspired by industrial research management and organisation.

MEW: Many of our readers work with their clients to publish scientific research in high-impact medical journals. What are your

perspectives from an academic viewpoint on the publishing industry as a whole?

RW: A major problem in academia is that the assessment of research quality by funding agencies and interview panels is often based – fairly or otherwise – on metrics directly derived from publications (e.g., journal impact factor). Sadly, it is quite normal to receive feedback on grant applications which focuses strongly on the quality of your journals rather than the quality of your work.

However, journal impact factor is not a good measure of either the quality or the impact of research. There are many examples of papers in high-impact journals which are simply not good quality science, and many excellent science papers in low-impact journals. Indeed, my most cited paper is published in the lowest impact factor journal of any of my publications.

Fundamentally, the entire concept of impact factors stems from an artificial scarcity (i.e., the limited number of papers per issue) which is a historical hangover from physical, printed journals. Online journals have essentially unlimited space in them, and yet the impact factor of a journal is entirely defined by editorial selection of the work, a feedback loop which can easily lead to fields having artificially inflated perceived value.

Many academics feel that the direction of the publishing industry is driven by profit, not by research quality, and that a major review is needed to combat issues such as artificially inflated publishing costs, exploitation of reviewers' time, and arbitrary biases arising from editorial decisions.

MEW: In the last edition of this magazine, Chris Winchester of Oxford PharmaGenesis presented some research showing that the pharmaceutical industry is actually better at disclosing the results of its clinical trials than academics. Do you feel this is likely to be true and, if so, why do you think that academics aren't publishing as much of their research as pharma?

RW: The research Chris presented is very interesting, and highlights a wider problem about publishing negative results. In an academic environment dominated by a pressure for high-impact journal papers, how can we expect researchers to spend time writing a paper with a negative result which will end up in a low-impact journal?

Chris's comments about deploying resources to meet legal and ethical obligations are accurate, but I think policies from funding agencies are exacerbating the situation. There is a massive pressure on academics to do research that can be translated into practical applications. If you get a negative result from trying to apply it (e.g., through a clinical trial) then you are disincentivised from publishing it.

There are all kinds of ideas for how to incentivise publishing negative or contradictory results linked to previous studies – things like journal policies which guarantee the publication of a refuting or contradictory perspective on an article – but in practice nothing seems to have been done about it, and no number of Nature Editorials has changed that!

MEW: The literature is becoming increasingly vast and complex, with new journals being introduced every year. However, medical writers often work at the cutting edge of drug research, and are expected to be fully conversant in the diseases that they are working on. How would you advise people to stay abreast of the topics that are of relevance to them?

RW: You might think that, with my background of computational analysis and general data geekery, I'd have some clever algorithm to search and curate the literature for me. I don't. I talk to people! Almost every really useful or inspirational article I have read has come from a recommendation. Of course, trying to gain a deeper understanding of a field will always take some serious searching and reading. However, to some extent, I think that academia's approach to reading the literature has reversed a bit. Nowadays, if you come up with an idea inspired by some key paper, it's almost easier to do the experiment, see if the result is interesting, and then work out how it fits into the existing knowledge, rather than the other way around.

MEW: I'm sure that travelling to Africa and back takes up a lot of your time, but what do you get up to away from the lab bench?

RW: I love illustration, design, photography, and playing the trumpet. I also like computer games, but frequently get distracted by reprogramming and redesigning them!

MEW: And finally, some quick-fire questions:

Oxford or Cambridge? (or Ghana?)
Oxford

Microscope or telescope?
Microscope

Craft beer or vintage bubbles?
Craft beer

Rock bar or baroque?
Rock bar

Chess or Monopoly?
I love playing *Race for the Galaxy*

Cat or dog?
I plead the fifth!

Sun-drenched summer or white Christmas?
White Christmas, it's all about the cold!

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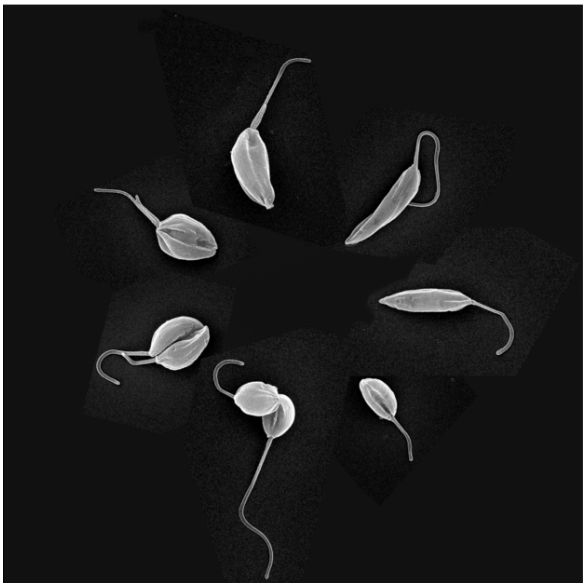
A common joke goes that, in this funding climate, Einstein wouldn't get funding to work on relativity, as he would have had to invent GPS first.



Different cell cycle stages of the Leishmania parasite, viewed by scanning electron microscopy. The cells are around 10–15 µm long and swim with the flagellum forwards (i.e., tail-first).

Journal Watch

Journal Watch is based on the French-language blog *Rédaction Médicale et Scientifique* by Hervé Maisonneuve available at www.redactionmedicale.fr.

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The vast majority of investigator brochures lack sufficient information to systematically appraise the strength of the supporting preclinical findings

The above title is one of the conclusions of an investigation of 109 investigator brochures (IBs) reported in an April 2018 issue of *PLoS Biology*.[1] Out of six German institutional review boards (IRBs), three accepted to provide the IBs of phase I and II trials; one IRB provided 97 IBs reviewed between 2010 and 2016. The IBs covered 8 of 12 therapeutic areas as distinguished by the European Medicine Agency. Seven studies were first in human, whereas all other mentioned at least some clinical evidence for the investigational product. All trials were privately funded, and 48 IBs were from the top 25 pharmaceutical companies. The authors assessed the content and properties of preclinical efficacy studies (PCESs) contained in IBs. They rated 708 unique PCESs (109 IBs) for their reporting on study elements that help to address validity threats, whether they referenced published reports, and the direction of their results. Less than 5% of all PCESs described elements essential for reducing validity threats such as randomisation, sample size calculation, and blinded outcome assessment. For most PCESs (89%), no reference to a published report was provided. Only 6% of all PCESs reported an outcome demonstrating no effect. For the majority of IBs (82%), all PCESs were described as reporting positive findings. Our results show that most IBs for phase I/II studies did not allow evaluators to systematically appraise the strength of the supporting preclinical findings. The very rare reporting of PCESs that demonstrated no effect raises concerns about potential design or reporting biases. Poor PCES design and reporting thwart risk-benefit evaluation during ethical review of phase I/II studies.

In February 2018, a series of papers in the *BMJ* reported the development of a new tuberculosis vaccine that failed: 2,800 infants had been included in trials conducted in South Africa.[2] The researchers were disappointed and later discovered that the animal studies had already raised doubts about the potential efficacy of the vaccine. An analysis of the IBs concluded that a selection of positive studies was done to influence the funding and approval for human trials. It was a public funded project.

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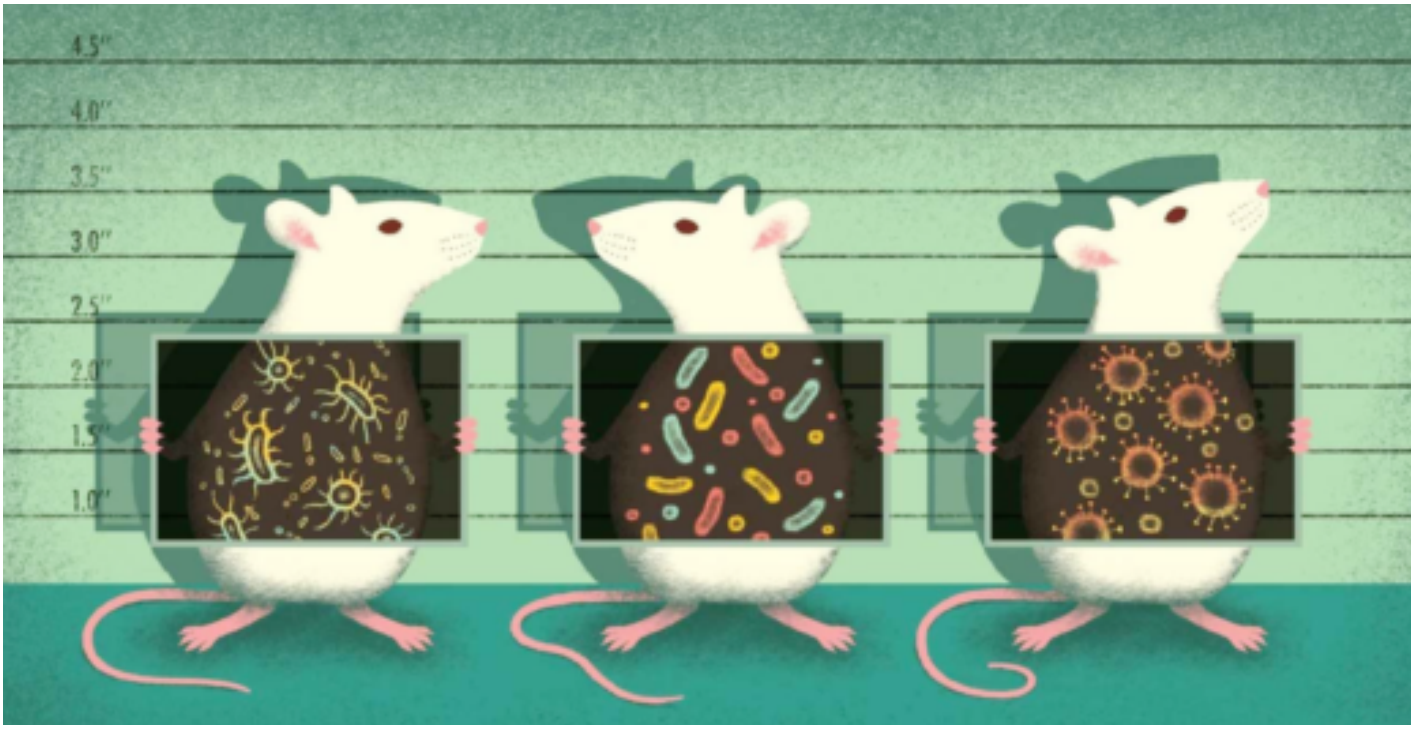

Prestigious journals start asking for disclosure of non-financial interests

Most journals limit disclosure to financial interest. Controversies about non-financial interests were discussed in a "Head to Head" published by the *BMJ*.[1] There are many interests that influence the decision of an expert – political, ideological, individual or religious. Individual interests could be past or current disputes between researchers, differences in schools of thought, etc. People are driven at least as much by non- financial motives as they are by financial gain. Fame may be more seductive than gain. Such declaration of non-financial interests must be handled with discretion. All experts have non-financial interests that cannot be eliminated. On the contrary, financial conflicts of interests can be eliminated or avoided.

Nature research journals recently updated their policies, asking authors of research articles, reviews, commentaries, and research analysis to disclose non-financial interests.[2] The Nature instructions are (https://www.nature.com/authors/policies/competing.html):

> *Non-financial competing interests can take different forms, including personal or professional relations with organisations and individuals. We would encourage authors and referees to declare any unpaid roles or relationships that might have a bearing on the publication process. Examples of non-financial competing interests include (but are not limited to):*
>
> - *Unpaid membership in a government or non-governmental organisation*
> - *Unpaid membership in an advocacy or lobbying organisation*
> - *Unpaid advisory position in a commercial organisation*
> - *Writing or consulting for an educational company*
> - *Acting as an expert witness.*

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A *Nature* special issue: How to grow a healthy lab?

A series of articles appeared in *Nature* (May 16, 2018 https://www.nature.com/collections/pmlcrkkyyq) on research integrity. An article introducing the series notes:

> *If you find a bad apple, check the barrel. Research-integrity specialists say that focusing too much on individual bad actors deflects attention from the environments that promote bad behaviour. The idea applies just as much to researchers who are unproductive, frustrated or unhappy, as this could be indicative of deeper problems.*

A *Nature* survey revealed the tensions bubbling in research groups around the world. A lack of research training exists in laboratories and personnel management is poor; it is one of the strongest contributors to an unhealthy lab culture. Senior and junior researchers live almost in separate worlds. The testimony of Catherine Winchester, research integrity adviser at the Cancer Research UK Beatson Institute, a non-profit organisation in Glasgow, is interesting.[1] She assists researchers and help teams to better do research and collaborate. She has been able to implement good practices: "*Perhaps the most complex undertaking so far has been developing practices for curating and preserving all the data that underpin a paper, including replicates*". In 5 years, no retraction and no serious issues with publications were observed.

The factors that lead to bad decisions can be represented by the mnemonic TRAGEDIES: Temptation, Rationalisation, Ambition, Group and authority pressure, Entitlement, Deception, Incrementalism, Embarrassment, and Stupid systems.[2] Recognising these and responding appropriately can save a career and strengthen science.

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Assessment of researchers should change to align the research system with society needs

A 20-page paper in *PLoS Biology* proposes strategies that are important for the future of research.[1] Currently, the reward system is based on poor metrics, such as the impact factor. The current quality of publications, the poor reproducibility of science must be improved. I extracted sentences from the abstract:

Assessment of researchers is necessary for decisions of hiring, promotion, and tenure. A burgeoning number of scientific leaders believe the current system of faculty incentives and rewards is misaligned with the needs of society and disconnected from the evidence about the causes of the reproducibility crisis and suboptimal quality of the scientific publication record. We completed a selective literature review of 22 key documents critiquing the current incentive system. From each document, we extracted how the authors perceived the problems of assessing science and scientists, the unintended consequences of maintaining the status quo for assessing scientists, and details of their proposed solutions. The resulting table was used as a seed for participant discussion. This resulted in six principles for assessing scientists and associated research and policy implications. We hope the content of this paper will serve as a basis for establishing best practices and redesigning the current approaches to assessing scientists by the many players involved in that process.

The six principles are:

1. Contributing to societal needs is an important goal of scholarship. Focusing on research that addresses the societal need and impact of research requires a broader, outward view of scientific investigation.
2. Assessing scientists should be based on evidence and indicators that can incentivise best publication practices. Several new "responsible indicators for assessing scientists" were proposed and discussed.
3. All research should be published completely and transparently, regardless of the results. Academic institutions could implement policies in the promotion process to review complete reporting of all research, and/or penalise noncompleted or nonpublished research – particularly clinical trials, which must be registered.
4. Openness – facilitating dissemination and use of research data and results by others. Researchers can share their data, procedures, and code in various ways, such as in open access repositories. Some journals are supporting this process by endorsing and implementing the transparency and openness promotion (TOP) guidelines.
5. Investing in research to provide the necessary evidence to guide the development of new assessment criteria and to evaluate the merits of existing ones.
6. Rewarding researchers for intellectual risk-taking that might not be reflected in early successes or publications. The need for a young researcher to obtain their own funding early often results in a conservatism that is inimical to ground-breaking work at a time when they might be the most creative. Changing assessments to evaluate and reward such hypotheses might encourage truly creative research.

Goodreports: A new tool to fill in the reporting guidelines checklists

The EQUATOR Network, in collaboration with Penelope (a website checking academic manuscripts before submission), has launched a simple and useful website available at www.goodreports.org. Authors choose the reporting guideline corresponding to their paper, and they fill in the checklists online. Checklists of 16 reporting guidelines are available. The authors then print and/or download the checklist in order to join it to their submitted paper.

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Medical Devices

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Useful links for medical device writing

Want to learn more about medical device regulations? Then read some of the presentations held at EMWA's medical device symposium this year: https://www.emwa.org/conferences/emwa-symposia/.

There are also several webinars on medical devices stored on EMWA's webinar archive https://www.emwa.org/training/emwa-webinars-programme-archive/.

For those who want to dig deep into the new regulations, the landing page of the **European Commission (EC)** Medical Devices Unit is a must: https://ec.europa.eu/growth/sectors/medical-devices_en

From there, you can access all relevant information https://tinyurl.com/mlhrsxs
The current regulation are :

- Council Directive 90/385/EEC on Active Implantable Medical Devices (AIMDD),
- Council Directive 93/42/EEC on Medical Devices (MDD), and
- Council Directive 98/79/EC on In Vitro Diagnostic Medical Devices (IVDMD)

These can be found, as well as the new medical device regulations replacing them:

- Medical Device Regulation 2017/745 (MDR)
- In vitro Device Regulation 2017/746 (IVDR)

Both were entered into force on May 25, 2017, but will only apply after a transitional period (MDR in spring 2020 and IVDR in spring 2022).

Relevant for medical writers, these guidelines describe the content requirements of study documents such as clinical study protocol (clinical investigation plan), patient informed consent, etc. They also describe new documents to be created in the future, e.g., the periodic safety update report.

The regulations are supplemented by guidance documents, the MEDDEV guidelines, which can also be accessed via this page (tab Guidance MEDDEV). Relevant for medical writers are:

- MEDDEV 2.1 guidance documents that relate to the scope, field of application and definition of medical devices
- MEDDEV 2.7/1 rev 4 specifies the content requirements of a Clinical Evaluation Report (CER)

The **European Competent Authorities for Medical Devices** https://www.camd-europe.eu/ is an umbrella group of national competent authorities. The group currently works on providing guidance and generating templates to facilitate the implementation of the new regulations.

See for instance:

- MDR and IVDR Transitional FAQs: https://tinyurl.com/ya245elb
- MDR/IVDR Roadmap: https://tinyurl. com/zyckuv9wt

Joint Action on Market Surveillance of Medical Devices (JAMS): https://tinyurl.com/y8mwl5du

The **Notified Bodies** are also quite active in providing support for the implementation of the new regulations, see the following links:

- https://www.bsigroup.com/en-GB/medical-devices/resources/ From here, you can also access the guide "Want to know more about the Notified Body?" This guide helps you understand terms like Notified Body, Competent Authority and CE-mark.
- https://www.tuv-sud.com/industries/medical-devices-healthcare From here, you can find information and webinars related to the new MDR https://tinyurl.com/y8babpjf.
- https://industries.ul.com/healthcare From here, you can, e.g., access the IVDR webisode series https://tinyurl.com/y8y97tdw.

You can also check out the page of EMWA's Medical Device Special Interest Group at https://www.emwa.org/members/special-interest-groups/medical-devices-sig/

Happy reading!

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In the Bookstores

Health Literacy From A to Z: Practical ways to communicate your health message (Second Edition)

By Helen Osborne, M.Ed., OTR/L
Aviva Publishing, 2018
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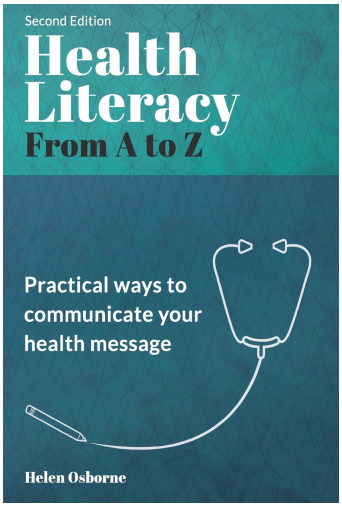
28.81 GBP. 256 pages



The EU Clinical Trials Regulation requires sponsors of clinical trials to produce a plain language summary that describes the results of the clinical trial in a format understandable to laypersons. According to the Multi-Regional Clinical Trials Center of Brigham and Women's Hospital in Boston and Harvard University, "The purpose of creating and disseminating [a plain language summary] to clinical trial participants is to ensure that study participants are informed about the trial results, that they know that their participation is respected and appreciated, and that they understand the value of their contribution to science and public health."[1]

The writing of plain language summaries is a new area of medical writing that will require many medical writers to acquire and develop different writing skills. As such, there is a need for the writer to appreciate the audience they are writing for and to understand how to communicate complex clinical trial results in a language that the layperson can understand.

Helen Osborne is a recognised expert in the world of health literacy, helping professionals communicate health information in ways that both patients and the public can understand. Her book, *Health Literacy From A to Z: Practical ways to communicate your health message*, is intended as an easy-to-use guide which can be used as a starting point for health communication between patient and doctor. The author uses her experience as an occupational therapist, training as an educator, and perspective as a patient and family caregiver to inform her recommendations for communicating health messages.

This is the second edition of *Health Literacy From A to Z*. The new edition includes the following new topics: the business side of health literacy; communicating when patients feel scared, sick, and overwhelmed; the general public: talking with patients about what they learn from the media; organisational efforts: health literacy at the community, state, and national levels; regulatory and legal language; and writing for the web. An expanded focus on knowing your audience, timely information about technology, stories from practice, and checklists are also all new additions to this second edition.

The book consists of 42 chapters which are arranged alphabetically. Each chapter contains a section on *Starting Points* (introductory information providing context for the strategies that follow); *Strategies, Ideas, and Suggestions* (loads of practical, how-to ways of communicating health messages clearly and simply); *Stories from Practice* (real-life experiences from a wide range of perspectives); *Citations* (references used in the chapter); and *Sources to Learn More* (a list of books, articles, web sites, podcasts, and additional resources to continue learning about each topic).

The first chapter of the book gives the reader insight into what health literacy is and how it began – including facts about the founders of health literacy, Len and Ceci Doak. It also gives a better understanding of why health literacy is so important in this day and age. When Len and Ceci met, Len volunteered as a tutor with people who could not read or write and Ceci was a health educator. She was concerned about how people with low literacy skills could understand medical advice, e.g., from their doctor. Thus began their journey into health literacy. The first chapter sets the tone for the whole book: easy and quick reading, which makes you want to learn more.

I thought all chapters contained interesting and useful material, but I especially benefitted from Chapters 6 and 7, which deal with confirming that laypersons have understood the information they have been given, and also provide some strategies and tools which could be put in place to make sure the patient understands what he/she is being told by a healthcare professional, e.g., a doctor. One of these strategies is the teach-back technique, where the patient repeats back to the healthcare provider what he/she has just been told. This is used to assess the patient's recall and comprehension of important information that has just been given.

The author discusses document design and provides some good ideas on how to structure written material, including web material, so as to be inviting and appealing to the reader (Chapter 9). Advice is provided on what font size to use (if writing for an older audience, use a bigger font size of at least 14), use of capital letters, alignment of text (left align text, because justifying text can lead to odd-sized spacing), use of bullet lists, and use of contrast (headings that are bolder than the rest of the text or pictures of varying sizes, and different colours to highlight certain parts of the page) – all strategies designed to keep the reader engaged.

To write an effective plain language summary, the writer must understand the audience they are writing for, and knowing your audience is discussed in several chapters of the book (Chapters 17 to 23). The author outlines various types of audiences that require medical advice, such as children and young people, people from different cultures and languages (if English is not their first language), people with differing emotions and cognition, people with hearing loss, people with different levels of literacy, older adults, and people with visual problems. Some different approaches for different audiences are described, including: when engaging with children one should talk directly to the child about health, prepare the child for medical procedures, encourage laughter, and teach in ways that children and parents can learn; and when engaging with someone from a different culture or language background, create a welcoming atmosphere, work with interpreters/translators, ask who

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makes the decisions, speak at a slower pace (when possible), use common words, and invite questions.

Chapters 33 to 36 concentrate on technology. The reader is introduced to podcasts – what they are, how they work, and how to find them. The author especially loves listening to podcasts and has her own series, *Health Literacy Out Loud*. The advantage of podcasts is that you can listen at your leisure, when and where it suits you. The author also discusses the use of blogs, social media, email and text messaging (which are increasingly being used to communicate health information), and interactive multimedia.

Throughout the book, the author provides useful resources to help the reader keep up to date and continue learning about health literacy.

I found the book very easy and quick to read, with simple, uncomplicated language (which of course is the aim). The chapters are short and the format of the chapters also makes for quick and easy reading. The majority of the paragraphs are short, and the author makes use of bullet points and boxed text, which draw the eye and keep the reader engaged. I particularly liked the *Stories from Practice* sections as they give insight into the public domain and the practicalities of everyday problems/issues with miscommunication and health literacy.

In conclusion, I found this book very interesting and would recommend it. It focusses on the healthcare environment and how best to provide laypersons with medical information which is easy to understand and digest. The author provides lots of tips and ideas on how to communicate with patients and how to make sure that patients understand everything that is being said to them.

Although the book does not provide all the necessary information for writing lay summaries, it does provide an understanding of how to communicate clearly with patients. There are many ideas and concepts in the book that could be of value to a medical writer new to this area of medical writing.

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Lingua Franca and Beyond

Editing for non-native speaking medical writers

SECTION EDITOR

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Maria asked: "Write an article about editing for non-native speaking medical writers. … does not need to be long, and preferably 'lightly' written. … [with] funny but at the same time educational stories to share in *Lingua Franca* …"

And that set me thinking.

Is editing for native English writers so different from editing for non-native English writers? Just because someone wasn't born and brought up speaking English doesn't mean that the quality of writing is inferior to that written by native English speakers. In fact, I've come across some native English speakers who are great experts in their particular field but whose ability to write clear and logical text in English eludes them. In addition, I've had the pleasure of working with experts who can present well-structured text but just can't spell … thank goodness for the spelling and grammar checker in Word; one of these co-workers had a job title of *Principal Statistician* but they would often sign off as *Principle Statistician*, an error that wouldn't be spotted by a spell checker.

Yes, there are some tell-tale signs when a text has been prepared by non-native English speakers; for example:

- Sentences that are extremely long with the verb appearing near the end; often, these have been written by someone from a country in mainland Europe.
- Colloquial terms from a writer's native language that don't translate well into English.

I suggest, however, that whatever you are editing and whoever has prepared it (text and images), key messages of editing apply, such as:

- Consider your reader – what's the message you want to get across to them and what do they need?
- Be consistent unless there's a good reason not to be so.
- Keep your text short and simple.
- And finally, try to retain the voice of the author(s).

For examples and if you'd like to know more, read the articles in this special issue of *Medical Writing* and look out for the Language and Writing workshops at EMWA conferences.

So, is there a fundamental difference between editing for native English writers and non-native English writers? You tell me or better still – tell Maria!

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New language: A matter of brain?

A language challenge

Have you ever struggled with a new language? Have you ever felt frustrated when other people talk and you don't understand or when you have something to say but you *cannot find* the right words? I did. English is *lingua franca*; all scientists must speak and write English adequately if they want to present their data or communicate with other researchers.

Does the ability to learn English depend on ethnicity (similar cultural roots) or biology? In other words: should those from Mediterranean countries be punished unlike North Europeans just because of a different cultural background? This might be part of the issue but probably not the most important one. When I was a teenager, I attended at a language high school in Milan: I studied English, French, and German. According to the *theory of roots*, we should be very good at French and less proficient at German and English. This is not always the case; one girl in my class was able to learn every language straightaway, as soon as she heard the first words. All of us were impressed (and a bit jealous) and I have always wondered why it was so easy for her to speak foreign languages as if she were a native speaker while we had to study hard and sweat trying to pronounce correctly.

A few years later when I started my PhD in the UK, I couldn't pronounce the word thaw, a four-letter word!!! How could I say that I had to take my cells out of the freezer? I used to say defrost, which is not the correct word, I know, but it was helpful to make me understood. Is there a scientific explanation for this? Have those superheroes a divine gift? No panic, no divine gift or superheroes and probably no penalty if you are Greek or Spanish or Italian. What really makes the difference is just our brain. A newborn can potentially speak every language in the world: I speak Italian because I grew up in Italy and my parents spoke to me in Italian but if I grew up in China or in an Amazonian tribe I would speak their language because humans are not born with speech but learn it through listening activities.[1] Newborns listen to a language and try to repeat it (babbling), activating the brain areas involved in language.

The human brain has two important sections: Broca's area and Wernicke's area, found in the left hemisphere (Figure 1). Specifically, Broca's area is located in the inferior frontal gyrus and involves the ability to speak one or more languages; Wernicke's area is located in the posterior superior temporal lobe and allows us to understand languages. Therefore, the more we practice, the more we stimulate Broca's area and the better will be our speech. This might explain why sometimes we can understand a language (involvement of Wernicke's area) but we cannot speak that language (involvement of Broca's area). This theory looks very handy: if we live for a while in another country, we will learn the host language. Is this enough?

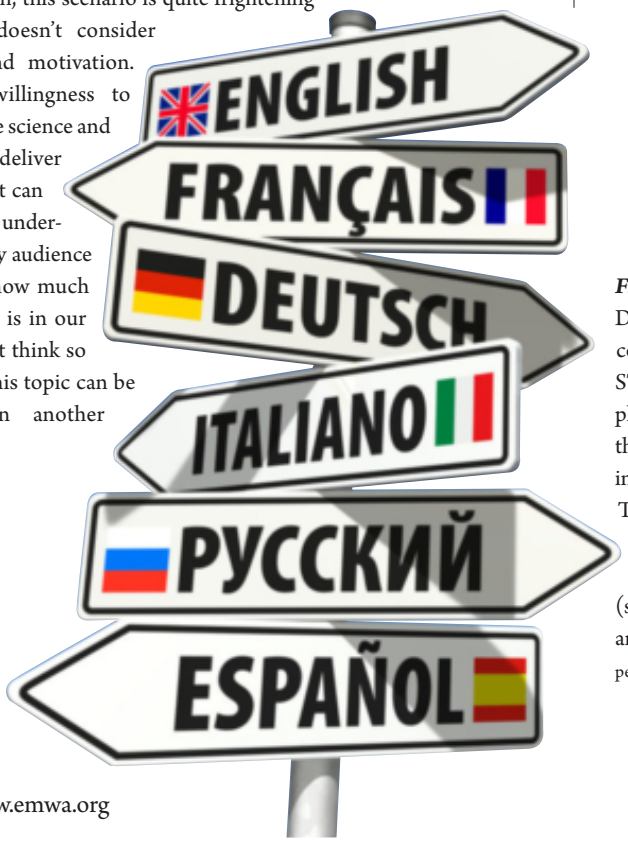
New neurobiological models

The Broca and Wernicke system provides a very simple explanation but science is always progressing; recent studies using modern

techniques suggest new complex models through which our brain can learn languages. Chang and colleagues[2] reviewed two models explaining similarities and differences: the first is the Hickok-Poeppel model and the second the Rauschecker-Scott model. Both argue a *dual stream* process for the stimuli starting from the auditory area and proceeding through Wernicke's area (Figure 2). The models also suggest a sensorimotor integration of the information. However, they differ in one feature: the Hickok-Poeppel model proposes a bilateral process with the involvement of both hemispheres while the Rauschecker-Scott model raises the possibility of a process occurring only in the left dominant hemisphere.[3] The dual stream models open a new scenario in *language learning* because we can now prove the involvement of multiple parts of the brain and not only the *classic areas* – Broca's and Wernicke's. Briefly, learning a new language is a complex process that involves all of the brain and indicates a generation of new connections.[1]

What does it mean in terms of neurobiology? Golestani's team in 2007 studied the differences in learning a new language in both fast and slow learners.[4] Scientists studied the ability of 65 native French speakers to understand the Hindi dental-retroflex contrast. Results, obtained with magnetic resonance imaging and diffusion tensor imaging, show that fast learners have a greater volume of white matter than grey matter and an anatomical asymmetry in the auditory cortex due to the larger amount of white matter in the left than the right side. Consequently, these people have more fibres, *fibre tracts*,[5] and more connections between the left auditory cortex and the language regions than slow learners. Furthermore, a study performed in 2013[6] demonstrated that white matter in children developed and stabilised at age 3-4 suggesting that teaching young children a new language may result in better-speaking adults. Therefore, if we learn a new language late in childhood or in adulthood, we have passed the more favourable time for brain connections and the babbling phase and go straight to sentence production.

Does the amount of white matter influence the ability to write? In other words, can we predict whether an individual is going to be a good medical writer by the amount of white matter in their brain? In my opinion, this scenario is quite frightening because it doesn't consider creativity and motivation. Does the willingness to communicate science and to clearly deliver messages that can be difficult to understand for a lay audience depend on how much white matter is in our brain? I don't think so but maybe this topic can be discussed in another editorial.



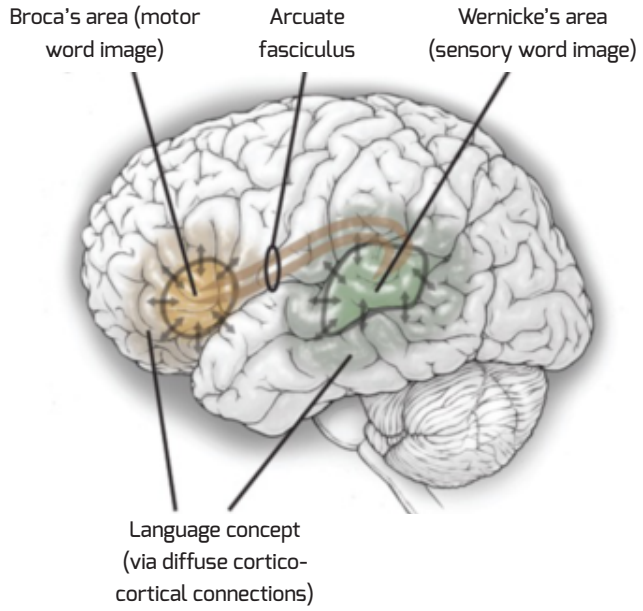


Figure 1.
Classical model of language organisation in the left hemisphere of the brain. Broca's area (gold) is located in the inferior frontal lobe and Wernicke's area (green) in the posterior superior temporal lobe, connected by the arcuate fasciculus. Language concepts (shaded) surround each canonical language area. Arrows represent diffuse cortico-cortical connections between Broca's/Wernicke's area and the widely dispersed language concepts.

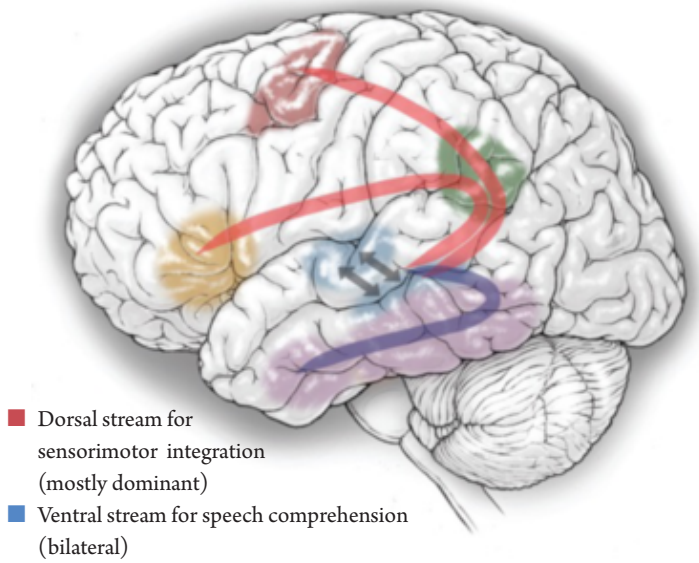
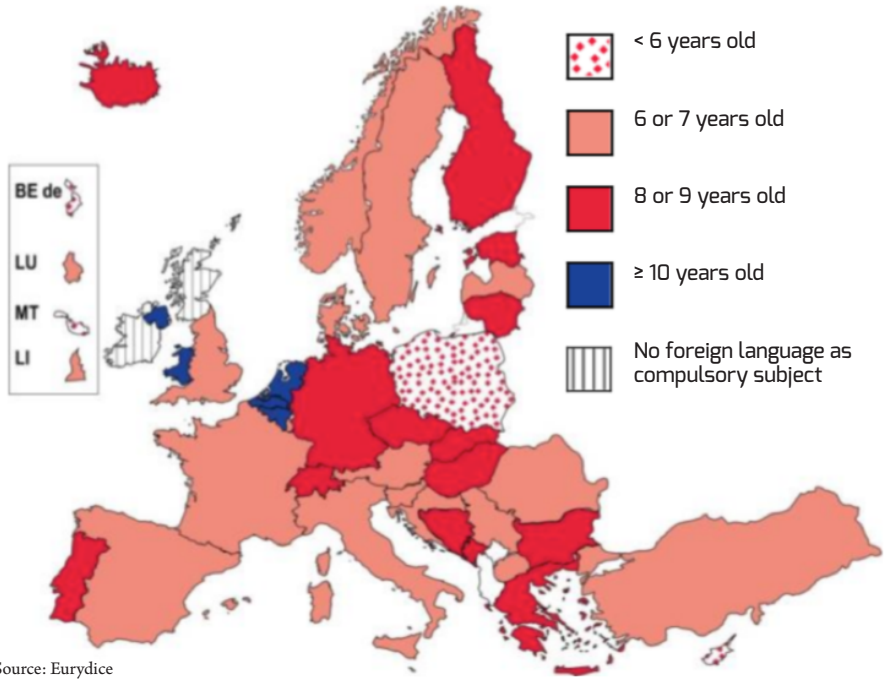
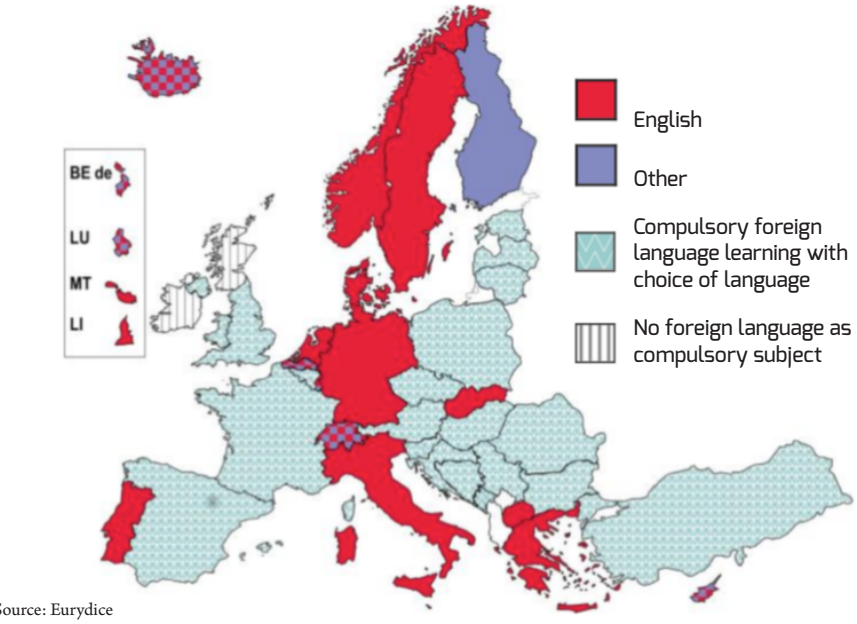


Figure 2.
Dual stream model of language. Regions shaded blue represent initial cortical processing of language in the STG (superior temporal gyrus) and STS (superior temporal sulcus), engaging in spectro-temporal and phonological analysis, respectively. The ventral stream (dark blue) flows through to the anterior and middle temporal lobe (shaded purple), and is involved in speech recognition and the representation of lexical concepts. The dorsal stream is believed to carry out sensorimotor integration by mapping phonological information onto articulatory motor representations. The premotor cortex (shaded red), inferior frontal gyrus (shaded gold), and the parietotemporal boundary region (shaded green) are involved in dorsal stream processing.



Source: Eurydice

Figure 3. Starting age of the first foreign language as a compulsory subject, 2015/16



Source: Eurydice

Figure 4. Mandatory foreign languages during compulsory education, 2015/16

Figures 3 and 4 are reprinted from Key Data on Teaching Languages at School in Europe – 2017 Edition (Eurydice Highlights) with the kind permission of Dr Wim Vansteenkiste.

Conclusions

In conclusion, the ability of an individual to learn a new language more easily than others is dependent on the anatomy of their brain and the possibility of generating new connections between several parts of the brain itself. Studies show that the sooner we expose our auditory cortex to new words and sounds, the better we learn them. English is the *lingua franca* in many fields – for example, economics, science, technology – and probably for this reason most countries in the European Community decided to introduce compulsory English teaching in school by the age of 6 (Figures 3 and 4).[7] This is a very good result compared with a few years ago when children started learning English later in childhood. More can be done, however, to ameliorate this trend to allow our little citizens to benefit more from a foreign language if learned at the age of 3 as we saw previously. Hopefully, more governments will understand the scientific basis of language learning and give their pupils the opportunity to build a solid future in a more connected and more unified Europe, also from a communicative point of view.

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Regulatory Public Disclosure

SECTION EDITOR

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Editorial

Welcome to *Medical Writing's* first regular section on regulatory public disclosure (RPD). In this fast-evolving area, individuals can feel it's almost impossible to keep up with developments. EMWA's established RPD Special Interest Group (SIG) – with its lively conference "talking shop", and resource-rich members' page (https://www.emwa.org/members/special-interest-groups/regulatory-public-disclosure-sig/) – is a great way to learn. This new journal section will support the RPD SIG – as a platform for sharing original articles, the latest regulatory guidances, news of general developments, and best practice. In addition, the journal – as a committed proponent of transparency and disclosure – will publish any full-length original article submitted to the new RPD Section as a feature article, which means it will be open-access.

The latest RPD SIG meeting (Barcelona conference, May 2018) report describes the activities and resources of the RPD SIG as a teaser to encourage you to attend future spring conference meetings.

The feature article (Cuadrado Lafoz et al., page 31) – by PPD colleagues – examines methods of anonymisation used in EMA clinical report submission packages in the 18 months since the opening of the EMA portal in October 2016. The findings provide a snapshot of how applicants have approached anonymisation to this point.

This RPD section is peppered with informational nuggets – much of which has come from you. As we all learn from each other, please send in your articles, tips, and points for forthcoming RPD Sections to help our community of medical writers get disclosure writing right!

Kind regards,
Sam

RPD SIG activities – an update from the 46th EMWA Conference in Barcelona

Following a short presentation given by committee member Holly Hanson, the committee answered questions and explored topics raised by attendees. Other committee members present answering questions were Tracy Farrow (RPD SIG co-chair), Christopher Marshallsay (RPD SIG co-chair), Alison McIntosh, Kathy Thomas-Urban, and Sam Hamilton. Many of the questions focused on EMA Policy 0070 issues.

Tracy and Christopher confirmed that the RPD SIG has an active area of the EMWA website (https://www.emwa.org/members/special-interest-groups/regulatory-public-disclosure-sig/). Resources on this website page include a glossary, key references and background reading.

Questions on any disclosure issues that might arise from day to day work can be sent to the RPD SIG. There is a question and answer log on the RPD SIG page of the EMWA website. RPD SIG committee members will try wherever possible to answer using their own experiences and knowledge of the area. If you have a new question, then please email your question to RPDSIG@emwa.org.

Tracy confirmed that with the fast changing environment of RPD, CORE Reference can also act as a useful resource. Within this user manual guidance information is provided to help medical writers navigate public disclosure "hotspots" (http://www.core-reference.org/). Sam confirmed that CORE Reference is a "living document" and she is gathering information affecting CORE Reference such as disclosure references including the FDA pilot scheme and Health Canada guidance.

There was a request for more guidance on how to anonymise information and for the provision of some examples of before and after anonymised text, especially for case narratives. The EMWA Professional Development Programme (EPDP) has developed several workshops in the area of public disclosure to provide training for EMWA members. Workshop DDF37 of the EPDP: Patient Data Protection in the Clinical Trial Disclosure Era: Compliance with EMA Policy 0070 and presented by Raquel Billiones has some content around anonymisation of patient narratives.

There was a discussion around anonymisation reports (ARs). These reports document how anonymisation was achieved and also provide an assessment of the risk of patient re-identification. To date, most published ARs have used qualitative methods to assess re-identification risks. More recently semi-quantitative methods have been employed. Alison highlighted that two

reviews of ARs using data gathered from the EMA website have shown the use of quantitative methods increasing. Both reviews are published in *Medical Writing*.[1,2]

Christopher reported that the EMA has identified the need to continue development of their guidance on anonymisation and has sought input from experts in the field by setting up a Technical Anonymisation Group (TAG) to assess best anonymisation practices (http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2017/03/news_detail_002717.jsp&mid=WC0b01ac058004d5c1).

It was recognised that medical writers have a key role to play in data anonymisation due to their involvement with patient level data. The medical writer should be writing their reports with anonymisation at the forefront. Tracy provided an example: by using Day X instead of just dates (DD Mmm YYYY) when writing safety narratives.

Christopher suggested that medical writers have to practice "effective, smart writing" by thinking ahead to the anonymisation required at the later stages of the Marketing Authorisation Application process. Sam suggested "tagging" information that may require later redaction and inserting a field to provide suggestions why this might be necessary. This also applies when writing protocols and statistical analysis plans as they too are subject to publication. It was acknowledged that medical writers have a role in educating reviewers about the need for later redaction of documents and should be actively encouraging process change. There should be an involvement of senior medical writer reviewers to identify data anonymisation variables.

Kathy responded to a question regarding identifying stakeholders involved in the disclosure of clinical trial summaries and data. Her assessment was that stakeholders were everyone involved in the planning, evaluation, and document preparation – and especially relevant were upper management who must be convinced that these requirements are legally binding and not just suggestions by special interest groups.

A request was made to provide a bullet point summary of Policy 0070 content. Discussions determined that as data anonymisation is a complex and new area for medical writers it will require some changes in working practices, as well as the development of new processes. If a medical writer is involved in this area they must become familiar with the practical aspects of data anonymisation. The EPDP offers several workshops to support medical writers with this topic. To develop processes addressing Policy 0070 requirements, there is a need for individuals to become knowledgeable about the relevant guidance and other associated supporting information to enable appropriate processes to be developed. It was thought that Policy 0070 requirements could not be summarised in a bulleted format. However, there was a request for a simple decision tree, or flow chart-type of representation of disclosure for clinical trials and this will be investigated further.

Kathy acknowledged that to keep up with changes in this area of medical writing self-education is required. The EMWA journal *Medical Writing* publishes helpful articles covering many different topics associated with regulatory public disclosure including a recent special issue of the journal with a focus on public disclosure. She also suggested that attending

Status updates ... from the regulators

Canada and the US

Health Canada's draft guidance on public release of clinical information – to support proposed changes to the Food and Drug and Medical Device Regulations – closed for public consultation on 25 June 2018. Watch this space for developments: https://www.canada.ca/en/health-canada/programs/consultation-public-release-clinical-information-drug-submissions-medical-device-applications/draft-guidance.html

The FDA Clinical Data Summary Pilot Programme has a new static webpage where FDA now archives all related press releases and publications. Watch it directly for updates, including published clinical study reports: https://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm589210.htm. FDA makes the redactions.

The first published clinical study report (pivotal study report for Erleada: https://www.accessdata.fda.gov/zdrugsatfda_docs/nda/2018/ Erleada_ 210951_toc.cfm) does not have the names of sponsor staff, including the names of medical writers, redacted, but does have the details for local sponsors redacted; does have selected formulation and other product-related information redacted; has sensitive information in patient narratives redacted; does have site ID, subject ID, date of death redacted from death listings; and does have site ID, subject ID, assessment date redacted from abnormal laboratory and other similar listings.

Europe

The European Commission (EC) is projecting that the EU Clinical Trial Regulation (CTR) 536/2014 will come into application during 2019. https://ec.europa.eu/health/human-use/clinical-trials/regulation_en
presents the EU CTR updated time planning, including merging of EMA Portal and the EU database.

EMA Brexit preparedness (http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2018/ 08/news_detail_002999.jsp&mid=WC0b01 ac058004d5c) is impacting broadly across EMA activities and this will specifically impact clinical data publication "... for which the launch of new procedures will be temporarily suspended as of August 1, 2018; data packages submitted for medicines until the end of July 2018 will be processed and finalised".

The EMA has published its first report on the Policy 0070 publication of clinical data (http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/ 2018/07/news_detail_002990.jsp&mid=WC0b01ac058004d5c1). The report provides information on the total number of documents published, the amount of commercially confidential information redacted and the anonymisation techniques used.

... from peer-review journal editors

As of July 1, 2018, manuscripts submitted to journals following the International Committee of Medical Journal Editors recommendations (http://www.icmje.org/ journals-following-the-icmje-recommendations/) require an individual participant data (IPD) "data sharing statement" to indicate:

- Whether authors intend to share individual de-identified participant data
- Which specific data they intend to share (including data dictionaries)
- Other study-related documents that will be available
- How the data will be accessible
- When and for how long data will be available.

As of January 1, 2019, clinical trials that begin enrolling participants on this date must include a data sharing plan in the trial's registration (http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/

meetings and workshops, such as those run by EMWA, can provide a good summary of the main and most relevant points associated with public disclosure.

For information, the EMA guidance on anonymisation is available from http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001799.jsp&mid=WC0b01ac0580b2f6ba.

The committee would like to thank all the attendees who gave their lunchtime to attend and ask questions including James Wolfe, Jennifer Clemens, and Louise Martinsson.

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CORE Reference

- CORE Reference (available for download from http://www.core-reference.org/core-reference/) identifies each point in an ICH E3-compliant clinical study report where anonymisation considerations should apply. Industry uptake is growing; downloads stand at 13,800 (September 2018).
- www.core-reference.org has an email list. Those subscribed receive disclosure news and information in "real time" direct to their inboxes. The General Data Protection Regulation email "opt in" exercise ended on May 25, 2018, and resulted in the purge of more than 370 "no response" contacts from our list. If you were purged, please consider re-joining, and also spread the word to your colleagues. All sign ups are via: http://www.core-reference.org/subscribe.

EMWA workshops on regulatory public disclosure and disclosed clinical documents

Learn about disclosure through EMWA's Workshop Programme. Conference courses include:

EMWA Workshop Course Code	Title	Workshop Leader(s)
DDF36	The Impact of Clinical Trial Disclosure on Trial-related Documents: Company Confidential Information, Personal Protected Data	Tracy Farrow Christopher Marshallsay
DDF37	Protecting Patient Privacy in the Disclosure Era	Raquel Billiones
DDF38	CORE Reference – Clarity and Openness in Reporting: E3-based	Sam Hamilton Tracy Farrow Debbie Jordan Vivien Fagan
MCA07	Writing Lay Summaries of Study Results According to the EU Clinical Trial Regulation	Thomas Schindler

Resources

PhUSE White Papers. Version 2.0 of white paper "Analysis and Displays Associated with Demographics, Disposition, and Medications in Phase 2–4 Clinical Trials and Integrated Summary Documents" is available: https://www.phuse.eu/documents/working-groups/version-control/css-whitepaper-demodispmed-v20-final-11696.pdf. This is one in a series of white papers developed by the PhUSE in collaboration with the FDA. The other white papers pertain to analyses and displays for adverse events, vitals, labs, ECGs, PK, and QT/QTc studies. For all final deliverables from Computational Science Working Groups, see www.phuse.eu, then click on Working Group Deliverables under the Resources tab.

Policy Makers and Data Sharing. In their paper "Data sharing for precision medicine: Policy lessons and future directions" (doi: 10.1377/hlthaff.2017.1558. Health Affairs 2018;37(5):702–9), Alessandro Blasimme and colleagues analyse data sharing guidelines issued over 20 years, and recommend how policy makers can innovate – on the themes of privacy, consent, and data quality – to mitigate what the authors describe as a "stalemate in data sharing".

Policy 0070 Webinar. AMWA has released a free (members only) recorded webinar entitled "Clinical Trial Transparency: What you need to know about EMA Policy 0070". Available at: http://amwa.mycrowdwisdom.com/diweb/catalog/item/id/1249916/q/n=1&c=185

TransCelerate's Common Protocol Template. Protocols are disclosed clinical documents. If you are using TransCelerate's December 2017 version (current) of their Common Protocol Template, (http://www.transceleratebiopharmainc.com/assets/common-protocol-template/), remember to consider including "estimand" in your protocol. Estimand is explained in ICH E9(R1), which is currently at Step 2 (draft guidance). http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E9/E9R1EWG_Step2_Guideline_ 2017_0616.pdf.

Other Interesting Reads. DeVito et al's JAMA research letter (https://jamanetwork.com/journals/jama/article-abstract/2679264) shows that non-commercial funders of clinical research have fallen behind the pharmaceutical industry in their promises on data transparency.

Hodgkinson et al's 2018 article entitled "The use of CSRs to enhance the quality of systematic reviews: a survey of systematic review authors" highlights the value of CSRs to the systematic review process, and the perceived barriers to their use. https://systematicreviewsjournal.biomedcentral.com/articles/10.1186/s13643-018-0766-x

Regulatory Matters

Patient narratives: Humanity within the data

SECTION EDITOR

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Nearly everyone remembers the childhood tale of *The Wizard of Oz*. Four characters searched for something they believed magic alone could create, only to find that they already possessed it. The image of the Tin Man comes to mind, who believed he did not have a heart because he was made of, well, *tin*. Although his metal chamber lacked a physical beating heart, his metaphorical heart was larger than life.

In the hurried world of preparing regulatory submission documents, patient narratives may not always be top of mind for medical writers and those who perform quality control (QC). Often the focus on time and prioritisation resides with the body of the clinical study report (CSR). Although the CSR contains the all-important aggregated data that allow conclusions to be made, the narratives, in my opinion, are the metaphorical heart of the document. And just like the Tin Man's heart, we may forget that it has been here all along. Reading these documents can bring the reader, and ultimately reviewer, closer to the study by sharing details of the courageous patients who gave of their time and entered the study with hopes of improving their health and furthering science. As noted in his book *The Gift of Participation,* Kenneth Getz hails the act of participation in clinical research as "a brave and selfless act".[1] Those who give of their time and information, anonymously without recognition or reward, deserve our utmost respect.

Part of my role is to train new editors how to conduct QC reviews of patient narratives. Our approach likens it to putting the pieces of a puzzle together and reviewing the narrative several times to focus on different items with each pass. One of these reviews includes simply *reading the story*. Why? By taking the emphasis away from the data, there is an opportunity to truly understand what the patient experienced.

When introduced to patient narratives years ago, my first impression was not glowingly positive. Frustration was felt as I scoured the trove of data sources in search of an informational nugget to validate the data. That changed one day while reviewing narratives about depression in children and how their illness affected, and sadly often ended, their young lives. I caught my breath while reading each new story. It was then that I realised how important it was to these patients and their families to share their stories, despite their pain and heartbreak, as a gift to further medical knowledge.

Those of us in the medical writing industry have a deep responsibility. In addition to applying our skills to translate complex information, we owe it to these patients to ensure their data, and their stories, are told correctly and reflected accurately. To comply with the new EMA Policy 0070, we also need to remember the sensitivity surrounding their data and treat them, and their data, with dignity.

In the recent EMWA workshop, *Patient Data Protection in the Clinical Trial Disclosure Era*,[2] attendees were reminded to include only the amount of data needed. Protecting sensitive data was an overarching theme of the EMWA conference as the new policy goes into effect. Patient narratives are therefore a critical area where writers and editors need to remember and apply the policy's guidance.

Just as the Tin Man realised that he had a heart all the while, we too can learn that our documents have a heart as well. I encourage everyone who writes or reviews patient narratives to apply our humanity to tell, hear, and feel the stories within the data.

References

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Medical Communication

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Editorial

Dear all,

At the start of a medical writing career, the quality control (QC) step can fill writers with a sense of dread. Someone is holding a magnifying glass to your carefully crafted (and at this point deeply loved) document and is trying to pick holes in it! At least, that's how it can feel.

However, as writers go through the process, they should (hopefully!) see pretty quickly how much a well-executed QC can add to their document rather than detract from it, and most experienced medical writers actually love the QC step.

The eagle-eyed among you will have noted the very deliberate use of *well-executed* in front of QC in the previous paragraph. My view is that QC is like most things in life – you get as much out as you're prepared to put in. However talented and skilled the QC specialist is, a writer will only gain the maximum benefit of this person's work and wisdom by understanding the optimal way to work with such a specialist on the document.

Claire Jones is an extremely experienced QC specialist, and in this article she uses her experience in the QC world to describe the role of QC and why it is so crucial to high-quality document production. She also provides some top hints and recommendations for medical writers to be able to get the most from their QC specialists.

This insider knowledge is so valuable to writers – even if you already know and love the QC step, I'm sure there is something in this article for everyone, to allow us all to improve our day-to-day working with our QC specialists.

Bestest,

Lisa

Getting the most out of quality control specialists: Practical guidance for medical writers

Introduction

Quality control (QC) is a process that usually occurs when a document is in a near-final or final state. It involves the checking of documents by QC specialists against source data (e.g., comparing data in tables and checking that analytical statements are supported by the data presented in the document) and/or for consistency (e.g., spelling, grammar, punctuation, formatting, style, and cross-references). QC specialists might also be referred to as "data integrity reviewers", "copy editors", and "proofreaders", but as my job title is "QC specialist", I will use this term throughout.

QC is an integral part of the medical writing process and relies on clear communication between medical writers and QC specialists. As a social sciences and healthcare researcher with recent medical writing and QC experience, I have some understanding of what it is like on both sides of the fence. As a medical writer I know it can be frustrating when QC specialists send back documents with lots of comments on consistency issues or wording of particular statements that you did not want checked or if they did not change the minor issues you expected them to. As a QC specialist it can be equally frustrating if medical writers are not clear about what they want you to check and how QC findings should be addressed.

My aim in this article is to use my experiences to outline the role of QC and why it is important, as well to provide practical guidance to medical writers on getting the most from their QC specialists.

Why quality control matters

Medical writers write a range of documents that include, but are not limited to, regulatory documents, protocols, and manuscripts.[1] Medical writers are highly skilled individuals, but even the best medical writers are not infallible. It is extremely easy to add incorrect data to tables when working with source tables that are over a hundred pages long, to make an analytical statement that is not wholly supported by data, or to forget to add a period at the end of a sentence before starting the next one. It might seem that consistency issues such as whether a space is inserted after a symbol are not as important as ensuring that data are accurate. In many ways they are not, but if a document is inconsistent in lots of the small things, and the document looks messy with no attention to detail, then it can detract attention from the key messages of the document – as Aristotle is credited as suggesting, "the whole is more than the sum of its parts".

Ultimately, research findings will be used by regulatory agencies, medical professionals, patients, and the general public to evaluate drug efficacy and safety and to advance medicine and healthcare.[1] Findings from clinical trials may also be used to inform future studies. Therefore, it is important that data are presented accurately and clearly for their intended audience(s) and that there is a safety net to catch errors and inconsistencies in documents should they arise – QC specialists are that safety net. They provide a fresh and objective perspective on documents and ensure that they are checked for consistency, correctness, and clarity.[2]

Understanding quality control specialists' skills and expertise

QC specialists can do so much more than just proofread documents for spelling, grammar, and punctuation or check whether numbers are presented to the right number of decimal places. QC specialists are highly skilled in their own right and it would be a shame to under-use their abilities. For example, QC specialists understand complex medical and statistical terms, and what it means if a study is underpowered or when it is not appropriate to use p-values. Therefore, QC specialists have the knowledge to comment when an analytical statement might be too strong, based not only on what is presented in the data, but also based on the methodology of the study. QC specialists are able to identify the elements of a well-written manuscript and understand how to communicate salient messages of a study in the discussion. QC specialists might also know more

about a journal's submission requirements or how to use journal portals for submitting articles than a medical writer with limited or no former manuscript experience. If a medical writer has only recently entered the profession, QC specialists can also be a resource for regulatory guidance and the latest updates (e.g., where to find them on the internet). These are all additional benefits that skilled QC specialists offer, but what about working with them on a day-to-day basis?

Improving the efficiency and effectiveness of the quality control process

I have identified five key stages, based on my experiences both as a medical writer and a QC specialist, which I have found useful in improving the efficiency and effectiveness of the QC process (see Figure 1 for an overview of the five stages). These stages are discussed below in more detail.

Proofread documents first

Proofreading a document before sending it for QC sounds obvious, but it is essential. If a medical writer sends a document to a QC specialist that has not been proofread beforehand, the document they receive back might contain a lot of comments and/or tracked changes making it difficult for the medical writer to see the most crucial corrections because they detract attention from the really important aspects of the document (e.g., whether the endpoints from the protocol are addressed in the results or whether conclusions on drug efficacy and safety are supported by the data).

QC is the final check of a document before it is sent to the client and then the intended audience (e.g., regulatory agencies, journals). Therefore, if the document contains lots of consistency and data issues, it may need to be checked again once the QC comments have been addressed. This additional check increases the time spent on a project that may already be time-critical and uses more resources.

Software to aid the consistency and quality of documents is becoming an established way of supporting the medical writing process.[3] In my experience, such software is relatively easy to use, can speed up the proofreading process, and can be helpful in identifying consistency issues that would take longer to identify and address if a medical writer or QC specialist were to only read through the document. An important caveat is that proofreading software does not *replace* the need for the medical writer to proofread a document because software will not identify issues with analytical statements or incorrect data, for example.

Allow a realistic amount of time

Medical writers need to be realistic about the time required for the QC process.[4] It is not realistic for a consistency and data check to be performed in one day on a 100 page clinical study report! Any good QC specialist will always tell a medical writer if they are concerned about the timeframe or if, on starting the QC, they think that checking the document might take longer than the medical writer and/or QC specialist envisaged. That being said, QC specialists understand that deadlines can shift and sometimes medical writers need their documents back quickly. QC specialists will do what they can to help with a quick turnaround as long as it does not affect QC quality.

Be clear about what you want and how you want it done

At the start of the QC process it is essential that medical writers clarify: 1. what they want the QC specialist to check and, 2. how any QC findings should be addressed. Medical writers should never presume that a QC specialist knows either of these two factors. QC specialists should always ask the medical writer what needs to be checked and how they want QC findings to be addressed. If QC specialists understand exactly what is being asked of them, medical writers will hopefully

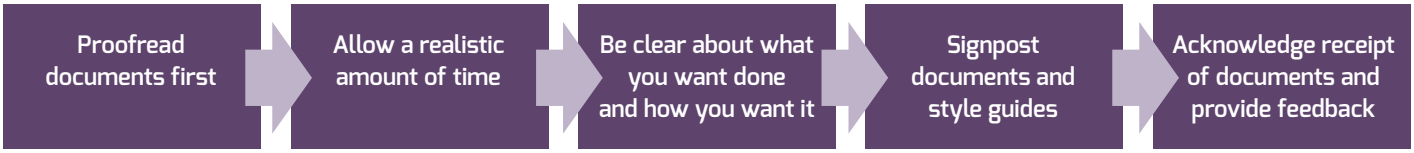

Figure 1. Five stages for improving the efficiency and effectiveness of the quality control process

receive documents that meet their expectations. Of course, there may be times when a medical writer tells a QC specialist that they do not need to check something (e.g., findings/data that have already been checked and have not substantially changed in a later draft) but if, during the course of doing the QC, the QC specialist notices that there are substantial changes (e.g., lots of new data and/or analytical statements) they should of course double check this with the medical writer concerned.

Signpost source documents and style guides

QC specialists need to know where source documents are located,[4] if there is a system for labelling them, and if there is a style guide.[4] Clearly labelling and signposting the source documents can save QC specialists a lot of time searching for sources and means that they are less likely to repeatedly ask medical writers where they can find a specific source. This means that clear signposting of sources improves the efficiency of the QC process because it prevents time being wasted trying to find documents and allows the medical writer to focus on writing rather than spending time answering lots of queries.

Acknowledge receipt of documents and provide feedback

QC specialists know that medical writers are often busy and possibly juggling several documents at a time. However, medical writers know how great it feels to have a client acknowledge receipt of their work and to thank them for writing a particularly tricky document or going above and beyond what they expected. Medical writers also know that having clients critique their work helps them to grow and develop as writers. QC specialists like, and need, those things too. Providing feedback – knowing what was good or helpful about a QC but also what did not work and could have been done differently – enables QC specialists to learn and to develop their skills in QC.[5] Providing feedback to QC specialists can also boost morale because it makes them feel valued – it's showing that medical writers care enough to take the time to comment on their work. When people feel valued they become more engaged, come to work more often, are committed, and feel accountable for their performance.[6] Thus, feedback is not just something that it is nice to do, it can be a very powerful tool for improving the QC process, which in turn leads to high quality documents.

Conclusions

QC specialists are a valuable resource for medical writers. Being aware of the added value that QC specialists contribute to medical writing, using QC specialists' skills and expertise, and incorporating the five stages of the QC process described here can enable medical writers to get the most out of QC specialists. This should improve the efficiency and effectiveness of QC and the writing of high quality, professional documents.

Acknowledgements

I would like to thank Sophie Rudert and Lisa Chamberlain James for reading the article and for their valuable feedback.

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Good Writing Practice

Syntactic structure

Circumlocution: Dependent clauses

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Introduction

Circumlocution is the usage of a multiword structure instead of a shorter syntactic unit, for example, usage of a clause instead of a phrase. The distraction consequence of circumlocution can be sentence pattern disruption and unintended over-emphasis of less important information.

The examples in this article are arranged firstly by section type (experimental, contextual) and secondly by actual sequence in a journal article (e.g., Materials and Methods → Results; Introduction → Discussion).

Experimental sections

Part 1 – Adjectival clause

Example 1: Materials and Methods section: experimental approach

A CR was defined as any movement during the CS period of the nictitating membrane which was equal to or greater than 0.5 mm.

Revision 1 (syntactic reduction)

A CR was defined as any movement during the CS period of the nictitating membrane ***equal to or greater than 0.5 mm****.*

Revision 2 (syntactic reduction + transposition)

A CR was defined as any movement ***(≥ 0.5 mm)*** *during the CS period of the nictitating membrane.*

Notes

In the Materials and Methods section, the objective is to convey multiple details as succinctly as possible. Toward this end, attenuated syntax is useful; that is, attenuated syntactic units and symbols prevail.

In Revision 1, the relative pronoun *which* and the linking verb *was* are deleted to obtain an elliptical adjective clause. In Revision 2, further concision is possible by conversion into a noun phrase/symbol, which is most pertinent when contiguous to *movement*.

Example 2: Results section: observation

On day 1 of dosing, the patient experienced a severe adverse event which was judged to be treatment related.

Revision (syntactic reduction)

On day 1 of dosing, the patient experienced a severe adverse event ***judged*** *to be treatment related.*

Notes

Attenuation by deletion of the relative pronoun *which* and auxiliary verb *was* results in a participle, which is less emphasised by length than the unattenuated adjective clause.

Part 2 – Adverbial clause

Example: Results section: data-based trend

The performance error for non-adaptive and adaptive schedules decreased for all learning sessions as shown in Figure 1.

Revision (syntactic reduction)

The performance error for non-adaptive and adaptive schedules decreased for all learning sessions ***(Figure 1)****.*

Notes

In the Results section of a journal article, an elliptical adverb clause is often used to convey the secondary information of table or figure location. However, the elliptical form of an adverb clause *as it is shown in Fig. 1* is unnecessarily emphasised by length and end-of-sentence position, especially for non-conceptual secondary information (i.e., data location). De-emphasis involves syntactic structure reduction into a parenthesised noun phrase.

Part 3 – Noun clause

Example: Results section: data preliminary interpretation

The fact that the chemicals were impure possibly caused the delay.

Revision (syntactic reduction + thematic focus)

The ***chemical impurity*** *possibly caused the delay.*

Notes

The noun clause is in apposition to the grammatical filler subject *the fact*. A test of the grammatical filler function of *the fact* is its replacement by *the chemical impurity*. Although this test may apply to all words to which an appositive is in apposition, if the word is a filler then it is unnecessary. The reduction in the number of words by four is accompanied by more thematically focused information, which also minimises the delayed predication.

Contextual sections

Part 1 – Noun clause

Example: Introduction section: research problem pertinent background

The main characteristic of TCP-PR is that it detects packet loss only by timers without using duplicate acknowledgements.

Revision (syntactic reduction)

The main characteristic of TCP-PR is ***packet loss detection*** *only by timers without using duplicate acknowledgements.*

Notes

The length-caused over-emphasis of a noun clause is similar to that of an adjective clause; furthermore, the noun clause over-emphasis also results from a wordy narrative pattern focused on agents and actions.

The use of two narrative words, the personal pronoun *it* and the verb *detects,* adds to the length of clause. Consequently, the narrative *that it detects packet loss* can be revised into the conceptually descriptive noun phrase *packet loss detection*. Although the reduction of words is small (two) the change in conceptual emphasis is not. In addition, the backtracking from *it* is eliminated.

Part 2 – Adjective clause

Example: Discussion section: hypothesis-support limitation

A series of tests under conditions that were identical often yielded results that were different.

Revision (syntactic reduction + transposition)

A series of tests under ***identical*** *conditions often yielded* ***different*** *results.*

Notes

In the Revision, the singular adjectives *identical* and *different* remaining after attenuation (deletion of the relative pronoun *that* and the verb *to be*) are transposed to the pre-noun attributive position of the noun being modified. In addition to circumlocution, another reason for attenuation is the syntactic number: repetition is more obvious between clauses than between words.

Summary

All three types of clauses (adjective, adverb, and noun) distract by their length: a disruption of sentence pattern and over-emphasis of lesser information. To revise such circumlocution, the clauses can be syntactically reduced to a noun phrase functioning as an adjectival or as an appositive, followed by transposition if necessary for modifier-modifiee contiguity. In contrast, the full clause may be appropriate to match the importance of the information. This matching of syntactic structure to rhetorical intent is the essence of syntactical fluency.

Of the six examples, four are in the experimental sections of journal articles and two in the contextual. This distribution may indicate that concision is more typical for the experimental sections (Materials and Methods; and Results sections).

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Manuscript Writing

Using problem statements to organise and write a manuscript on original research

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Preparing clear, convincing scientific manuscripts is a challenge. In my experience, the biggest problem for most writers is not an inability to write well in English but rather a lack of clarity regarding what their article is supposed to be about. The subject matter might be clear to them, but coming up with a clear and coherent concept for the manuscript is often challenging. Writers need to consider more than just the declared study objective (if there is one) – they need to consider what background information is essential and what the conclusions and key messages should be. Fortunately, there is a simple and effective method for sorting this all out called "the problem statement" approach, first described in *Medical Writing* by Marina Hurley in 2012.[1]

How to compose a problem statement

A problem statement is simply two to three sentences defining (a) the problem and (b) what the manuscript does to address it. The focus here is on the purpose of the manuscript rather than the study.

All aspects of a manuscript can be related back to the problem statement (Figure 1). The introduction is an elaboration of both parts of the problem statement; the methods describe how the problem was addressed; the results describe what new information was added (outcomes) as a result of attempting to address the problem; and the discussion describes whether the objective or purpose was met, what the individual results were and what they meant, what important considerations there might be, and what the problem looks like with the new information learned.

When composing a problem statement, use the fewest words possible. For the first part, not all aspects of the problem need to be explained, just the main one: What specifically is insufficient or unacceptable?

The second part of the problem statement only needs to describe the bottom line of what this manuscript is attempting to do. Some useful starting words for this sentence include "This article describes..." and "This article shows…".

Here is an example problem statement:

> *Current influenza vaccines are not fully effective and must be given annually due to antigenic drift by influenza viruses. A more broadly protective vaccine is needed. This article describes the results of a clinical trial examining the immunogenicity and safety of a candidate broadly protective vaccine that targets the conserved stalk region of the influenza haemagglutinin protein.*

In this example, both parts of the problem statement are clear: The problem is that the current situation is insufficient (existing influenza vaccines are not good enough and an alternative is needed). The intention of this manuscript is to address this by describing the results of a study on an alternative approach (a possible broadly protective vaccine).

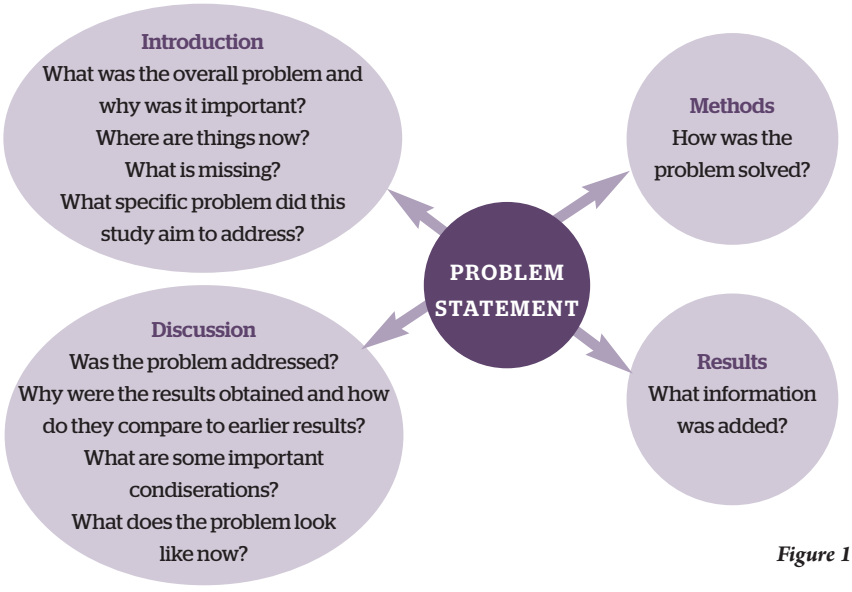

Figure 1

Where to go from the problem statement

Once the problem statement is defined, building the manuscript becomes much simpler. The problem statement can be easily converted to a basic outline or skeleton and from there to a detailed outline and first draft.[2,3]

To create the introduction portion of the outline, simply elaborate the problem statement into the overall problem and why it is important, the current situation and what is missing (or insufficient), and, finally, what this study examined. For the methods and the results, refer to CONSORT or other relevant reporting guidelines for what items to include.[4] Finally, for the discussion, be sure to explain whether the objective of the study was met, describe individual detailed results and their relationship to what has been published previously; include considerations, strengths and limitations (with rebuttals); conclusions; and recommendations for applying the conclusions and for further work.

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Getting Your Foot in the Door

Editorial

GYFD congratulates the EMWA Internship Forum team for another great event in Barcelona.

Also in this edition, first time attendee Clare Chang shares with us some insights she gained in her quest for getting that first medical writing job. I am sure we will hear more from Clare in our forthcoming issues.

Raquel Billiones

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Barcelona Internship Forum recap

A little less than half a decade ago I completed my EMWA foundation certificate and began my search for a position as a professional medical writer. Although I was pleased with the workshops and the level of instruction provided by EMWA, I was still without relevant professional experience and felt discouraged by how many open positions required such experience.

At the 2015 Autumn conference in Den Haag, I met Danae Rokanas, another prospective medical writer. Our conversation soon turned to the topic of how one breaks into the medical writing industry without having had a job in it. We thought about how we could use EMWA's resources to develop some kind of a scheme where aspiring medical writers seeking experience could be matched with companies willing to provide such experience. The EMWA Internship Forum was born, and 6 short months later, we had our first event at the 2016 spring conference in Munich.

Beatrix Doerr kindly served as the chair of the Internship Forum for our first two events. After last year's Internship Forum in Birmingham, she passed the baton to me. Even though the Internship Forum was partly my idea to begin with, I have to admit I found it daunting to actually have to lead and organise it!

> I am looking forward to organising the next event and making it even more beneficial for all participants.

As the Internship Forum is a relatively young endeavour, the Internship Forum team and I have tried to make adjustments and improvements for each subsequent event. Some of these changes have been logistical, such as the space and time allotted for the event. The ultimate goal is to make the Internship Forum as beneficial as possible for the applicants and the companies that participate.

For the most recent Internship Forum held this past May in Barcelona, we tried to address two possible barriers to participation for prospective medical writers, namely language and location. Many people entering medical writing will be required to demonstrate professional, (near) native-level English skills even though English is their second language. For some prospective medical writers, travelling to the Internship Forum or moving to another city for an internship (or both) may not be possible.

Sara Rubio was a recent addition to this year's Internship Forum team and was indispensable in shaping our approach to this year's event. Sara gave an opening presentation on her experiences and perspectives as a non-native English speaker working professionally as a medical writer. Being a Barcelona native, Sara also worked behind the scenes in soliciting participation from local medical writing companies, thus giving local applicants the opportunity to find an internship that did not require relocation.

We also had talks from Phil Leventhal on gaining experience for a first medical writing job, and from Stephen Walker on his experiences in offering internships through the Internship Forum. Jackie Johnson was on site to offer CV and career coaching. And of course, we had companies (both Barcelona-based and from elsewhere in Europe) offering internships.

Looking back on the first three Internship Forums, I am of course pleased at what we have accomplished in this short period of time. I am also relieved that my own initiative did not crash and burn when left under my guidance (a big thanks to the Internship Forum team, Sara, Aimée, and Nathan, for their help!) I am looking forward to organising the next event and making it even more beneficial for all participants.

Bis zum nächsten Mal, in Wien! (Until next time, in Vienna!)

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Regulatory medical writing for academic scientists

I'm a classic born and bred research scientist. I'm like one of those lifelong students who has just ridden the education train all the way to the last stop and earned a glowing Ph.D. It's a known fact that there is a gap we need to cross when we move into the clinical research side of things. However, like many before (and after) me, I thought that taking on projects in applied sciences and translational science would help me bridge that distance. Little did I know that when I started scratching the surface of clinical research to get to regulatory medical writing, that I would be entering a whole new world (Table 1).

What is regulatory writing and why do I need to know about clinical research?

Regulatory medical writing is the development of clinical documents that follow the life-cycle of a product that will enter clinical trials all the way to market authorisation and into post-marketing studies. These are also documents that are sent to the health authorities for assessment. Based on this definition, I think it's pretty self-explanatory why knowledge of clinical research is fundamental to regulatory writing.

Shifting my academic research goggles

Scientific training in academia has a very specific mode of thinking when it comes to experimental design and analyses. When one is working with in vitro and animal models, the stakes are not as high; we're moulded to really emphasise innovation and cutting-edge technologies.

Table 1. Differences between academic and clinical research

Area	Academia	Clinical Research
Specimen	• Non-human subjects (cells, tissues, pre-clinical models)	• Humans
Writing	• Individual authorship is important – publish or perish • Do not need to consider regulatory requirements but need to adhere to good publication practices and journal guidelines • Writing and publishing results is an academic requirement to graduate and move up the ladder	• Individual authorship is not important (team effort – usually in the form of an institution or company) • Ethical, legal, and regulatory requirements are important • Writing up results is an ethical and legal requirement
Datasets	• Small (few samples) to large (big data e.g. sequencing datasets) • Open access or accessible if you subscribe to the journal	• Large to very large (can get up to hundreds and thousands of patients) • Clinical trial data transparency
Data analysis	• Less validation requirements	• Qualified statistician does the statistical analysis on the results using validated software
Documents	• Short to long • Page limit restrictions • Examples: dissertations, publications, abstracts, posters, slides	• Long • Less strict with page limits • Examples: clinical study report, investigator brochures, common technical documents, risk management plans. Patient informed consent forms are the exception and are usually short and have a page limit
Audience	• Scientists within similar fields such as supervisors, other academics, and peers	• Varied audience including health authorities, ethics committees, clients, patients, and healthcare professionals
Focus	• Innovation • New breakthroughs • Impact factors • Generating publications • Soliciting research funds	• Safety of patients • Quality of the products • Efficacy of the products • Bringing products to market • Ensuring ongoing safety (pharmacovigilance)
Timelines	• More laid back; long timeline (e.g. 3-6 years for a Ph.D)	• Fast-paced work environment (time is money!)
Communication	• Other scientists • Supervisors • Physicians	• Clients • Health authorities • Key opinion leaders • Biostatisticians • Medical affairs department • Regulators • Healthcare professionals • Clinical researchers

The sexier the molecular tools, the better. All in all, a good proof of concept study is all you need. This means that we're more focused on innovation and discovery and tend not to think about risks, safety, quality, and efficacy. As a consequence, when a hypothesis is formed, the way the experiment we design tend to omit safety. Imagine my personal paradigm shift when I started learning about clinical development, especially when it came to the design and interpretation of results of clinical trials. The quality, safety, and efficacy of treatment products are central to clinical research. Although it's rather straightforward, I was not used to implementing systems (or even thinking about such systems) when I designed an experiment.

So where did I start?

As I was going through my Facebook feeds one day, someone from the Cheeky Scientist Association posted an article entitled, "Get A Clinical Research Job – The Beaver Method." The author of this wonderful piece addresses the frustrations many job hunters go through with finding a clinical research job (highly recommended reading). Essentially, the first thing is to "broaden your understanding about clinical research". Luckily there are many free resources online. The University of California, San Diego on Coursera offers a fantastic programme on drug development that takes you through a thorough understanding of what you have to think about during the different clinical trial phases. Johns Hopkins University on Coursera has a course on the design and interpretation of clinical trials. Not only do they get you into the clinical research mindset, but also get you familiar with the clinical jargon. Following this, I recommend reading the ICH guidelines on Good Clinical Practice (E6), General Considerations of for Clinical Trials (E8) and Structure and Content of Clinical Study Reports (E3). Finally, the US FDA hosts education events for small businesses (Small Business and Industry Assistance Education Events). Most of these are free and you can attend them in person or online. The recorded webinars are also posted on http://sbiaevents.com/past-sbia-events/. I recently attended one and also received an attendance certificate. Honestly, there are so many events and free resources out there – put on your thinking cap, be resourceful!

But I have no experience! How do I overcome the Catch 22 situation?

There is only one word: Networking. I don't want to believe it either because I'm also a rather introverted person. As academics, we pride ourselves in our technical skills, our academic excellence, and being able to shoulder it all. On top of that, maybe one of the reasons why academia is attractive is because of the solitude and being able to work on our own projects. Over time, we're surrounded by more and more academics and it becomes hard to envisage that the world actually values other skills. Networking isn't about going out and meeting a bunch of people, begging for a job, or trying to impress a future boss. Networking is taking an interest in the people you're engaging with. Listen to their stories. What do they need and how can you help? Network to help you expand your professional network and to talk to industry professionals and hear about their lives. Large companies might be a dream, but you won't know what it's really like on the inside unless you know an insider! When you start networking and reaching out, people will start taking notice of you. You need to let people know who you are and why they should care.

Tools of the trade?

You can find professionals on LinkedIn and through LinkedIn groups. One way of networking online is by writing a simple email to compliment someone's blog or writing. In-person networking such as career fairs and local networking events gives you that personal touch. It also helps to be targeted by joining professional associations (such as EMWA). Finally, networking takes time. Rome wasn't built in a day. You need to stay committed. Remember to follow up. It took about 3 to 6 months before most of my contacts warmed up to me. Some may never and that's fine, too. It's important to find the right chemistries for you. Networking is a marathon for your entire career. It has taken me a little over a year since my first (out of 200+) applications to find the right position. I have just been offered an Associate Manager, Medical Writing position for a small CRO in Shanghai. There is a saying from China that roughly translates to "Sometimes you don't hold on because you see hope, rather, it is because you held on that hope appeared".

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My First Medical Writing

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Editorial

We all have been at the first stages of our careers, knowing what we want to do but without much experience. This is the case of many aspiring medical writers who come out of academia with a burning desire to become medical writers but without much knowledge of the industry and, sometimes, not confident of whether they have what it takes.

This new section serves two main purposes: to offer an opportunity for those who want to showcase their first medical writing work and, most importantly, to receive feedback on the quality of their writing and have an opportunity for improvement.

As the section editor, I'm committed to providing comprehensive feedback for all submissions and to working together with the author on improving quality while also training writing skills, dealing with feedback, and gaining experience.

We welcome all submissions from aspiring medical writers about the topic of their choice. However, we encourage authors to explore making scientific topics accessible to the general public. You can write about the topic of your research in academia, a health issue that you are passionate about, or a recently published paper.

For the debut of this section, we would like to thank Bhavana Achary, a PhD in biochemistry and molecular biology from Singapore, who is passionate about bringing science closer to the lay public.

If you are an aspiring medical writer, don't miss this opportunity of having your work read by experienced medical writers all over Europe (and ever further away, I would dare say). If you know someone who could benefit from this opportunity, spread the word… and the love!

Evguenia

Understanding precision medicine: Bringing the bench closer to the bedside

Five years ago in 2013, the actress Angelina Jolie underwent an elective double mastectomy. Her decision was based on her family history of cancer and a mutation that increases her risk of developing breast cancer by 87%.[1] Her courageous account brought the words "BRCA1 mutation" out of the doctor's office into our everyday conversation. In recent times, we have learnt how genes influence our health. These advances in our understanding of the underpinning causes of disease are resulting in more precisely targeted treatments, hence the term *precision medicine*. Precision medicine can help treat rare conditions as well as improve the currently available treatments for common diseases. There are a number of challenges in this evolving field. They include the need for a regulatory framework that protects consumer data while ensuring that the information is accessible to all. There is also a need to balance the costs of developing new lines of treatments that beneficial to all.

Precision medicine is a move away from the "one size fits all" principle, which suggests that most drugs work similarly in all individuals. We all share experiences that contradict the above-mentioned principle. Precision medicine is tailored to a specific group of individuals sharing certain characteristics such as genetic makeup, family history, and environment. While the term *precision medicine* might be new, the basic tenet of *personalising* the treatment to the individual is not. Historically as we learnt more about the differences in physiologies amongst individuals, knowledge of these differences have dictated *personalised* treatments. Examples of these are blood typing routinely performed prior to transfusions or how drug allergies influence treatment options.

In the past two decades, there has been an explosion of information regarding the genetic and molecular causes of diseases, resulting in clinicians thinking differently about these diseases starting with how they classify them.[2] Traditionally, most diseases are classified based on where in the body they originated. For example, cancers are classified as breast cancer, lung cancer, etc. However, these different cancers might share similarities in their molecular markers and genetic mutations suggesting a need for new classifications based on common root causes that can be targeted more effectively.

Cancer is a key focus area of precision medicine.[3] Currently, doctors have more knowledge about the genetic mutations and molecular markers associated with specific types of cancer. These markers can predict disease and indicate the treatment prognosis. Lung cancer treatment is hailed as an exemplary model of precision medicine. Using next-generation sequencing platforms to profile for most common mutations associated with lung cancer, the choice of drug treatments are tailored to those specific mutations. Significantly, most of these genetic variants are considered *actionable,* indicating that treatments are available targeting

these mutations.[4] The genetic profile of the cancer cells allows physicians to identify the drugs that will or won't be effective in an individual patient; thereby reducing the severity of side effects and possibly the cost of treatment. Similar progress has recently been reported in the treatment of pancreatic and breast cancer.[5,6]

Precision medicine is not limited to "matching" mutations to known drug treatments. It also helps to treat conditions with fewer drugs or lower doses. For instance, psychotropic medications for mental health conditions have different levels of efficacy for different people. Often, due to the low efficacy or the side effects of the drug, many patients discontinue their prescribed medication. Genetic testing combined with information on the drug metabolism predicts how individuals with different genetic makeup respond to various psychotropic medications. Patients who metabolise the prescribed drug faster are more likely to respond, albeit at a higher dose and suffer from lesser side effects. Poor metabolisers might not respond as effectively and are more likely to suffer from side effects.[7] These genetic tests such as GeneSight, CNSDose, and Millenium PGT help doctors to tailor the chosen drug and dosage to the individual.

Regenerative medicine is another example of how precision medicine is revolutionising the field. The substantial progress in biomaterial development, cell biology, and tissue engineering allows one to foresee a future where replacements for defective or damaged organs are designed from cells harvested from the same individual. Such replacements can circumvent the potential complications such as rejection of donor tissue and result in improved function of the repaired organ over prolonged periods.[8]

As in any evolving field, there are a number of challenges to overcome. Identifying patients with similar genetic mutations to participate in clinical studies is a challenge as genetic testing is not yet a common procedure. It is difficult to show the effectiveness of a treatment in clinical studies with a small number of patients as such studies do not always arrive at statistically significant results. This poses a problem as insurance companies are reluctant to cover the costs of treatment unless the drug is shown to be effective in a clinical study.[9] Additionally, the costs associated with developing drugs that benefit only a small percentage of people with a disease can be high. For instance, the drug ivacaftor is very effective in about 5% of cystic fibrosis patients with a specific mutation. However, the costs of developing the drug added up to 300,000 US dollars per patient and the drug is ineffective in the remaining 95% who do not have the same mutation.[10]

While there is tremendous value in genetic testing and contributing this data to research, the layperson needs to be aware of the limitations of genetic testing and analysis, especially those that are not stringently regulated. Direct-to-consumer genetic testing, like those offered by companies such as 23andMe, have regulations restricting what they can say about a consumer's health. However, consumers use other companies for data analysis, which are not subject to similar regulations, to report on genetic linkages to diseases. Sometimes these results are misleading due to false positives, either because the person does not carry the mutation or the mutation is not linked to the disease.[11] Many of the detected genetic mutations might be classified as variants of unknown or uncertain significance or if they are linked to disease, they might not be actionable.[12] False negatives or mutations that are not detected by the genetic tests are equally alarming to doctors, as people might not visit their doctor when they should and the opportunity to treat diseases at an early stage might be lost. These limitations associated with precision medicine are at times lost in the hype surrounding it.

The rapidly diminishing costs of genome sequencing herald a future when DNA sequencing is a routine part of one's health check-up. This is already happening in Pennsylvania, USA. Geisinger, a health care system recently announced that DNA sequencing report will be part of their routine clinical care.[13] In the near future, just like high cholesterol levels alerts one to the possibility of developing heart disease and prompts individuals to alter their lifestyle; knowledge of one's genetic makeup and its implications in health and lifestyle choices might be commonplace. Precision medicine is paving the way in reducing the gap from the lab bench to bedside.

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Out on Our Own

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Editorial

Welcome readers,

This edition of Out on Our Own (OOOO) is all about the Freelance Business Forum (FBF). It's where I, only two congresses ago, embraced EMWA and delved into the world of the FBF. Just in the last year, I have been a table leader, written an article for OOOO, and become a freelance business group subcommittee member, and now here I am as section editor. It is with pleasure that I take over as section editor from Satyen Shenoy, who has been remarkable at developing the section but also the FBF. The EMWA FBF is unique, providing a much-needed platform for freelancers, and future freelancers, to meet. The medical writing field is relatively small, and even more so for freelance medical writers, I feel that forming a network and connecting with others is key to a freelancer's success. This is the principle behind the EMWA FBF. This year in the majestic city of Barcelona, freelancers, and those tempted by the freelance world, got together to chat, share experiences, suggest solutions and drink a little sangria. It was truly a success, with over 70 registered attendees, and 10 roundtable discussions that followed on from an encouraging talk by Helen Baldwin. Check the FBF 2018 report for more details. In this issue of OOOO, two first-time EMWA attendees, Mariana Rickmann and Francisco López de Saro paired up to summarise their experience. First meeting in a workshop, they then navigated to the FBF. Mariana, as a new freelancer, was keen to get a good discussion flowing at her table as she had accepted to be a table leader, and Francisco, with already 2 years of experience as a freelancer, by attending the FBF still learned new techniques for working with clients.

Beate Walter, a second-time FBF attendee, had a different perspective this time around, as between the first and second FBF she has taken that exciting and challenging step of becoming a freelancer. Here, she describes what it takes to become a freelancer in Germany, getting that first client and stepping into the freelance world, developing a business, finding accountants, etc. It's not all about writing!

Get inspired, register for the next EMWA FBF, and join us for these insightful discussions. See you in Warsaw.

Laura A. Kehoe

Here is what happens when new freelancers attend an EMWA conference for the first time

Barcelona, grey and cold at the beginning of May. One may think that in Barcelona the sun always shines. Which it does.

But they also say "Hasta el 40 de mayo, no te quites el sayo", which means until the 40th of May don't take your coat away.

That was precisely the case for the Friday afternoon when Mariana and Francisco were attending a workshop at the EMWA conference.

Who would want to be outside enjoying the beach and a lovely energetic city when there is so much going on inside the EMWA conference?

Two scientists turned writers sit next to each other to begin an exercise on establishing a robust dialogue for problem-solving during a writing project.

What do two Spanish people do? Yes, they chat (sorry Alison!). Wasn't it about dialogue, anyway?

Indeed, the Spanish communication gene is also expressed in scientists. Perhaps, at a lower level than the general population, but detectable and even with surprising results in some cases. Immediately they noticed they had something in common: love for basic science and a new career in writing.

Here, they describe their experiences of EMWA and the FBF.

This is how the freelance medical writing world got real for me at EMWA

Joining EMWA and going to the conference in Barcelona was one of the first business strategies on my list when I decided to start my new life as a freelance medical writer.

The extensive amount of resources for freelancers available on EMWA's website gave me the trust I needed to invest in becoming a member and attending the conference.

More importantly, Barcelona is the starting point for the most significant events in my life: studies, work, family and friends.

It was immediately crystal-clear for me that I should start my new professional road there as well. Plus, I had accommodation, family vacation and babysitting all in one! How could I miss it?

After finishing my PhD in Barcelona, I joined the pancreatic cancer research group in Munich: the place to be if you are in the field. Science and projects were exciting and very time-demanding.

After my second maternity leave and the end of my temporary contract, I had some time to think about my next steps.

What can I offer to society? What do I like? What do I want to do?

All these questions and their answers simmered together and guided the route to where I want to be: to help people understand the scientific facts behind news, products or projects with my writing skills. And I am still on my way, so ask me next year!

By planning my days at the Congress in Barcelona, I was immediately overwhelmed by the number of workshops, sessions and intense rhythm.

It was challenging to keep my focus since every session was exciting for me as a newcomer. I decided to select the workshops that complemented the training on writing that I had just finished and registered for several foundational seminars.

In "managing your freelance project", I was lucky enough to sit next to Francisco. I learnt a lot from the workshop, but also by meeting people like him, who are ahead of me on the freelance path.

And being a new freelancer, it was almost an obligation to go to the Freelance Business Forum (FBF). I was curious, nervous, excited and my senses were sharper than they were, at least during the last year (remember: I come from maternity leave, with little sleep time).

Especially important for me was to participate as a moderator (table leader) of the table discussion session. Guess what topic I moderated? How to find the balance between life

and work. I hope at least one person could benefit from the vivid discussion I had with another new freelance mom. Check the FBF 2018 report!

I arrived at the EMWA Congress in Barcelona thinking that the workshops will push my writing skills forward and that the FBF will open the door to some new business relationships.

Yes, I did learn a lot from the workshops. Yes, I did get some business ideas from the forum.

But, what impacted me the most, what I benefited the most from, was the interpersonal relations, the quick chats during coffee breaks, lunch, the networking event, the group works during the workshops, the freelance discussion tables and the after-congress activities.

Being myself an introverted scientist, I did not quite envisage the length of solitude that I would have to experience as a freelancer.

I instantly connected with so many friendly and helpful professionals and got the invigorating energy of human interaction.

Incredibly talented scientists like Francisco and so many others gave me the motivation and encouragement to put all my effort into this new career step I am taking now.

The imaginary freelance medical writer world that grew in my mind since I started working on it, suddenly got real. And it was great.

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Transferring a life of scientific experience into writing services

Although I had immensely enjoyed my life as a basic research scientist for 25 years, it got to a point in which the efforts of surviving in academic life became less and less appealing, for many reasons.

With short-term contracts and ever-shrinking budgets, sustaining a small biochemistry and molecular biology lab could be very frustrating.

But also, I felt that most of what I had published, on DNA replication and repair, was only remotely connected to real-life health problems: just satisfying my own curiosity about things was not a good-enough reason to spend taxpayers money.

Working from home with total freedom was for me extremely appealing, so the decision to become a freelance medical writer 2 years ago was easy.

It also helped that my daughter had just been born, and the intensity of scientific life would make logistics too complicated. My wife, who works in the pharmaceutical industry, provided me with a first few contacts, and soon I developed a good client base, which has been expanding ever since.

At first, I could hardly believe that I could be paid substantial amounts of money for writing papers and grants, the very same kind of work that I used to do for pleasure. Discovering that I could make a living from my experience in writing and publishing papers was a revelation.

But not everything is perfect in medical writing: I do miss the discussions with colleagues on current scientific topics and giving talks on my own research.

Now, I spend endless hours typing in quiet solitude, so last winter I was looking for any good reason to spend a few days away from my home-office.

Attending the EMWA conference was the perfect occasion to combine travel and professional interests, and I was eager to meet other people with the same professional pathway as mine.

Being a newbie at these meetings, I did not know exactly what to expect. I was overwhelmed by the number of seminars, courses, lectures that were going on at the EMWA conference, and I found it hard choosing the topics or events that I wanted to attend. However, all the activities that I joined were insightful for me.

Personally, I had rarely met other medical writers (MWs are a rare breed in Spain), and I was curious about the kind of people I would find doing the same as I. I was fortunate to meet Mariana and other scientists now successfully working throughout Europe as MWs, and these social interactions were by far the most rewarding aspects of the conference.

At the FBF I enjoyed the cheerful talk by Helen Baldwin and the discussion tables. I joined one on project budgeting and pricing, which seemed to be very popular with other attendees. I learned quite a few things, such as that other medical writers sign formal contracts on every project they do.

I still find budgeting one of the most troublesome aspects of being a freelancer and I wish there were some general rules or guidelines to follow.

I was eager to meet other people with the same professional pathway as mine.

I returned to my desk in Madrid energised and with some fresh ideas on how to grow as a freelancer but, most importantly, with new friends on whom to rely for professional advice and companionship on this adventure.

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My way into freelancing and the first 6 months in business

Looking back about a year, I would have never guessed that I'd start my own business and go freelance within the next couple of months. I was in a permanent position as a medical writer (MW) in a small CRO in Germany, doing regulatory and scientific writing. I did that for about 3 years.

And then, the medical writing department shut down, and I was being 'let go'. It came totally out of the blue. But, when I started to look for a new job (what else), a former client of mine contacted me on LinkedIn (one reason I would always recommend being on LinkedIn). He wanted to keep working with me and, a long story short, he gave me the idea of becoming a freelancer. Due to my "lucky" timing, I could register just in time for the EMWA Freelance Business Forum (FBF) in Cascais in November 2017 to sneak a peek of what other freelancers thought and get answers to some of my questions.

My first FBF was overwhelmingly welcoming and interesting. Everybody was so encouraging when I talked about my idea and my experiences. I've only worked in medical writing for about 3 years, wasn't that too early to go freelance?

One thing I have always appreciated about MWs in general, but now in freelance MWs especially, is the support you get and the lack of competitiveness. Instead of other freelancers thinking "oh no, here comes another one" they share strategies and give hints on what needs to be done, when and how.

So, coming back from Cascais the theory became more real. I wanted to become a freelancer. In Germany, that means a bit of paperwork (or actually a lot): Looking for an accountant to take care of my taxes, my tax ID, and register me as a self-employed MW; an insurance consultant that would check out my existing insurances for necessary adaptations or whatever insurance(s) I would require; health insurance had to be arranged; and because I was still in the status of "unemployed" the whole business of applying for a founding grant (*Gründungszuschuss*). Again my "lucky" timing. When you're unemployed in Germany and want to start your own business (with a few requirements you have to fulfil) there are means to apply for grants that get you over the first hump (the first months when work isn't chasing you down yet). In order to apply for this money, you have to write a business proposal, a business plan for the first 3 years including calculations of income and expenses. Basically, get your crystal ball out and predict your future. What a blast. Or not. I thought making my own website (a whole other story) was hard, figuring out my business name, getting the necessary hard- and software, etc., but no, the income you have to predict for 3 year to come, this led me to complete meltdown status. How should I know? How do I do that? Do I lie and fib a little? Help!

Instead of other freelancers thinking "oh no, here comes another one" they share strategies and give hints on what needs to be done, when and how.

My experience in the CRO and the projects I had completed helped me to accomplish this in the end. My "client No. 1" wanted to do two projects with me to start off: observational studies with medical devices, between 50 to 100 patients, they wanted the database, the analyses, the reporting and possibly a manuscript (I did the exact same thing for him before, so I knew what would come and how much time it would probably need). This was my foundation, everything else was just made up, what I was expecting (or better hoping for); manuscripts and projects that resembled the ones I described.

One more thing, that only works for freelancers in Germany, is the Künstlersozialkasse. It has been described in the OOOO section before, so I applied there too. Because, funnily enough, a "scientific author" counts as an artist. Until now, (July 2018) I am still waiting on a reply. I had to send in proof of my work as a "scientific author" more than once, so I'm unsure whether or not I have much chance. But, if you mainly write manuscripts or other scientific content and not so much the regulatory documents, it is a good option. They pay half of the health and pension insurance (and in turn your clients have to give a deductible to the Künstlersozialkasse).

January 2018, and the time had come. Officially, I was in business. I had my own business website, or at least, the domain. I bought a new laptop and gear to arrange my new office at home. January and parts of February flew by with getting my website filled with information and hooking it up with Google in order to be found there, contacting my network and letting people know that I was "back" in business and eager to work. And then, the waiting game started. Why didn't they call? Or send a message? Oh well, I did a few webinars (EMWA and others, like software and basics in business development) and read a lot, tried to fill my time with "productive" tasks. I was constantly antsy. I didn't want to leave my "office" for too long in case someone would call or write. And then, they called and wrote. New clients that found my profile on LinkedIn or my website, and also old clients that knew me and appreciated my work. Boy, it felt great. I was in business, for real, or for at least another month or two. My nervous state of mind got a bit better with time. Whenever I didn't or don't have completely filled days, I do things I could never do while employed. Like, going to the gym mid-morning (so much more relaxing and less claustrophobic) or read or paint or garden or knit or whatever my heart desires. Even flying to family visits without feeling the tension of holiday constraints, I just packed my laptop and work phone and worked as it was necessary between playdates with my nieces and coffee with my friends and family.

Learning to relax and taking the days and work as they came was a big issue for me, but my biggest issue yet after my first 6 months, is to balance the need for business development. I haven't mastered the art of always being busy. We discussed this in the last FBF in Barcelona, and I still have a few things I haven't tried out so far. But isn't there always? There are busy times followed by free time. Recently, I started working with a recruiter that only works with freelancers. Yet another way to expand my opportunities. So, fingers crossed, I will find new clients and keep my current ones, keep learning and growing my business and network, because basically, networking is, besides the actual medical writing content, the most important thing for freelancers. Isn't it?

One more thing I heard a lot from people who have either worked with me or even from those who declined to work with me so far, is, that my attitude, my personality were nice to either work with or get to know, because I love what I do and that transfers. Plus being professional and sticking to timelines is one of my strengths. Nevertheless, the "lack" of experience got in my way a few times. But, I feel this will get better with every project and contract I will do. A bad attitude is a lot harder to fix. Becoming a freelancer took a lot of guts, there are uncertainties you don't have when you're employed, but the positive outweighs the risks for me, and it was the best decision I could have made by far.

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Upcoming issues of **Medical Writing**

December 2018:
Patient-reported outcomes

Patient-reported outcomes are outcomes reported by the patient rather than by healthcare professionals. This issue will include articles on their design, quality, feasibility, analysis, use, and future.
The deadline for feature articles is September 10, 2018.

March 2019:
Careers in medical writing

By choice or by chance? Medical writing work is very diverse and so are the careers of people in this field. This issue will focus on stories about medical writing careers.
The deadline for feature articles is December 10, 2018.

June 2019:
Generics and biosimilars

This issue will introduce readers to generics and biosimilars; provide and discuss their key legal and regulatory aspects in the US and Europe; and discuss their economics and how they affect pharmaceutical companies.
The deadline for feature articles is March 10, 2019.

CONTACT US

If you have ideas for themes or would like to discuss any other issues, please write to **mew@emwa.org.**

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