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Themes of upcoming issues of *Medical Writing*

September 2015: The theme will be 'The medical writing business'. The issue will include articles on different kinds of medical writing business models (e.g. freelance, contracting, contract research organisation, and networks), along with issues related to outsourcing and medical writing management. *This issue is now closed to new submissions.*

December 2015: The theme will be 'Writing for lay audiences'. The issue will include articles on writing patient education materials, informed consent forms, writing for special populations, medical journalism, and websites. *The deadline for feature articles is 2 September 2015.*

If you would like to submit an article, have ideas for issue themes or articles, or would like to discuss any other issues, please write to editor@emwa.org.

Risk management

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Editorial

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The thalidomide tragedy of the early 1960s cost several thousand lives, but it ultimately led to changes that will undoubtedly save many thousands more: it triggered a chain of events involving the WHO and the ICH that resulted in the pharmacovigilance systems we have today.



A key aspect of pharmacovigilance – the safety monitoring of drugs after their licensing – is risk management, which aims to better understand the benefit-risk profiles of drugs

and minimise their risks to patients. A rapidly evolving area, risk management is the theme of both this issue of *Medical Writing* and the 3rd EMWA Symposium in Dublin.

In December 2008 the European Commission unveiled the so-called 'EU Pharma Package', a set of proposals to give EU citizens better access to information on medicines and better protection from the harms caused by genuine and fake medicines. This package was followed by new pharmacovigilance legislation – *Directive 2010/84/EU* and *Regulation (EU) 1235/2010* – which came into force in July 2012, and a revised good pharmacovigilance practices (GVP) guideline from the EMA, published in April 2014: *Module V – Risk management systems (Rev 1)*.

Writing in this issue of *Medical Writing*, **Tiziana von Bruchhausen** and **Kerstin Prechtel** explore how these recent changes have affected safety medical writing, increasing document complexity and helping to create a new role: the pharmacovigilance medical writer. They identify some of the personal qualities pharmacovigilance writers require and outline the processes by which they can prepare Risk Management Plans (RMPs) for different purposes.

In Europe, an RMP must be submitted to the EMA with each new marketing authorisation application. Since July 2012, the EMA's RMP has had a modular format. **Sandra Götsch** guides us through its seven

parts (I–VII) and eight modules (SI–SVIII), providing insights, tips, and – for those of us who are new to RMPs – reassurance!

RMPs are further covered in a feature article by **Lesley Wise**, who describes how the risk management of approved medicines has seen an increasing focus on continued benefit-risk activities throughout a medicine's lifecycle. Lesley examines the historical background to benefit-risk assessment, changes to the content and format of RMPs in the EMA's revised GVP guideline (see above), and the new ICH standard for periodic benefit-risk evaluation: the Periodic Benefit-Risk Evaluation Report (PBRER).

Looking to the future (perhaps the not-so-distant future), **Massoud Toussi**, **Lisa Chamberlain James**, and **Alasdair Breckenridge** explore the possible role of social media in adverse event (AE) reporting. They explain the value of AE data from social media and highlight technological and other developments that are needed for such data to be properly captured and used, potentially revolutionising pharma's pharmacovigilance activities.

The Geoff Hall Scholarship winners

Are medical writers ghostwriters?

In this issue, we also announce the winners of the Geoff Hall Scholarships, which are annual scholarships in honour of a former EMWA president. They are awarded to new medical writers on the basis of an essay competition. This year's theme was 'Are medical writers ghostwriters?' The winners are **Andreas Sakka** and **Nicholas Churton**. Their excellent essays give us newcomers' views about this controversial topic.

Reaching out to non-native English-speaking medical writers

Non-native English-speaking medical writers are an important but perhaps underserved part of our association. Much of this has to do with English being the *lingua franca* of medical writing and

therefore EMWA, but some medical writers write in their own language or at least translate to and from their own language. To reach out to these non-native English-speaking medical writers, Maria Koltowska-Häggström started a new section, **Lingua Franca and Beyond**, in the last issue of *Medical Writing*. In this issue's instalment, she invites native English speakers to her section to learn about the work and needs of their non-native English-speaking colleagues. Also in this section, Laura C. Collada Ali, a medical translator living in

Italy and a member of EMWA's Executive Committee from 2013 to 2015, writes about the importance of having non-native speakers of English involved in EMWA and the Executive Committee. Laura also brings her fantastic energy to the pages of *Medical Writing* by rekindling **Gained in Translation**, our regular feature dedicated to medical translation. She further contributes her regular **Profiles** section, in which she continues her series of interviews of medical writers and translators from all over Europe.

President's Message

Julia Donnelly, Sam Hamilton

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I can't believe that my two years on the Executive Committee are now complete – what a journey from Manchester and Barcelona in 2013, Budapest and Florence in 2014, and finally Dublin in 2015. Apart from travelling many

miles, I have had a great experience and have worked with some quite inspirational individuals.

Over the past two years I have been involved with all the aspects of EMWA: the finances, education, PR, website, journal, conference, constitution and head office. Until I became Vice President, I had no idea just how much goes on behind the scenes, or indeed how many volunteers are involved with seamlessly delivering the EMWA institution. I am particularly proud of the new website that was introduced last year and the fruition of the webinar programme. Personally, I have enjoyed working with other professional bodies, and am delighted to see our collaborations increasing. From presenting at SfEP (Society for Editors and Proofreaders), PharmaNetwork Careers fairs, a joint ISMPP, EMWA, AMWA webinar, and the 2nd International Congress on Medical Writing in Ajman. We now have reciprocal agreements to advertise future conferences with ISMPP and DIA and have worked with ISMPP and GAPP to distribute relevant surveys which will help to promote our profession. The Budapest Working Group (BWG) is an expert collaboration, and the EMWA-AMWA all-new CORE Reference is a huge undertaking with an ambitious goal.

I have enjoyed the past two years far more than I had expected, and I encourage anyone who is interested in getting involved to make contact. Finally, I would like to thank Andrea Rossi my predecessor and wish Sam Hamilton every success; I know she is going to be a wonderful president!

Best wishes,
Julia



Thank you Julia and the Executive Committee for making my busy year as Vice President so enjoyable.

EMWA's future will build on a solid 22-year foundation; our modern public face – through a strong social media presence – has paved the way for a lasting global identity. As incoming President, I will guide EMWA to live up to all our expectations, some of which were already realised in Dublin.

Our 3rd Symposium Day nudged educational content beyond the advanced workshop programme, by introducing developing topics. Spurred on, we devised and delivered the inaugural Expert Seminar Series (ESS) to further extend learning opportunities. Six experts presented diverse cutting-edge topics tailored for the more experienced medical writer. We are already working hard to develop the 2017 ESS programme, and we welcome ideas and contacts for the topics that interest you.

Julia's penchant for new collaborations has infiltrated my work too, with the blossoming of the EMWA-AMWA BWG partnership to develop the CORE Reference. Our resource for authoring ICH-compliant clinical study reports aligned with the principles of responsible clinical trial data sharing is under development. Our BWG representative is part of an established industry effort to develop clinical study protocol guidance. These two projects should bear fruit by May 2016. Similar projects are planned, opening doors for experienced members – I encourage you to volunteer.

EMWA is a diverse organisation mindful of all its members' needs. A medical communications-focussed 2017 Symposium Day is planned. Individuals contribute their personal knowledge, so if you have a particular expertise, then please step forward and make the difference.

I hope you'll agree that member experience is continually being enriched. Together, we will professionalise and shape our industry. I look forward to the challenges of the year ahead, and to meeting many more of you in The Hague in November 2015.

Best wishes,
Sam Hamilton

The changing face of (benefit-)risk management

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Abstract

Over the last 20 years the focus of post-approval management of medicines has changed from risk management to the assessment and management of benefit-risk. In the EU this has been reinforced by changes in the legislation underpinning pharmacovigilance and the introduction of Good Pharmacovigilance Practice (GVP) modules. The documents used by companies to present and manage the benefits and risks of a product to regulators changed in 2012, requiring a change in focus for companies and regulators which needs to be reflected in increased cross-functional working and continued benefit-risk assessments.

Keywords: Benefit-risk, Signal, PSUR/PBRER, Risk management, Risk Management Plan (RMP), Lifecycle

Background

In the late 1950s and early 1960s thalidomide was used as a hypnotic and anti-emetic. It seemed to have a low level of obvious side effects in patients, although some side effects were noted by Dr Florence and reported in the *British Medical Journal* in 1960.¹ Then as the use of the drug spread, some obstetricians started to notice congenital abnormalities in babies born to mothers who had taken thalidomide during pregnancy.² This was the start of the unfolding of what is described as the thalidomide disaster, which was responsible for the initiation of systems to monitor the safety of marketed medicines in many countries of the world.³ These systems encourage health care professionals to report suspected side effects of medicines to national regulatory authorities and have been very successful in detecting safety concerns in marketed medicines over the years.^{4,5}

However, by the late 1990s there was a move to be more proactive about drug safety management. In 2001 a concept paper was agreed by the

International Conference on Harmonisation to define a risk management guideline (ICHE2E), which was finalised in 2004.⁶ The aim of this guidance was to better define what was known about the safety profile of a medicine when it was licensed, in terms of the number of patients studied and the types of risks identified, as well as plans for obtaining further data and managing the known risks. It was anticipated that such an approach would help to ensure that the safety profile of a product early in the post-marketing phase would be closely monitored to detect any new safety concerns early, and also to ensure that the safety profile as seen in the clinical studies was reflected in clinical use.⁷

The European Medicines Agency (EMA) adopted this guideline in 2005 as part of Volume 9A of the Rules Governing Medicinal Products in the European Union.⁸ The EMA Risk Management guidance was mainly aimed at new products and those with an emerging safety signal that might require management beyond labelling. All products submitted for a marketing authorisation were required to have a risk management plan as part of the submission. To improve consistency across products, the EMA introduced a risk management plan template in 2006. Whilst the guidance was clear and the template was relatively easily managed, there was no attempt to combine information on benefits and risks and no information for the lay reader. As familiarity with the template and guidance grew, it was also clear that there was a lot of duplication in the document and concern that the risk management plans may not be achieving all they had set out to do.

There have been a number of reviews of the impact of the guidance on the risk management of medicines, both internal⁹ and external¹⁰ to the EMA, and some of the perspectives from these were taken into account for the new guidance and template which came into effect in 2012 as part of the implementation of the European pharmacovigilance legislation.

2012 PV legislation

The European pharmacovigilance legislation introduced in 2012 through Regulation (EU) No 1235/2010 and Directive 2010/84/EU was a major revision of medicines legislation in European countries which also took into account emerging trends in the healthcare sector such as increased transparency, provision of patient accessible information, and a focus on consideration of both benefits and risks. The outworking of the legislation for the companies, the individual European regulatory authorities, and the EMA is guided by a number of modules on Good Pharmacovigilance Practice (GVP)¹¹ which replace Volume 9A of the Rules Governing Medicinal Products in the European Union. The GVP modules of key interest in this article are GVP modules V and VII, which cover risk management planning and the periodic benefit-risk evaluation report (PBRER) as defined in ICH E2C(R2). Please note: This is described in the EU as the Periodic Safety Update Report (PSUR), but this article will retain the ICH document naming convention.

The RMP and PBRER are now orientated more towards the management of the benefit-risk profile of a product rather than just the risk profile and have ensured an increased and continuing focus on benefit-risk assessment and management.¹²

As a consequence of this increased focus on benefit-risk management, regulatory authorities, the pharmaceutical industry, and academia are now paying far more attention to benefit-risk assessments, and the quality and communication of those assessments. For example, a major work package within the EU-PROTECT research project addressed quantitative benefit-risk methods.¹³ EU-PROTECT was a public-private partnership which was part of the Innovative Medicines Initiative (IMI). It aimed to assess the utility of various benefit-risk methodologies and particularly how the benefit-risk assessments can be visualised. Other approaches have been investigated by the Centre for Innovation in Regulatory Science (CIRS), most recently with the Unified Model for Benefit-Risk Assessment (UMBRA) initiative.¹⁴ At the same time, regulators, pharmaceutical industry associations, and academic groups are working on guidance to improve standardisation of the assessments and to develop methods that will help in the display and review of the benefit-risk of products. This is also being taken forward by the recent ICH working group established to update section 2.5.6 of the CTD (ICH M4E(R2)).¹⁵

New requirements for the RMP

The new requirements for risk management plans introduced within GVP V¹⁶ retained the principles of ICH E2E. The format of the risk management plan is now modular with the aim of increasing the ease of updates. Additionally there is now some guidance in GVP V on how to define important identified and potential risks, and what might constitute missing information relevant for inclusion in the risk management plan. The document now contains specific sections on the benefits of the treatment as well as a section designed for non-scientific readers which is publically available on the EMA website. This is all in line with the comments above on increased transparency, provision of patient accessible information, and a focus on consideration of both benefits and risks. There are also some sections common to both the RMP and the PBRER, as discussed in the PBRER section below.

In summary, the RMP is a document where information on the population studied (size, demographic distribution, duration of treatment, and clinical trial inclusion/exclusion criteria) is provided along with information on the important identified and potential risks and the missing information (e.g. relevant populations not studied, long-term safety). This information is accompanied by proposals for obtaining more safety information (the PV plan), information on benefits and proposed risk minimisation measures for the important identified and potential risks and for the missing information (Risk Minimisation measures). The effectiveness of these risk minimisation measures becomes an integral part of the benefit-risk assessment.

For companies an important point to note is that updating of the RMP has now been decoupled from the PBRER in terms of regulatory RMP submissions. However, given the sections common to both the RMP and the PBRER, companies may decide to maintain an internal updated RMP document for consistency reasons.

New requirements for the PBRER

The updates introduced to the PSUR as part of the GVP guidance were much more major than those for the RMP and reflect changes agreed at the ICH level in ICH E2C(R2).¹⁷ The new PSUR document, renamed the PBRER, focuses on the review and discussion of the safety and efficacy data from the most recent time period, as well as the cumulative data and how the overall benefit-risk profile has changed during the current reporting period. It also introduces the concept of the difference

between benefits and clinical study endpoints, and encourages companies to clearly identify the benefits of treatment. EMA GVP module VII¹⁸ implements ICH E2C(R2) and provides clear guidance on the need to understand the risks in the context of the benefits and the need to understand both the benefit and safety information in the context of the uncertainties in each of these. For example, a relatively small treatment-exposed population may imply uncertainty in both the benefit estimate as well as the risk estimate. The impact on the benefit estimate is that we will be less sure about the overall extent of the benefit and aware that it may be smaller than we have seen. The impact of a small population on our confidence in the safety data is that we may be concerned about risks that we have not yet had the opportunity to see (because either the safety population is too small or too refined or the studies were too short). The consequent impact on understanding of the benefit-risk profile of such a product is that there is more concern about the unknowns in the safety profile in the context of concern about the generalisability of the benefit information. Each PBRER requires a formal assessment of the benefit-risk of the product which takes into account all the data for the product and how effective the risk minimisation measures are in reducing either the risk of a side effect or the severity of the side effect if it occurs. This assessment will consider the importance and the magnitude of the benefit and will weigh against that the important risks in the context of their frequency and seriousness AND the context of the benefit.

Benefit-risk in the product lifecycle

As we move through the product lifecycle the key benefit-risk related product activities remain the same (signal detection, evaluation, management of potential and identified risks, evaluation of that management). What changes is the amount and type of data we have on which we can base our assessments. For example, there may be new studies in different indications, which change the types of benefits we consider and may also increase the amount of safety data available. Additionally, there will be reports of suspected adverse reactions from the safety monitoring systems mentioned in the Background section of this article. These reports can identify new safety signals that will need to be evaluated¹⁹ and, if considered real, may need to be considered as part of the benefit-risk assessment. They may also help to provide new information on known risks. Figure 1 describes the overall benefit-risk lifecycle for a typical product.

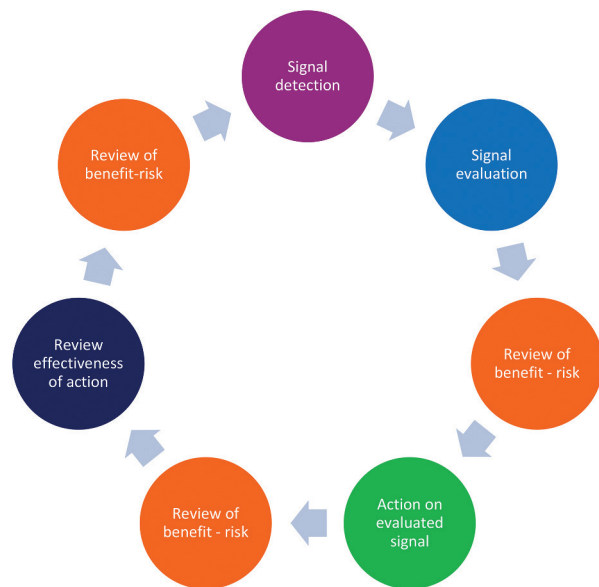


Figure 1: A life cycle approach to benefit-risk management.

As the product lifecycle continues, new safety risks will emerge from regular reviews of the data. These new risks will need to be evaluated and managed and the benefit-risk of the product will need to be re-evaluated. As more data accumulates, it may be possible to identify sub-groups of patients who respond better to the product (or less well), and subgroups who have a greater risk of more serious side effects. Trying to identify and characterise these subgroups is an important part of maximising patient benefit and minimising risk.

Conclusion

Over the last 20 years the focus of post-approval management of medicines has changed from risk management to the assessment and management of benefit-risk. The assessment of benefits and risks needs to consider the importance and the magnitude of the benefit and to weigh against that the important risks in the context of their frequency and seriousness AND the context of the benefit.

The overall benefit-risk assessment is described and reported periodically in the PBRER and should take into account all the data available on both the benefits and the risks of the product for a given indication. This assessment requires cross-functional working within global companies and also an understanding of the place of the product in the health care systems of different territories. It also requires a good understanding of how patients view both the benefits and the risks associated with the treatment, which often depends on the underlying condition being treated and the alternatives to the treatment.

Interestingly, thalidomide has been licensed once again, this time with stringent risk management measures in place to prevent the tragic consequences to the foetus if exposure occurs during pregnancy. The indications for treatment with thalidomide vary between different countries of the world but reflect the need for the benefit to outweigh the risks. Examples include leprosy and cancer. In the EU thalidomide is licensed to treat multiple myeloma, a disease with limited treatment options. Patients are educated about the benefits and the risks, and the effectiveness of the risk minimisation is monitored closely.²⁰ This illustrates the importance of managing risks in the context of the benefits and identifying those diseases or patients where the benefits of treatment outweigh the risks.

Conflicts of interest and disclaimers

Lesley Wise works as the Head of Global Risk Management and Pharmacoepidemiology for Takeda Development Centre Europe Ltd. The information and views set out in this article are those of the author and do not necessarily reflect the corporate opinion or position of Takeda.

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Pharmacovigilance medical writing: An evolving profession

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Abstract

The preparation of pharmacovigilance documents is a global and cross-functional activity. The pharmacovigilance medical writer has a key position in this complex activity, leading the whole document creation process. This process includes drafting the document, coordinating the input of the involved functions, providing valuable expertise on the required format and contents and detailed guideline knowledge, and coordinating the review and consolidation of comments. Furthermore, different submission scenarios and document requirements exist, depending upon, for example, the medicinal product, therapeutic indication, and authorisation procedure. The result should always be a high-quality state-of-the-art document meeting all requirements for an electronic submission to health authorities worldwide.

Keywords: EU pharma package, Pharmacovigilance medical writer, Lifecycle, RMP

Introduction

Medical writing is an established professional field in the pharmaceutical industry that takes account of changing legislation and requirements for professional medical communication. Based on the new pharmacovigilance legislation issued in the context of the so-called 'EU Pharma Package', the EMA introduced the Good Pharmacovigilance Practices¹ (GVP) in 2012. This framework (in the following referred to as EU Pharma Package for the purpose of this article) provided the opportunity for a new medical writing role to develop: the pharmacovigilance medical writer. The ideal profile description of a pharmacovigilance medical writer includes pharmacovigilance expertise; extensive knowledge of formal requirements and guidelines; document, format, and content expertise; and writing, communication, and project management skills. Moreover, the pharmacovigilance medical

writer often needs to look beyond the preparation of a single document and to take into account further regulatory aspects regarding document planning and assessment (as described in the examples below).

The lifecycle of a medicine

In pharmacovigilance, document-related activities do not end with the submission of a document to health authorities, but continue throughout the lifecycle of a medicine, along with pharmacovigilance and risk minimisation activities (see Table 1 for some examples) and benefit-risk analyses. The EU Pharma Package emphasises the concept of lifecycle with regard to the risk management system for a medicine (Figure 1) and reflects this concept in the new contents and requirements for Risk Management Plans (RMPs)² and Periodic Safety Update Reports/Periodic Benefit Risk Evaluation Reports (PSURs/PBRERs).³ At the time of marketing authorisation, only limited clinical experience and knowledge about the risks of a medicine are available. Marketing authorisation is granted based on clinical trial data indicating that the benefits exceed the risks (i.e. the benefit-risk profile is positive). Pharmacovigilance activities are planned to further characterise the risks (e.g. to assess risk frequency or severity) or to investigate whether subsets of patients within the target population (e.g. patients with hepatic impairment) are at higher risk. Measures aimed at minimising risks associated with the use of a medicine are planned at the time of marketing authorisation. The EU Pharma Package introduced the requirement to assess the effectiveness of these measures in the post-authorisation phase. Depending upon this assessment, different risk minimisation measures (RMMs) may need to be planned (Table 1). Risk management according to the EU Pharma Package is not just managing risks, but also understanding risks in the context of benefits and

Table 1: Pharmacovigilance activities and RMMs

Pharmacovigilance activities		RMMs	
Routine	Additional	Routine	Additional
<ul style="list-style-type: none"> ● Periodic reports (DSURs, PSURs/PBRERs) ● Signal detection and evaluation ● Monitoring ● Specific adverse reaction follow-up questionnaires^a 	<ul style="list-style-type: none"> ● Non-clinical studies^a ● Clinical studies^a ● Non-interventional studies^a ● PASS^a ● PAES^a ● Pharmacoepidemiology studies^a ● PK studies^a ● Further pre-clinical work^a ● DUS^a ● Registries^a 	<ul style="list-style-type: none"> ● SmPC^{a,b} ● Package leaflet^{a,b} ● Labelling^{a,b} ● Pack size and design^{a,b} ● Legal (prescription) status^{a,b} 	<ul style="list-style-type: none"> ● Education programme^{a,b} ● (different educational tools depending upon the target audience, e.g. patient alert cards)^b ● Controlled access programme, pregnancy prevention programme, direct health care communication^b ● Surveys (including questionnaires for data collection)^b ● Studies, PASS, etc. ● Prescriber guides

Abbreviations: DSUR, Development Safety Update Report; DUS, Drug Utilisation Study; PAES, Post-Authorisation Efficacy Study; PASS, Post-Authorisation Safety Study; PBRER, Periodic Benefit Risk Evaluation Report; PK, Pharmacokinetic; PSUR, Periodic Safety Update Report; SmPC, Summary of Product Characteristics.

^aGVP Module V Rev 1.²

^bGVP Module XVI Rev 1.⁵

maximising the benefit-risk balance of a medicine. In fact, the effectiveness of the medicine in real-life settings might differ from the efficacy shown in clinical trial settings. A subset of patients within the target population might turn out to be at higher risk or to benefit to a lesser or greater extent from the use of a medicine. This would impact the benefit-risk balance of the medicine. Last but not least, post-authorisation safety and efficacy studies may be needed to further characterise risks, assess the effectiveness of RMMs, or maximise benefits.

In a nutshell, the link between risk management and pharmacovigilance medical writing is the RMP, which gives a detailed description of the risk management system, contains information on a medicine’s safety profile, and explains the measures

taken to prevent or minimise the medicine’s risks in patients. As a medicine progresses throughout its lifecycle, emerging evidence on safety and efficacy/effectiveness needs to be evaluated in the context of baseline knowledge, and pharmacovigilance activities and RMMs are planned dynamically and proportionally to risks. In this sense, the RMP is also dynamic and proportionate to risks. Unlike other regulatory documents (e.g. clinical study reports, clinical summaries, periodic safety reports), an RMP is a living document that is updated continuously throughout the lifecycle of a medicine during the pre- and post-authorisation phases. Updates may be needed at any time point of the lifecycle of the medicine.

After marketing authorisation, the PSUR/PBRER periodically evaluates risks and benefits of a medicine and the effectiveness of the RMMs in place. Evidence on risks and benefits that emerges during the reporting interval is presented in the context of baseline knowledge and culminates in an integrated benefit-risk analysis. The PSUR/PBRER and the RMP are closely related: if new safety concerns arise in the context of PSUR/PBRER preparation, an RMP update is needed in parallel and new pharmacovigilance activities and RMMs are planned.



Figure 1: The risk management cycle. Source: GVP Module V Rev 1.²

A task for pharmacovigilance medical writers

Prior to the EU Pharma Package, RMPs and PSURs/PBRERs were normally prepared by drug safety professionals. With the new pharmacovigilance legislation, both RMPs and PSURs/PBRERs became complex, multidisciplinary documents with a new modular format, requiring a large amount of

data and analyses that encompass the pre- and post-authorisation phases. In other words, a task for highly specialised pharmacovigilance medical writers.

A multidisciplinary document requires a skilled writer who ensures clear data presentation, effective medical communication, and content- and style-wise consistency across modules. Furthermore, the pharmacovigilance medical writer plays a critical role in managing a high number of document files and versions, and ensuring that all contributions are provided and reviewed in a timely manner. Moreover, the pharmacovigilance medical writer must have sound knowledge of guidelines and should ensure that all contributions comply with the GVP requirements. They must also ensure that information contained in other submission documents (e.g. clinical summaries) is in line with the data presented in an RMP. Last but not least, in view of their expertise and knowledge of guidance and requirements, the pharmacovigilance medical writer adds value to planning of the most appropriate document format (of, for example, an RMP) and the level of detail of data presentation; discussions on risks and their categorisation as safety concerns (Table 2); and the strategic planning of submission of different yet related documents.

Table 2: Definition of safety concerns

Identified risk	An untoward occurrence for which there is adequate evidence of an association with the medicinal product of interest
Potential risk	An untoward occurrence for which there is some basis for suspicion of an association with the medicinal product of interest but where this association has not been confirmed
Important identified risk and important potential risk	An identified risk or potential risk that could have an impact on the benefit-risk balance of the product or have implications for public health
Missing information	Gaps in knowledge about a medicinal product, related to safety or use in particular patient populations, which could be clinically significant
Safety concern	An important identified risk, an important potential risk, or missing information
Risk-benefit balance	An evaluation of the positive therapeutic effects of the medicinal product in relation to the risks, i.e. any risk relating to the quality, safety, or efficacy of the medicinal product as regards patients' health or public health

Source: GVP Annex I Rev 3.⁶

There are many different situations a pharmacovigilance medical writer could face. The next section presents a few of them in reference to RMPs.

Pharmacovigilance medical writing task: Preparing RMPs for different authorisation procedures

In Europe four different authorisation procedures exist: centralised, decentralised, mutual recognition, and national. Depending upon the type of medicinal product, the intended therapeutic indication, and several other legal regulations, a new marketing application is submitted via one of the four procedures. Detailed guidance regarding the application type is given on the EMA homepage.⁴

An RMP is part of the submission dossier and is required for all new marketing applications which are planned for submission in the EU/European Economic Area (EEA), regardless of the authorisation procedure. Unlike other regulatory documents, the RMP is not a classical single-file document but is set up in a modular fashion, meaning that an RMP consists of several parts, some of which are further subdivided into several modules or appendices. Each part/module can be updated and re-submitted independently from the others. Also, not all parts/modules of an RMP might be required for an initial application.²

In general, the RMP undergoes a preparation phase, followed by a writing and review phase, a finalisation phase, an agency review phase, and finally the post-approval phase (Figure 2).

In the following examples, different submission scenarios and their impact on RMP writing are presented.

Example 1

A new active substance for a new marketing application is planned for submission via the centralised procedure in the EU/EEA.

In the preparation phase, the pharmacovigilance medical writer conducts kick-off meetings with the team. These kick-off meetings serve to raise the team's awareness of the upcoming task and to clarify timelines, responsibilities, and deliverables. They also permit discussion of the content, required analyses, planned pharmacovigilance activities, and RMMs, to name a few topics. As a next step, the pharmacovigilance medical writer prepares a so-called 'shell RMP', which contains all required information that can be provided independently of the statistical data outputs. For example, epidemiological, non-clinical, and pharmacokinetic information is usually available well in advance and



Figure 2: RMP lifecycle phases.

can be finalised at an early stage. The aim of this front-loading approach is to agree in advance on the key outline of the RMP and the required analyses, pharmacovigilance, and RMMs, and to free up the team's capacity for the interpretation of data during subsequent writing and review (see below). The preparation of a shell RMP includes one or two review cycles in the team and discussion of comments meetings. To the extent possible, the pharmacovigilance medical writer then finalises the shell RMP before the statistical analyses arrive.

The next step is the writing and review phase. Taking into consideration the statistical data analyses and the accompanying implications for the medicinal product (e.g. Are the safety concerns observed so far in line with expectations? Are additional measures required?), the pharmacovigilance medical writer creates first and final draft versions of the RMP. These draft versions are reviewed and thoroughly discussed in the team before they are sent to management for review and company approval. Alignment with other documents of the submission dossier also takes place in this phase, as it is important that the entire dossier is consistent and tells the same overall story. Also, a thorough quality check against the source data is performed at this stage.

In the finalisation phase, the pharmacovigilance medical writer takes the last management decisions into consideration and then finalises the RMP content-wise. The RMP is now ready to undergo the last technical steps in the electronic document management system, which are required to deliver a high-quality state-of-the-art document for electronic submission. These technical steps include checking of format, setting of hyperlinks, and electronic approval in the system. After successful

completion of all these steps, the RMP is now available for electronic submission to the agency.

The RMP now enters the agency review phase. In the case of the centralised procedure, the agency review follows a defined review schedule. The advantage of this procedure is that the timelines of the agency questions are known well in advance. This facilitates internal capacity and timeline planning enormously. Depending upon the type of questions received, the RMP will be updated several times during an agency review procedure. In addition to the RMP update, the pharmacovigilance medical writer also helps the team with the responses to questions on the RMP. Questions can, for example, refer to re-classification or addition or demotion of the proposed safety concerns, additional data analyses, requests for post-approval measures, and changes to the proposed labelling (i.e. Summary of Product Characteristics and Package Leaflet). Towards the end of the approval procedure the frequency of the agency interaction increases and RMP updates can be requested several times at extremely short notice. Good team interaction and internal processes allowing for these demands are crucial here. Finally, if positive opinions are obtained from the Pharmacovigilance Risk Assessment Committee and Committee for Medicinal Products for Human Use, the new medicinal product is given approval by the European Commission. During this last phase, agency review of RMP Part VI (the public summary of the RMP written in lay language) also takes place.

The first task in the post-approval phase is the preparation and submission of RMP Annex 1 within the required timelines. RMP Annex 1 provides the key information regarding the RMP in a structured electronic format and can also be prepared by

a pharmacovigilance medical writer, in collaboration with selected team members. After this task has been completed, the RMP is now subject to various updates as long as the product is on the market.

An RMP update is required upon request of the EMA or a national competent authority within the EU/EEA, or whenever the risk management system changes (i.e. when new information leads to a significant change in the benefit-risk profile or when the result of an important pharmacovigilance activity is obtained or a risk minimisation milestone is reached).²

Example 2

A new active substance for a new marketing application is planned for submission via the decentralised procedure in the EU/EEA. The RMP follows the same preparation, writing and review, and finalisation phases as described above for the centralised procedure. Differences exist with regard to the agency review phase: the applicant does not receive consolidated comments by one agency but several comments from different national agencies, according to various local requirements and also different review timeframes. A major challenge for the applicant is to consolidate all these comments content- and timeline-wise. For example, will the changes requested by one national agency be implemented globally in the RMP, and therefore apply to other countries as well? Or are these requested changes applicable to this one particular country only, and is it therefore advisable to create 'local' versions of the RMP? Other differences include the requirements for RMP Annex 1 and the handling of RMP Part VI, as these procedures follow local requirements as well. In the post-approval phase, RMP updates can be requested at any time by any of the national agencies involved and not only by a single central body like the EMA. This can lead to the same questions as in the agency review phase, such as whether requested updates apply to all countries or are country-specific.

Example 3

A generic medicine, on the market for decades, is planned for submission via the national procedure in a new EU/EEA country. The initial RMP for generic medicines can follow an abridged format:² epidemiological, non-clinical, clinical, and post-authorisation data can be omitted, as well as the RMP module on important risks and, in most cases, the parts on pharmacovigilance activities and efficacy studies. What happens if the reference medicine is no longer on the market? Should

epidemiological data for the indication/target population and non-clinical data, possibly based on the scientific literature, be provided to discuss the risks of the medicine? Would it make sense to present proprietary data, for example on post-marketing experience with the generic medicine? Should the company's own risk analyses be provided? The pharmacovigilance medical writer plays a key role in facilitating solutions to these often complex issues. National competent authorities may appreciate a proactive, tailored approach that follows the general principles of the GVP guidance.

Conclusions

With the recent implementation of the EU Pharma Package, complex pharmacovigilance documents and new processes were introduced. The pharmacovigilance medical writer has a key position in this novel context, leading the document creation process and providing oversight and guidance to the multidisciplinary authoring team.

Acknowledgements

We would like to thank Sven Schirp and John Sherrill for discussions and constructive feedback.

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Publications: Is help from medical writers acceptable and useful?

In the October 2014 issue of *Current Medical Research & Opinion*, Jackie Marchington and Gary Burd present a survey in which they asked academics and clinicians about the value of professional medical writers.¹ In 2012, they sent out a 9-question SurveyMonkey survey to 260 academics/clinicians. The survey covered various aspects of medical writing assistance and included one open question: ‘*Is there anything you would like to tell us about your experience of working with professional medical writers?*’

Regrettably, only 76 people (29.2%) responded, but their responses are revealing. The highest number of respondents (61/76) felt medical writers were useful for ‘*Editing for grammar, spelling, journal style (including referencing), etc.*’ By contrast, only 9 respondents (12%) valued a medical writer’s scientific expertise. These findings mirror my experience as an in-house science editor, working with professors and physicians: the ‘*Science*’ in my job title sometimes felt superfluous.

The survey also aimed to ‘*evaluate academic/clinician authors’ perceptions regarding the acceptability [...] of using [medical writers] in the development of publications.*’ 83% of respondents felt that it was OK. However, extreme selection bias – the people surveyed were all current or former clients of the communications agency Marchington and Burd work for – limits the value of the data relating to this question.

Only 13 people answered the open question, and some of their answers are not useful, so it’s difficult to draw conclusions. One person commented that the medical writer

should be the first author, but this would normally contravene ICMJE (International Committee of Medical Journal Editors) guidelines.² Another felt that medical writers *could* be authors, depending on their contribution, while acknowledging that this isn’t really their role.

Happily, most respondents valued the assistance of medical writers (63/75) and reported positive experiences of working with them (61/70), although there are issues with validity: four people rated their experience of working with medical writers but reported having no such experience. The study’s flaws are clear, but it does provide welcome insights into the views and experiences of researchers who have sought professional help with their publications.

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A shot at demystifying the risk management plan for medical writers

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Abstract

A risk management plan (RMP) is a complex regulatory document which is now required in the European Union as part of a medicine's approval process. This article offers practical guidance for medical writers who are interested in writing an RMP. In a step-by-step approach, the medical writer is led through the RMP template with the aim of taming this mystical beast.

Keywords: Risk Management Plan, European Medicines Agency, Medical writing, Pharmacovigilance

Writing a risk management plan (RMP) for the first time can be a daunting prospect. This article aims to provide some tips for medical writers who are new to preparing RMPs. Most of you will know that the RMP is a legally binding regulatory document submitted to health authorities. It is now mandatory for all new marketing authorisation applications in the European Union (EU), except for those for homoeopathic medicinal products registered via the simplified registration procedure and traditional herbal medicinal products. Once an RMP is accepted by the health authorities, the Marketing Authorisation Holder (MAH) has a legal obligation to perform the activities described in the RMP.

Objectives of the RMP

The RMP gives a detailed description of pharmacovigilance activities and interventions designed to identify, characterise, and manage risks relating to a medicinal product (MP).¹ The ultimate goal of the RMP is to improve the benefit-risk balance by combining risk assessment and risk minimisation.

First, the RMP describes what is known and not known about the safety profile of the MP. Once that has been established, the RMP outlines measures to prevent or minimise the risks and how the effectiveness of those measures will be

assessed and monitored. In addition, the RMP proposes pharmacovigilance activities to study further safety concerns during use of the drug in the real-life setting and documents the need for efficacy studies in the post-authorisation phase.

Structure of the RMP

The RMP is structured in a modular format and consists of seven parts, where part II ('Safety specification') is further divided into eight modules (see Table 1 for an overview of the parts and modules of the RMP alongside their respective aims). Normally, all parts of an EU-RMP should be submitted. In certain circumstances, some parts or modules may be omitted unless they are requested by the competent authority. For example, generic applications based on Article 10(1) of Directive 2001/83/EC do not require RMP part II modules SI-SVII.

Check reference RMPs

Before you start writing the RMP for your product, always consider whether RMPs are available for products with the same active substance or within the same pharmacotherapeutic group. These should be taken into account even if they are approved for a different indication and posology. Also, reference to other products with similar indications and/or risks can be useful.²

In the case of a generic drug, check if RMPs exist for the innovator, the reference product, or a generic. The RMP for a generic should comply with the RMP for the reference product, unless some safety concerns are clearly no longer relevant. Addition of further safety concerns in a generic RMP (in relation to the reference product) has to be thoroughly justified. Provided that the reference MP has no additional pharmacovigilance studies or stipulated efficacy studies imposed as a condition of the marketing authorisation, RMP parts III and IV may be

Table 1: EU-RMP structure and objectives of the respective parts

RMP structure		Objectives
Part I	Product overview	Provide administrative and active substance information
Part II	Safety specification	Identify what is known and not known about the medicinal product
	Module SI: Epidemiology of indication(s) and target population(s) Module SII: Non-clinical part of the safety specification Module SIII: Clinical trial exposure Module SIV: Populations not studied in clinical trials Module SV: Post-authorisation experience Module SVI: Additional EU requirements for the safety specification Module SVII: Identified and potential risks Module SVIII: Summary of the safety concerns	
Part III	Pharmacovigilance plan	Plan a programme to identify new safety concerns and characterise known ones
Part IV	Plans for post-authorisation efficacy studies	Investigate effectiveness in everyday medical practice
Part V	Risk minimisation measures	Take steps to prevent or minimise known or suspected risks and evaluate the effectiveness of risk minimisation measures
Part VI	Summary of the risk minimisation plan	Provide a public summary of the RMP written in lay language
Part VII	Annexes	

omitted for generics. Part VI should be based on an appropriately modified version of the public summary for the reference MP.¹

How to write an RMP – A step-by-step approach

First of all, get yourself acquainted with the formal requirements for content and submission of EU-RMPs as outlined in Good Pharmacovigilance Practices (GVP) Module V published by the European Medicines Agency (EMA).¹ Use the guidance on format of the RMP which is available for download on the EMA website as either an integrated template with all modules in one document, an abridged format suitable for generic medicines, or the complete set of individual modules.³ Don't be surprised to find that this template is very repetitive and tables will have to be copied again and again in different parts.

Due to the complexity of the RMP, you will most probably work together with a multidisciplinary team (e.g. toxicologists, pharmacologists, pharmacovigilance, clinical and regulatory experts), who will advise on the evaluation of risks and the proposed measures for prevention and risk minimisation.⁴ Note that the RMP is a stand-alone document and cross references to other parts of the dossier should therefore be avoided. Table 2 indicates the location of information in the

common technical document (CTD) according to GVP guideline Module V.¹

Part I - Product overview

This section is straightforward to prepare. It provides administrative information on the RMP and an overview of the product it covers. It also includes active substance information, pharmacotherapeutic group (Anatomical Therapeutic Chemical [ATC] Classification System), mode of action, indication, posology, and pharmaceutical forms/strengths.

Part II - Safety specification

Part II is organised in eight modules. Apart from module SVI, which includes additional elements required to be submitted in the EU, all other modules correspond to safety specification headings in ICH-E2E.⁵ The purpose of the safety specifications is to provide a synopsis of the safety profile of the MP and should include what is known and not known about the MP.

Module SI: Epidemiology of the indication(s) and target population(s)

This module provides background information on the proposed indication(s), explaining what events occur as part of the disease and what events can be expected in the target population. The following issues have to be discussed:

Table 2: Mapping between RMP modules and CTD according to GVP guideline Module V

RMP	CTD
Part I - Product overview	Module 2.3: Quality overall summary Module 3: Quality Module 2.5: Clinical overview
Module SI: Epidemiology of the indication(s) and target population(s) Module SII: Non-clinical part of the safety specification	Module 2.4: Non-clinical overview Module 2.6: Non-clinical written and tabulated summaries Module 4: Non-clinical study reports Module 2.7: Clinical summary – briefly Module 5: Clinical study reports Module 2.5: Clinical overview Module 2.5: Clinical overview – briefly Module 2.5: Clinical overview (including benefit-risk conclusion) Module 2.7: Clinical summary SmPC
Module SIII: Clinical trial exposure	Module 2.5: Clinical overview Module 2.7: Clinical summary
Module SIV: Populations not studied in clinical trials Module SV: Post-authorisation experience Module SVII: Identified and potential risks	Module 2.5: Clinical overview Module 2.5: Clinical overview – briefly Module 2.5: Clinical overview (including benefit-risk conclusion) Module 2.7: Clinical summary
Module SVIII: Summary of the safety concerns	Module 2.5: Clinical overview Module 2.7: Clinical summary
Part III - Pharmacovigilance activities	Module 2.5: Clinical overview Module 2.7: Clinical summary
Part IV - Plans for post-authorisation efficacy studies	Module 2.5: Clinical overview Module 2.7: Clinical summary
Part V - Risk minimisation measures	Module 2.5: Clinical overview Module 2.7: Clinical summary

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- epidemiology of the indication(s), including
 - incidence and prevalence
 - demographics of the target population(s)
 - risk factors for the disease
 - main treatment options
 - mortality and morbidity
- concomitant medications in the target population(s)
- important co-morbidities found in the target population(s)

Preparing this part of the RMP will provide no real challenge for medical writers, especially if they have some experience in writing clinical overviews.

Module SII: Non-clinical part of the safety specification

This module is basically a summary of the non-clinical parts of the CTD, so any experience with preparing non-clinical overviews will be very helpful. You are asked to present a summary of the important non-clinical safety findings, such as toxicity, general pharmacology, drug interactions, and other toxicity-related information or data. Justify inclusion or exclusion of non-clinical findings as important risks depending on their relevance for humans and also note missing information. Safety concerns arising from non-clinical data should be carried forward to module SVIII.

Module SIII: Clinical trial exposure

Again, this is a pretty straightforward section, where meticulous work is required to provide a tabulated and/or graphical summary of a variety of exposure

measures from clinical trials, such as duration of exposure, dose levels, or age groups.

Module SIV: Populations not studied in clinical trials

In this module, you should discuss which subpopulations within the expected target population have not been studied in clinical trials (e.g. pregnant women or patients with severe renal impairment). The relevance of inclusion and exclusion criteria should also be explained, especially when exclusion criteria from study protocols are not proposed as contraindications in the Summary of Product Characteristics (SmPC). Typical populations to be discussed in this section are children, the elderly, pregnant or lactating women, and patients with hepatic or renal impairment.

Only safety concerns which are still outstanding should be carried through to module SVIII.

Module SV: Post-authorisation experience

Post-authorisation experience is only required for updates of the RMP and is therefore not further discussed here.

Module SVI: Additional EU requirements for the safety specification

This module is special insofar as it contains some safety topics not included in ICH-E2E:

- harm from overdose (either intentional or accidental)
- transmission of infectious agents
- misuse for illegal purposes (e.g. use as a recreational drug)

- medication errors
- off-label use
- specific paediatric issues (including potential for paediatric off-label use, safety and efficacy issues identified in the Paediatric Investigation Plan)

Safety concerns from this module have to be carried through to module SVIII.

Module SVII: Identified and potential risks

This module should provide more information on the important identified and potential risks. Note that this should be a concise chapter and not a collection of adverse events from clinical studies or lists of adverse reactions from section 4.8 of the SmPC ('Undesirable effects'). Make sure it only contains important adverse reactions, important interactions, and important pharmacological class effects.

For each important identified risk and important potential risk, a variety of information has to be provided, such as frequency, severity, and nature of risk, risk factors, and preventability.

Module SVIII: Summary of the safety concerns

A safety concern may be:

- an important identified risk (confirmed by clinical data);
- an important potential risk (not refuted by clinical data or of unknown significance); or
- missing information (e.g. high likelihood of off-label use or populations not studied such as pregnant and lactating women, children, or patients with severe hepatic/renal impairment).

Safety concerns identified in modules SII, SIV, SVI, and SVII are included here. Also, each risk listed in SmPC sections 4.3 ('Contraindications') and 4.4 ('Special warnings and precautions for use') should be regarded as an 'important risk'. However, do not include adverse drug reactions mentioned in SmPC section 4.8 ('Undesirable effects') as important identified risks if they are currently considered unlikely to affect the benefit-risk assessment of the product. Carefully check the SmPC for evidence of missing information.⁶

Part III - Pharmacovigilance plan

The Pharmacovigilance plan (PhV Plan) describes how the MAH identifies and characterises safety concerns by proactive monitoring. It does NOT include actions intended to reduce, prevent, or mitigate risks.¹

For each safety concern summarised in module SVIII, the planned PhV activities have to be listed and can be divided into routine and additional PhV activities. If safety concerns are well characterised, routine post-authorisation PhV will suffice. Additional PhV activities may be non-clinical studies, clinical trials, or non-interventional studies.¹ For safety concerns with additional PhV activities, provide an action plan and a summary table including expected dates of milestones.

Part IV - Plans for post-authorisation efficacy studies

Whereas parts II, III, and V are concerned with drug safety, part IV deals with the efficacy of the MP. The PhV legislation provides the legal basis for requiring post-authorisation efficacy studies for products

- where there are concerns about efficacy in everyday medical practice; or
- when knowledge about the disease or the clinical methodology used to investigate efficacy indicates that previous efficacy evaluations may need significant revision.

For paediatric medicines and advanced therapy medicinal products (ATMPs), long-term follow up of efficacy is required. This section may be omitted for generics if the reference MP does not have any efficacy studies imposed as a condition of the marketing authorisation.¹

Part V - Risk minimisation measures

Risk minimisation measures (covered in more detail in another article in this issue – see page 62) fall into two categories: routine and additional activities. No general guidance is possible on which activities are to be used as this is a case-by-case decision. However, the proposed activities should always be proportional to the risks.

It is possible that routine risk minimisation activities will be the only proposed risk minimisation activities. They include appropriate information and warnings in the product information (SmPC, package leaflet, and labelling), and may also relate to package size and legal status of the product (i.e. prescription status). Additional risk minimisation activities are all measures which go beyond the above and should be confined to the most serious risks. An action plan needs to be provided on how the effectiveness of additional activities will be evaluated. Further information on additional risk minimisation activities can be found in GVP Module XVI.⁷

Part VI - Summary of the RMP

Part VI is split into two sections. Section VI.1 ('Elements for summary tables in the European public assessment report (EPAR)') contains summary tables from parts I, III, IV, and V.

Section VI.2 ('Elements for a Public Summary') is the publicly available scientific summary of the RMP written for the lay reader. This section has several subsections to summarise all the key aspects of the RMP, including a short chapter about disease epidemiology, treatment benefits of the drug, unknowns relating to treatment benefits, and a summary of safety concerns. Furthermore, a summary of the risk minimisation measures, which puts the MP's risks in the context of the treatment benefits,⁸ has to be provided, along with the planned post-authorisation development plan (if applicable). Section VI.2 can be regarded as one of the key challenges for the medical writer as it represents the 'public face' of the RMP and should be a useful resource for patients and physicians.⁶

Part VII - Annexes

This part consists of 12 annexes, including the current or proposed product information, worldwide marketing authorisation, and other supporting data such as referenced material.

Conclusion

The RMP is a complex document, but it is structured in a clear manner and can be mastered by following a step-by-step approach. Medical writers, with their attention to detail, writing expertise, and communication skills, are a valuable part of the authoring team. For someone with experience in regulatory writing, preparing an RMP can be a rewarding challenge.

Author information

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Acknowledgements

Thanks go to Johanna Klocker for her comments on the manuscript.

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Using social media as the patient's voice in the benefit-risk assessment of drugs: Are we ready?

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Abstract

There is no doubt that the public interest in health-care-related issues is growing. This, coupled with the surge in the use of social media, leaves the pharmaceutical industry with a set of unique opportunities and challenges. The screening and reporting of adverse drug reactions (ADRs) is of vital importance, and Marketing Authorisation Holders (MAHs) have a responsibility and liability for their drugs. Patients increasingly use social media to share their healthcare experiences, and this is a welcome opportunity for MAHs to learn more about the real-world experience of their products. However, currently this source for ADR reporting is largely underutilised; partly because the data generated are unstructured, but also because our technology for assessing and analysing this information is lagging behind. There is an urgent need for policy, methods, guidelines, and technology platforms to allow patients' voices through social media to be adequately 'heard' and incorporated into the benefit-risk assessment of drugs.

Keywords: Social media, Benefit-risk, Adverse drug reactions, Data gathering

The information gathered through digital media is increasing exponentially, especially through the data contributed by social media. Additionally, the majority of the data responsible for the exponential growth of knowledge are unstructured, and include tweets, comments on social media sites such as Facebook, and videos posted on websites such as YouTube. While the public's interest in discussing healthcare-related issues is growing, our technology for assessing and dealing with this

type of information is struggling to keep up. Although marketing departments of pharmaceutical companies have already begun using social media to understand the perceptions of patients about their drugs, other departments – such as safety and pharmacovigilance – are still sceptical about the validity of the knowledge extracted from social media.

Should we be interested in social media reports of adverse drug reactions?

The European Medicines Agency's (EMA) Good Pharmacovigilance Practices (GVP) defines an adverse drug reaction (ADR) as a response to a medicinal product which is noxious and unintended. ADRs are considered as serious if they involve death, a life-threatening condition, inpatient hospitalisation or prolongation of hospitalisation, persistent or significant disability or incapacity, a congenital anomaly, or a birth defect. An individual case safety report (ICSR) describes one or several ADRs that occur in a single patient at a specific point in time.

The criteria for an ICSR to be valid include:

- at least one identifiable reporter,
- a single identifiable patient,
- at least one suspect adverse reaction, and
- at least one suspect medicinal product.

It is challenging to apply these definitions to social media reports of ADRs, but the importance of ADR reporting cannot be overestimated. The continuous surveillance of the safety and efficacy of pharmaceutical products used in clinical practice helps the early detection of drug safety problems

in patients and, thus, serves to reduce drug morbidity and drug mortality.¹ ADRs can also have negative effects on treatment adherence and, consequently, increase the risk of resistance and disease. Furthermore, the treatment of ADRs incurs additional healthcare expenses due to hospitalisation or other medical interventions.² Therefore, the screening and reporting of ADRs is of vital importance.

Marketing Authorisation Holders (MAHs) are legally responsible for the safety and effectiveness of medicines on the market, and are required to report ADRs to the national pharmacovigilance centre, a medicines regulatory authority, or the World Health Organization, as appropriate.²

MAHs are required to operate appropriate pharmacovigilance and risk management systems to ensure responsibility and liability for marketed products and to ensure that appropriate action can be taken when necessary. To be able to fulfil this requirement, the MAH must have a thorough understanding of the ADRs caused by their products. According to EMA GVP Module VI, MAHs should regularly screen internet or digital media under their management or responsibility for potential reports of suspected adverse reactions. If the MAH becomes aware of a report in any non-company sponsored digital medium, the report should still be assessed to determine whether it qualifies for reporting. Within the European Union, MAHs are legally obliged to forward adverse events (AEs) to the EMA. In addition, there are other voluntary programmes in place to improve ADR reporting, e.g. the U.S. Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS)³ and The Yellow Card Scheme in the UK.⁴

However, given that patients are increasingly using social media to post and discuss their experiences with diseases, drugs, and treatments, a vast amount of data is now generated specifically concerning reactions to medicines that MAHs are required to monitor, assess, and act on, as appropriate. Current tools and techniques for the analysis of unstructured data, especially in the domain of pharmacoepidemiology and safety, are very limited. Also, discussions about the validity and reliability of data traditionally have excluded unstructured data provided by patients from the range of acceptable ‘evidence’ in the evaluation of the benefit-risk balance of medicinal products. Consequently, very few studies have been conducted on the extraction of knowledge from these sources, and there are methodological and technological gaps in this area which must be filled.

What makes digital media an attractive source of knowledge on healthcare?

Digital media refers to audio, video, and images that exist in a computer-readable format and includes websites, web pages, blogs, vlogs, social networking sites, internet forums, chat rooms, and health portals. To this list, one should also add the ‘internet of things’ which is the interconnection of uniquely identifiable embedded computing devices within the existing internet infrastructure (e.g. GPS devices, cars, cameras, ‘coach’ watches, sphygmomanometers, glucose measuring devices, insulin pumps, bathroom balances).

An unprecedented volume of information now exists on these media, with the number of social media users growing phenomenally over the past few years. For example, the number of registered Google Plus active users increased from 500 million to 1 billion within a period of less than a year in 2012.⁵ It is estimated that an individual who is already an active user of social media spends around 13 to 16 minutes per hour on social media websites,⁶ and may engage in collaborative projects (e.g. Wikipedia), share information on social networking websites (e.g. Facebook), participate in virtual games and social worlds (e.g. World of Warcraft, Second Life), or create and share videos (e.g. on YouTube, Vimeo).

It is estimated that these websites will increase the amount of recorded data to 44 zettabytes by 2020 (1 zettabyte = 10^{21} bytes), as compared to 1 zettabyte in 2010. This is a massive amount of unstructured data compared with the estimated 5 zettabytes of data from structured sources by 2020. It is estimated that 9% of all unstructured data will be related to healthcare, of which half will be related to drugs.⁷ Internet-based applications are also easily accessible and within the reach of large groups of people, and thus can be updated immediately and with high frequency.

Validity and usefulness of patient postings in social media

Traditionally, AE reporting relies on physicians and drug safety groups, who serve as gatekeepers to validate the reports. Patients are increasingly using social media to share their experiences with drugs, medical devices, and vaccines.⁸ However, currently this source for ADR reporting and pharmacovigilance is largely underutilised. To date, there are only five articles on PubMed that discuss tracking ADRs with the help of social media.

In a study described in one of these articles, Freifeld and colleagues identified more than 4000 posts on Twitter that resembled AEs and showed that they were significantly correlated with data

from FAERS by System Organ Class ($P < 0.0001$).⁸ Internet data on ADRs from consumers may also serve to identify areas for service improvement or topics about which patients need more education or information. For example, analysis of 3785 items from five social media sites found that patients with glaucoma had stronger positive feelings towards complementary therapies and treatments with a poor evidence base than towards medically proven therapies,⁹ suggesting a lack of awareness or education about the clinically proven treatments.

Web-based patient-reported outcomes can provide an opportunity for MAHs and regulatory bodies to understand the benefits and risks of medicines in the real world. However, there are concerns about the validity of data from social media sites. Guidelines developed in consultation with industry, patients, regulators, academic groups, and prescribers are urgently needed to suggest methodologies to collect, analyse, and process this large pool of information,¹⁰ which could potentially help in early detection of unrecognised side effects. Such methodologies and may serve as complimentary tools for MAHs and the FDA for receiving patient feedback.¹¹

In addition, knowledge of social media discussions will help physicians to better understand how patients perceive their ADRs and to manage the adverse effects of drugs and develop strategies for improving treatment adherence. A mixed methods study examined the content related to aromatase inhibitor (AI)-associated side effects posted by breast cancer survivors on 12 message boards between 2002 and 2010. Of the 25,256 posts related to AIs, 18.2% mentioned at least one side effect. Furthermore, 12.8% mentioned discontinuing AIs and 28.1% mentioned switching AIs.¹²

Online communities may also highlight topics that are of concern to patients (e.g. medication convenience

or packaging) and side effects that are not discernible in clinical trials.¹³ In addition to ADRs, social media data can also help assessment of the risk perceptions of patients. Analysis of patient narratives on popular social media websites for health-related topics in France before and after withdrawal of all medicines containing benfluorex found that there was drastic change in the patients’ perceptions after withdrawal. Prior to the withdrawal date, most posts concerned efficacy, while those after the withdrawal date discussed cardiovascular side effects.¹⁴

Do we have the technology for tapping these unstructured data?

The studies described above are small scale and ‘one shot’ examples. Given the large volume of unstructured data available on the internet, an efficient data solution is needed to detect ADR reports on social media and bring them to the attention of MAHs for validation and further actions.

Few examples exist today which could provide insights into the technical possibilities of detecting safety signals through the internet. One such example is IMS Health’s Nexus™ Application Suite and its module AETracker. This module provides a cloud-based engine for AE monitoring, off-label usage, and other legal, regulatory, and reputation risks in company-sponsored digital assets including social media accounts and mobile apps. In real time, pharmacovigilance experts review and confirm any false positives or alert the client within 1 hour of an AE being reported (Figure 1).

In a test project, the system processed websites such as Twitter, Facebook, forums, and Wikipedia pages and generated 281,971 records related to a specific drug, of which 15% were flagged as potentially interesting signals by AETracker and 1.7% were confirmed

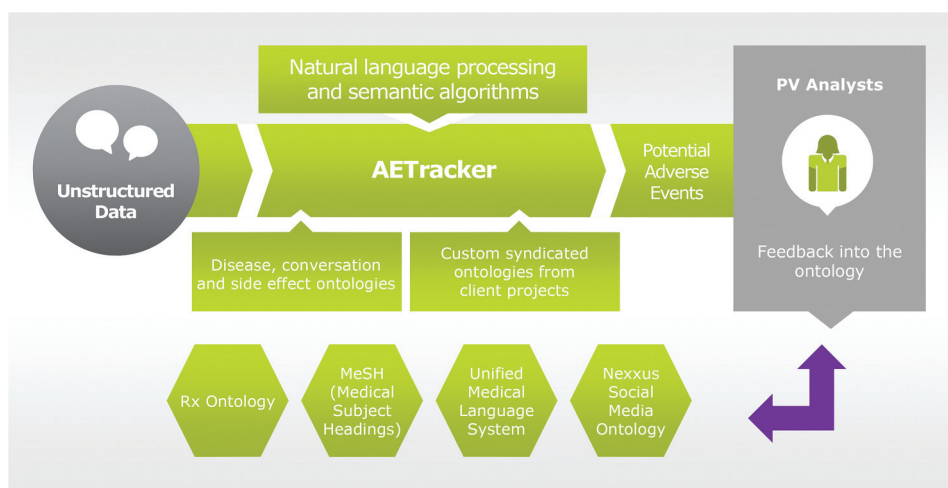


Figure 1: AETracker: A solution for ADR tracking on the social media.

following analysis. Notably, the system flagged every record that looked like an AE with 100% accuracy. This approach showed that technological advances such as the Hadoop system, natural language processing, and logical programming could provide useful methods allowing robust analysis of internet-based safety signals. Also, it showed that MAHs could save 85% of costs related to pharmacovigilance as compared to a moderation approach.

Beyond the interest related to the detection of safety signals, such tools also allow MAHs and healthcare professionals to gain a better understanding of the information exchange about a drug, and to better understand patient and consumer perceptions about that drug. For example, the use of AETracker resulted in an observation that Copaxone is perceived to be a highly effective first-line injectable for multiple sclerosis, followed by Rebif, Avonex, and Betaseron, in decreasing order of efficacy. Betaseron and Betaferon were perceived to be easier to use and associated with fewer side effects (e.g. injection site reactions) than Rebif and Avonex. Extavia and Avonex were perceived to be more cost effective than Rebif, Copaxone, and interferon β-1b drugs. According to social media conversations, side effects were the main cause for patients to switch treatments (unpublished observations, Figure 2).

In the UK, the WEB-RADR initiative is being led by the MHRA. This initiative seeks to investigate technologies for gathering ADR data, and will develop tools and recommend policy. WEB-RADR

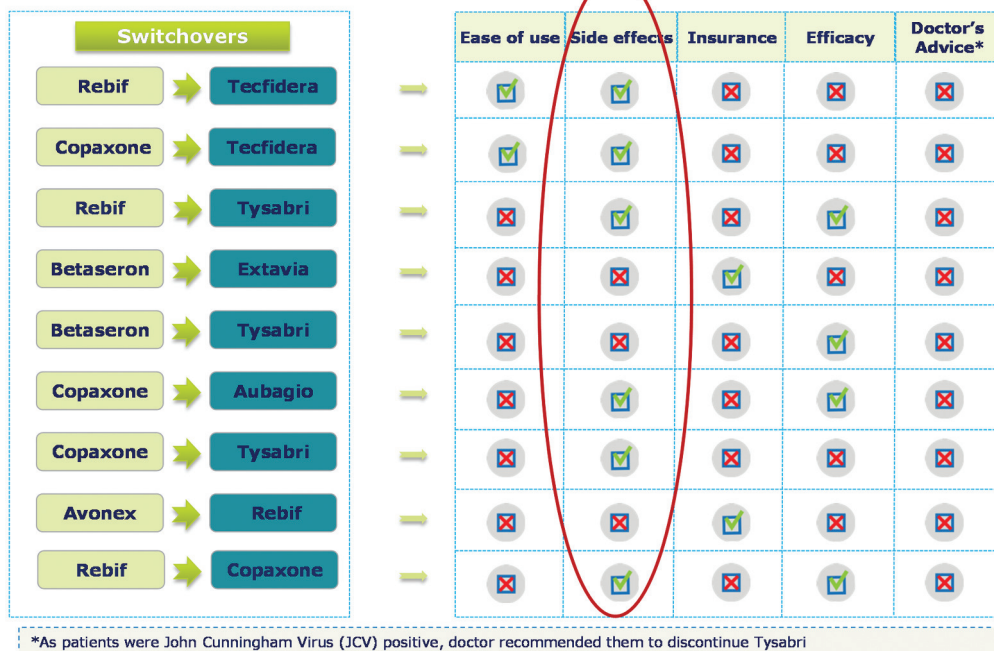
is a multi-stakeholder initiative and comprises the development of a mobile app for collecting ADR data. The data collected via this app should add information to the established safety profiles of medicines, enable earlier detection of new signals, reveal new patterns or trends in reporting, and even provide a means for geo-pharmacovigilance.

Technologies in development such as WEB-RADR will allow patients to report ADRs through apps or social media sites. Ideally, these reports would be analysed alongside other sources of pharmacovigilance data, and any signals identified and regulatory action agreed. Feedback can also be provided directly to the patient, but this two-way communication should be handled with care because of ethical and legal implications. Data gleaned from social media are also subject to validation, assessment, and duplication issues. Currently, collaboration between IMS Health and Facebook allows de-duplication of the majority of reports in AETracker.

Conclusion

There is no doubt that ADR reporting methodologies are changing and that the amount of data generated through social media is rapidly growing. This provides an opportunity for MAHs and healthcare professionals as information on ADRs shared on social media can be used as a source of information and insights for the benefit-risk evaluation of drugs.

Side effects were seen as a major reason for switchover based on social media conversations



Massoud Toussi – February 5, 2015, ECPM, Basel, Switzerland

Figure 2: Summary of social media conversations on the use of injectable drugs in multiple sclerosis.

There is an unmet need for policy, methods, guidelines, and technology platforms describing the tracking of adverse reactions through social media. A big data-based technology solution is required to assess and analyse this new data set and produce insightful and robust knowledge from it. A number of initiatives have been undertaken by governments and agencies to fill the gaps and unmet needs, and a first step would be the development of guidelines or position papers. A multi-stakeholder approach seems necessary for the development of such guidelines, including at least industry, patients, regulators, academic groups, and prescribers. One of the barriers to the use of social media by drug companies is the fact that if they analyse social media – even for other purposes other than drug safety – this may generate a lot of ADR information which could go beyond their ICSR processing capabilities. However, the future of ADR reporting is data intense and is almost upon us. It’s time to arm ourselves with the technology and guidelines to maximise our understanding of the patient’s voice.

Conflicts of interest and disclaimers

IMS Health produces the Nexxus™ Application Suite. No other conflicts to declare.

Acknowledgements

The authors acknowledge the assistance of Dr Pradnya Kulkarni from Trilogy Writing in the preparation of this manuscript.

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Special section

Winners of the Geoff Hall Scholarship essay competition

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The Geoff Hall Scholarships (GHSs) are given in honour of a former President of EMWA. Geoff was a very special person, an extremely valued member of EMWA, and a very good friend to many EMWA members. He firmly believed that the future of EMWA lies in our new and potential members, and so it's a very fitting legacy that we have the Scholarship Awards in his memory.

The Scholarships are awarded annually on the basis of an essay competition, and the title of this year's essay was 'Are medical writers ghostwriters?'. There was a record number of entries, and although it sounds like a cliché, it's genuinely true that the essays caused a lot of debate and discussion among the GHS committee and it was not an easy task to choose just two winning entries. However, two were eventually chosen, and the very worthy winners were Andreas Sakka and Nicholas Churton.

Andreas Sakka has worked as a professional medical writer at Caudex Medical since June 2014. After graduating from Imperial College London

with a BSc in Biochemistry, Andreas moved into industry. He has worked for a number of companies, including Smiths Detection and GE Healthcare, primarily developing *in vitro* and *in vivo* diagnostic technologies for various diseases. Following redundancy, Andreas decided to leave the lab to join the world of medical communications.

Nicholas Churton works as a medical writer at ICON Plc involved in medical writing projects concerning clinical study reports, patient narratives, safety documentation such as developmental safety update reports, editorial reviews and book reviews. Before this, Nicholas was a student at the University of Bath, UK, where he studied for a MSc in Biology. After this he moved to the University of Southampton, UK, to study for a PhD in microbiology. He is currently awaiting examination.

Andreas' and Nicholas' winning essays are presented below, and we wish them the very best at the start of their very promising medical writing careers.

Are medical writers ghost writers?

By Andreas Sakka

Are medical writers ghostwriters? Yes.

At least they may appear to be to the layperson. Ostensibly, medical writers and ghostwriters are professional writers, providing a service to paying clients, creating literature that is published under somebody else's name. This much is true and, with such a concise and unambiguous description, one may think that there is little to dispute regarding the difference between the two. However, a deeper look at the subject reveals a crucial difference that clearly separates medical writers and ghostwriters.

The fundamental distinction between medical writers and ghostwriters is that of visibility. Ghostwriters are typically paid to create literature, in whole or in part, on behalf of an author but their own identity and contribution is never

revealed. Without insider knowledge, it would be impossible to recognise that an author did not create a piece of work on their own or what level of assistance was given. The ghosts are invisible, and the invisible cannot be held to account.

Ghostwriting -along with the associated practices of ghost authorship and non-declaration of funding sources or conflicts of interest- has, in the past, contributed to incomplete and misleading publications of scientific data pertaining to various therapies. Ultimately, this caused harm to patients prescribed inappropriate drugs. Two of several such scandals involved Merck's drug Vioxx and Wyeth's hormone therapy drugs. Between these two cases, ghostwritten articles were used to mitigate apparent risks, failed to report adverse events (including

patient deaths) and promoted unsupported benefits and off-label uses of the drugs.¹⁻³ Merck and Wyeth used ghostwriters as part of a campaign to produce literature beneficial to their companies, with leading academics listed as authors to provide 'a veneer of independence and credibility'.⁴ Without transparency in authorship and funding, readers could not have realised the conflicts of interest within these publications and therefore a balanced judgement on their integrity and validity was impossible. These scandals led to Senator Charles Grassley investigating ghostwriting practices in medical literature where he expressed his concerns for the 'lack of transparency that exists in medical ghostwriting'.⁵

Pharma companies must balance an inescapable and inherent conflict of interest: they develop medicines used for the public good but are required to generate revenue and profit for shareholders. To make money, pharma must sell drugs. To sell drugs, they must raise awareness of them and convince clinicians to choose their medicine over that of their competitors. This creates a commercially driven pressure to optimise the way in which a drug is perceived; a pressure that may encourage unethical behaviours such as the poor publication practices described above. In his criticism of Merck over the Vioxx scandal, Dr Eric Topol wrote 'sadly, it is clear to me that Merck's commercial interest in rofecoxib [Vioxx] sales exceeded its concern about the drug's potential cardiovascular toxicity'.⁶

Contrary to the secrecy of ghostwriting, medical writers are clearly identifiable in the material they produce. For example, it is typical for medical writing assistance to be detailed in the acknowledgment section of a journal article. Transparency, and its implication of accountability and openness to judgement, encourages ethical behaviour by making unethical behaviour difficult to hide. In this way, information on new medicines is disseminated to the medical community and public for the benefit of all.

There are a number of industry-developed publication guidelines in which medical writers are trained and adhere to in their work. These guidelines shape the way in which medical writers produce literature and interact with other members of the medical and pharmaceutical industries to ensure that information is communicated ethically. Examples of recommendations within the good publication practice (GPP2) guidelines include: granting authors full access to study data and allowing them the freedom to make public or publish the study results; disclosing potential conflicts of interest and identifying funding sources;

following established reporting standards such as CONSORT, PRISMA, MOOSE, etc.⁷ GPP2 continues to develop in order to maintain and improve the highest standards of publication practice. GPP2, used alongside authorship guidelines such as those of the International Committee of Medical Journal Editors,⁸ help to ensure clear, accurate, complete and unbiased reporting of scientific data, regardless of whether outcomes are positive or negative, and appropriate authorship with authors who are publicly accountable for the published work.

Furthermore, both the American Medical Writers Association and European Medical Writers Association have published position statements on ghostwriting.^{9,10} Examples of statements made within the EMWA position statement include 'involving the named author(s) early in the publication process', 'refusing requests to develop publications without sufficient involvement of the named author(s)', and 'refusing requests to develop publications in an unethical or irresponsible manner.'

Ghostwriters do not need to hold themselves to the high standards set out by a Medical Writers Association or GPP2 guidelines; they can simply write what they are told to by their paymasters, regardless of concerns over ethics, accountability or the potentially disastrous public health impacts of misrepresented science. In this regard they are the polar opposite of the professional medical writer, who must strive to ensure the integrity and transparency of reported science by adhering to internationally recognised and accepted guidelines. Through ethical publication practices, the medical writer can help prevent harms to patients such as those that ghostwriting contributed to in the Merck and Wyeth scandals.

In summary, medical writers provide an important resource to aid academics, investigators and pharmaceuticals companies to publish data ethically with completeness, transparency and integrity. This is achieved by adhering to various publication, authorship and reporting guidelines and provides a critical 'check and balance' to pharma companies who are driven by the conflicted requirements of doing public good while making private gain. In so doing, the medical writer can help promote the benefits of publicising the latest science, build trust and credibility in the pharmaceutical and medical industries and avoid the medical failures that unethical publication practices and ghostwriting have contributed to in the past.

Are medical writers ghostwriters? Absolutely not.

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Are medical writers ghost writers?

By Nicholas Churton

Are medical writers ghostwriters? I feel a chill go down my spine when I hear those words. Perhaps that is because I dislike that statement or perhaps it is just the ghost in me trying to escape. I once spent ten minutes talking to my father-in-law about what I did for a living as a medical writer since leaving the realms of academia. After ruling-out administrator, typist and office assistant, the word ghostwriter begrudgingly slipped out of my mouth, and I was greeted with a response of 'Ah ... now I understand.' I smiled but felt somewhat misunderstood.

The term ghostwriter applies to the situation where the true author of a piece of work is not directly credited and as such it is often associated with suspicion and distrust.¹ However, conventional ghostwriting can be considered an elegant art and is seen in categories such as autobiographies, fictional and non-fictional stories, magazine articles as well as academic literature. The topic of ghostwriting in the academic field has been hotly debated in recent years, attracting the attention of professional medical writers in both Europe and America.^{2,3} The controversy of academic ghostwriting stems from the fact that the author paid to write the publication did not take part in the design or execution of the work they are writing and as such there is a risk that the study will be misrepresented. In a recent article in the *British Medical Journal*,⁴ Dr. Richard Smith and Dr. Peter Gøtzsche discussed with deputy editor Trish Groves the ethical implications of industry-driven publications and the use of

ghostwriters. Although well-argued, the article generated extensive response, including an eloquent response from members of the Global Alliance of Publication Professionals stressing the importance to exercise caution when distinguishing between ghostwriters and professional medical writers.

In essence, a professional medical writer is not a ghostwriter. A medical writer can be defined as a specialist writer who generates scientific documents in a clear and effective way whilst ensuring compliance with all necessary regulatory guidelines. The key word in that description is specialist. To generate complex medical documents such as clinical study reports, safety reports or patient narratives, the medical writer must simultaneously comprehend the roles of the clinicians, statisticians, publishers, auditors and, most importantly, the client. But to someone who is not immersed in the world of clinical research, the role of a medical writer is sometimes hard to explain. In many respects, the term ghostwriter is not that far-off; we do not devise the studies we write, we are not always credited, and we are paid according to the complexity of the document. The fundamental difference between a medical writer and a conventional ghostwriter is that we are governed by guidelines and policies laid out by The International Conference on Harmonisation (ICH)⁵ and those of the European Medical Writers Association,⁶ the American Medical Writers Association,⁷ and the International Society for Medical Publication Professionals,⁸ which ensures writers adhere to ethical practices

and thus prevent the publishing of misconstrued and fraudulent information.

Furthermore, the argument that medical writing services are detrimental to research needs rethinking.^{1,9} Medical writers provide a professional, high-quality and cost-effective way of communicating scientific information. The partnership between a medical writer and the client they write for is founded on shared professional standards which can result in a positive and long-lasting relationship. Ultimately, it is the responsibility of the medical writer to represent a given product in a fair and ethical way based on the data available and in accordance with the ICH guidelines⁵ and medical writing policies,^{6–8} but responsibility also lies with the client to ensure that the final document accurately depicts the true nature of the product or study. Consequently, recent debate over ghostwriters in academia^{1,2} should not result in writers themselves becoming the scapegoats.

A personal and frank account of a medical writer, and self-proclaimed ghostwriter, can be seen in an article by Linda Logdberg.¹⁰ In this article, Logdberg describes her disillusion with a career in academia and the initial appeal medical writing had; namely, the knowledge that her work was helping the sick, whilst enjoying the flexible hours and good pay. A thought shared by many! At first her career was enjoyable, working directly with the physicians responsible for the work and relishing the role she played. But as her career progressed the initial charm of the work disappeared and as she started working for larger companies the gap between the writer and the researchers grew and the ethical burden of what she was writing became more apparent. In her own words, she ‘... was unwilling to turn this ugly duckling ... into a marketable swan’. I am sure that this experience has been shared by many medical writers at least once in their career and highlights some of the issues medical writers encounter, but I do not believe, and I hope, that this is not the norm. My experience of medical writing, limited as it is, has been extremely positive. The members of the team I work with are highly-skilled, ethical writers, many of whom have been published academics. Each writer takes pride in their work and, although they may not be credited, there is a strong sense

that the work generated is their work and that only work of an exceptional quality should be delivered to the client.

The outsourcing of services such as medical writing is an increasing phenomenon in the medical and pharmaceutical industries and the perception of a medical writer as a ghostwriter is likely to continue for some time. However, what perceptions do we encounter if we extend that concept to all services provided by a global clinical research organisation? Do we consider the clinical trials Ghostwriters? Do we consider the clinicians Ghostclinicians? No we do not, and nor should we consider medical writers as ghostwriters. Professional medical writers should be considered as highly-skilled, ethical individuals with a strong medical and scientific background who facilitate the ever-increasing need for effective scientific communication.

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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

The articles included in this section are a selection from the EMA's news and press release archive for December – February 2015. More information on the work of the EMA can be found on its website: www.ema.europa.eu.

Adaptive pathways: a future approach to bring new medicines to patients?

December 12, 2015 – “Adaptive pathways should be the preferred approach in the near future to bring new medicines to patients.” A number of scientists, including members of the European Medicines Agency (EMA) and its scientific Committees take this position in a co-authored article published in *Clinical Pharmacology and Therapeutics*.

The concept of adaptive pathways foresees an early approval of a medicine for a restricted patient population based on small initial clinical studies. The first approval is followed by progressive adaptations of the marketing authorisation to expand access to the medicine to broader patient populations based on data gathered from its use and additional studies.

Under the header ‘From adaptive licensing to adaptive pathways: delivering a flexible life-span approach to bring new drugs to patients,’ the authors, who are part of the New Drug Development Paradigm (NEWDIGS) initiative, analyse the key drivers of adaptive licensing. These include:

- The patients’ demand for timely access to medicines, in particular where there are unmet medical needs. With adaptive licensing, new treatments would be made available to some patients earlier, on a smaller evidence base, if efficacy has been observed in this patient population.
- A better understanding of pathologies which has led to the identification of subgroups of patients who are likely to better respond to

certain medicines than others. For many of these subgroups, a progressive approach to licensing while learning from real-world experience may become the only viable access route to new treatments.

- The growing financial pressure on healthcare systems and a call for a more targeted use of medicines to increase their therapeutic value.
- The pressure on industry to make the development of medicines, in particular for chronic diseases, sustainable. Development programs targeting smaller, better defined populations would lower the threshold for financing a drug’s development and allow for more medicines to be brought forward.

A number of recent developments are fostering the transition from a traditional approach, which implies large trials and a marketing authorisation for broad groups of patients, to an adaptive approach. These include the development of innovative clinical trial designs, learning healthcare systems and the inclusion of patients in decision-making processes to better understand what level of uncertainty they are willing to accept.

EMA adaptive pathways pilot project

EMA launched a pilot project on adaptive pathways (formerly known as adaptive licensing) in March 2014 to explore this approach with real medicines in development.

As of November 2014, the Agency had received and assessed 29 applications as part of the pilot, nine of which had been selected for discussion with the applicant.

Stage I of the pilot project will close at the end of February 2015. The Agency will then focus on stage II of the project. This will include in-depth, face-to-face meetings with the applicants for the applications selected.

After 28 February 2015, EMA will still consider new applications for stage II face-to-face meetings if they are well-developed. Applicants are invited to contact EMA at adaptivepathways@ema.europa.eu for advice on the content and suitability of their request to be considered for stage II of the pilot.

EMA is planning to publish a report on initial experience gained as part of the pilot project by the end of 2014.

EMA recently changed the name of its pilot project from adaptive licensing to adaptive pathways to better reflect the idea of a life-span approach to bring new medicines to patients with clinical drug development, licensing, reimbursement, and utilisation in clinical practice, and monitoring viewed as a continuum.

Europe to boost international cooperation on generics

January 19, 2015 – The European Medicines Agency (EMA) is ready to share its assessments of applications for generic medicines in real time with collaborating regulatory agencies outside the European Union (EU). This initiative aims to facilitate the timely authorisation and availability of safe, effective and high quality generic medicines worldwide.

The information-sharing initiative is part of the International Generic Drug Regulators Pilot (IGDRP). It started in July 2014 using the European Union decentralised procedure as a model, and it is now extended to the centralised procedure.

The EU is leading this initiative with the aim to both save global assessment resources and to facilitate and strengthen the scientific assessment process for medicines. It is expected that this sharing of assessments will allow authorisation of generic products in concerned countries in a coordinated and resource effective way.

The first phase of the pilot project will involve the EU, Australia, Canada, Chinese Taipei and Switzerland. Other members of the IGDRP may decide to take part in the pilot programme at a later stage. These include Brazil, China, Japan, Korea, Mexico, New Zealand, Russia, Singapore and South Africa. The European Directorate for the Quality of Medicines & Healthcare (EDQM) and the World Health Organization (WHO) participate to IGDRP as observers.

In the initial phase, 10 applications for generic medicines will be selected for participation in the pilot; further products might be considered after evaluation of first results.

Companies are invited to express their interest in participating in the pilot programme. Further information has been published today on the EMA website.

About IGDRP

The IGDRP was launched in April 2012 to strengthen collaboration and convergence between regulatory agencies worldwide and mitigate challenges of global generic development and approval programs.

This information-sharing initiative is one of the work packages of the IGDRP. The EU is also involved in other areas of cooperation which aim to explore work sharing possibilities in the area of active substance master file, inspection of sites conducting bioequivalence and bio-analytical studies and information sharing on pharmaceutical quality issues.

Regulatory information - Paediatric guidance revised to reflect changes to European Commission guideline

January 21, 2015 – The European Medicines Agency has published revised documentation related to paediatric investigation plans (PIPs) to reflect recent changes to the European Commission's guideline on PIPs. The guidance documents relate to the procedures for submission of PIP/waiver applications, re-examination and compliance check.

The revised documents take into account the changes and simplifications that have been introduced by the European Commission in the recently published guideline on the format and content of applications for agreement or modification of a paediatric investigation plan and requests for waivers or deferrals and concerning the operation of the compliance check and on criteria for assessing significant studies.

New international standard to improve safety of medicines

January 21, 2015 – The European Medicines Agency (EMA) has published a guide to support the implementation of a new international standard for the safety monitoring of medicines in the European Union (EU). The so-called ISO ICSR standard improves the reporting of suspected side effects of medicines in Individual Case Safety Reports (ICSRs). The use of the new international standard will take effect on 1 July 2016.

ISO ICSR aims to establish the same format for the reports on individual cases of suspected side effects in patients due to a medicine across the world. It also is expected to include better information on medicines that might be associated with an adverse drug reaction and on the therapeutic uses of those medicines. In addition, the standard also strengthens personal data protection in the records of ICSRs collected by pharmaceutical companies and regulatory authorities.

This will improve the quality of data collected, and increase the ability to search and analyse them. Regulatory authorities will be able to detect

and address safety issues with medicines more quickly, and therefore better protect patients.

The new guide developed jointly by EMA and the Heads of Medicines Agencies (HMA) will be of interest to pharmaceutical companies and medicines regulatory authorities in EU Member States and will support them to prepare for the use of the standard. The guide specifically defines the electronic transmission process of ICSRs, the format and content of the ICSR, the business rules for report validation as well as classification and data quality principles. It will also assist software providers and IT developers as pharmacovigilance databases are being developed.

The finalisation of the guide is a major step in EMA's preparation for an enhanced EudraVigilance system, the European database of all suspected adverse reactions reported with medicines authorised in the European Economic Area (EEA), as required by the EU pharmacovigilance legislation.

Notes:

- This guide is based on the ICH E2B (R3) guideline and the corresponding ISO ICSR standard as referred to in Article 26 of the Commission Implementing Regulation (EU) No. 520/2012. The guide will apply with the use of the ISO ICSR standard as of 1 July 2016.
- The next step for the development of the EudraVigilance system based on the new ISO ICSR standard and related EU guide are further outlined in the News bulletin for pharmacovigilance programme update - Issue 2.

Public consultation on application of transparency rules of EU Clinical Trial Regulation

January 21, 2015 – The public consultation on how the transparency rules of the European Clinical Trial Regulation will be applied in the new clinical trial database is launched by the European Medicines Agency (EMA) today. Stakeholders are invited to send their comments before 18 February 2015.

The European Clinical Trial Regulation aims to create an environment that is favourable to conducting clinical trials in the European Union (EU), with the highest standards of safety for participants. The Regulation ensures that the rules for conducting clinical trials are consistent throughout the EU. It also transforms the level of information publicly available for each clinical trial carried out in the

EU by requiring transparency on the authorisation, conduct, and results of the trial. The Regulation will apply to clinical trials that are registered once the Regulation is in operation (not before 28 May 2016).

The key instrument to deal with clinical trials in a transparent way is the new clinical trial portal and database. It will be used for submission and maintenance of clinical trial applications and authorisations within the EU. It will serve as the source of public information on the clinical trial applications assessed, and all clinical trials conducted in the EU. According to the Regulation, EMA is responsible for the development and maintenance of the portal and database, while the authorisation and oversight of clinical trials will remain with the EU Member States.

The public will be able to access extensive details of each trial including the major characteristics of the trial, the start and end of recruitment, end date of the trial and substantial modifications to the trial. These details will be made public as they occur starting with the decision on the trial. A summary of results and lay summary will be published 12 months after the end of the trial. For those trials included in a marketing authorisation application in the EU, clinical study reports will also be published 30 days after the procedure for granting the marketing authorisation has been completed or the application has been withdrawn.

The Regulation requires that the clinical trial database shall be publicly available unless one or more of the following exceptions apply:

- protection of personal data;
- protection of commercially confidential information, in particular taking into account the marketing authorisation status of the medicine, unless there is an overriding public interest;
- protection of confidential communication between Member States in the preparation of their assessment;
- protection of the supervision of clinical trials by Member States.

The document under consultation sets out proposals for the application of the transparency rules of the European Clinical Trial Regulation for stakeholders to review and comment on. The proposals aim to balance the right of patients and the public to access extensive and timely information on clinical trials, and developers' and researchers' need to benefit from investments. This will support the EU as a suitable location for

innovative, cutting-edge research and development of medicines.

How is this public consultation linked to EMA's policy on the publication of clinical data?

This public consultation refers only to the practical application of transparency rules for the clinical trial portal and database that is established within the European Clinical Trial Regulation. The European Clinical Trial Regulation is distinct from EMA's policy on the publication of clinical data, which has already come into force (January 2015). There are several important differences between the provisions of the European Clinical Trial Regulation and EMA's policy. Under EMA's policy, the Agency proactively publishes the clinical study reports submitted as part of marketing-authorisation applications for human medicines. This means that the policy applies to clinical reports of studies that are beyond the scope of the European Clinical Trial Regulation as it, for example, also includes clinical trials that are conducted outside the EU but submitted to EMA for marketing authorisation in Europe.

Note:

- The Clinical Trial Regulation EU No. 536/2014 requires that the Agency develops and maintains the clinical trial portal and database to act as a single portal for submission and maintenance of clinical trial applications and authorisations within the EU, to support the coordinated assessment and exchange of information between Member States on the processes of authorisation and supervision of clinical trials, and to serve as the source of public information on clinical trial applications assessed, and clinical trials conducted in the EU, from the time of decision on each trial up to the inclusion of the results of those trials.

Regulatory information - Transitioning to mandatory use of electronic application forms

February 5, 2015 – The European Medicines Agency (EMA) is announcing the transition to the mandatory use of electronic application forms for initial marketing authorisations, variations and renewals for human and veterinary medicines.

As of 1 July 2015 it will be mandatory for companies submitting applications for centralised procedures to use the electronic application form.

From 1 January 2016 the application forms in Word format published by the European

Commission will no longer be available and only the latest version of the electronic application form will be used for all EU procedures, including national procedures.

The electronic application forms offer a convenient, online version of the currently used paper versions, which are published and maintained on the European Commission's EudraLex website. These electronic forms are designed to reflect and capture the same content as the paper-based application forms. EMA first made these forms available to companies in July 2012, following a successful pilot phase. Since the initial release, the forms have been significantly improved and a further release based on change requests will be made available this Spring.

The mandatory use of these forms is expected to reduce the administrative burden for both the regulatory authorities and the industry, while at the same time improving data quality and consistency during data entry.

Further information on the new requirements can be found on the eSubmission website where an information leaflet on the mandatory use of the forms has been published.

Regulatory information - EMA introduces weekly start dates for the assessment of type II variations from March 2015

February 20, 2015 – Starting March 2015, the European Medicines Agency introduced weekly start dates to facilitate the assessment of certain type II and worksharing variation applications for medicines for human use. These changes are one of the outcomes of the Agency's structural reorganisation which was initiated in September 2013 to improve the efficiency and effectiveness of its operations. They are expected to offer more flexibility to applicants and streamline the assessment of applications by allowing certain variations to conclude outside of the plenary meeting of the Committee for Medicinal Products for Human Use (CHMP).

The new process will be applicable to most type II including grouped and worksharing variations. For these variations, companies will be able to send their applications to the Agency according to the weekly submission slots and the assessment will start on a weekly basis. The CHMP will adopt its scientific opinion at different time points either outside the CHMP meeting or at the meeting, depending on the start date of the review.

Assessment of responses to requests for supplementary information will also follow the weekly-start timetables.

The validation period between submission and procedure start as well as the assessment timelines as provided for in the legislation will remain unchanged. Linguistic review of product information changes for these variations will continue to follow the monthly review cycle starting five days after the CHMP monthly plenary meeting.

The new process will not apply to variations for which amendment of the marketing authorisation

by the European Commission is required within two months from CHMP opinion. Similarly, it will not apply to variations involving the Pharmacovigilance and Risk Assessment Committee (PRAC) or the Committee for Advanced Therapies (CAT) either. These variations will continue to follow the existing monthly-start timetables.

Further details can be found in the post-authorisation guidance on type II variations which has been revised to reflect these changes. The new weekly-start timetables have also been published on the Agency's website.

Profile

An interview with Ingrid Edsman on why attending EMWA conferences is so rewarding!

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Ingrid Edsman, with 17 years of increasingly senior clinical research positions in the Pharmaceutical Industry, is an expert in the preparation of regulatory and clinical documents. She obtained a Medical Degree at the Karolinska Institute in Stockholm in 1986, worked five years as a medical doctor and joined the pharmaceutical industry in 1991. Work in big pharma included clinical safety, project management, and clinical data analysis and system development from the user perspective. All positions involved extensive writing, and the combination of science and writing suited her well, so in 2006 she became medical writer, and in 2008 she took the leap into self-employment.

Ingrid has been a member of EMWA since 2007 and has so far attended all conferences but one. We therefore turned to her to find out what keeps Ingrid coming to conferences and what EMWA has offered her as a member of a professional association.

Medical Writing (MEW): How did you learn about EMWA and what persuaded you to join our association at the very beginning of your career?

IE: When I became medical writer in 2006, I attended a medical writing course in Prague where the lecturers were the EMWA veterans Stephen de Looze, Barry Drees and Alistair Reeves. They encouraged the participants to join EMWA, and when I learned about the educational programme and networking opportunities, it was an easy decision to join.

MEW: How has EMWA influenced your professional pathway as a freelancer? How different do you imagine your career would be, if you worked as an in-house employee in a big pharma company?

IE: Through EMWA I have realised that medical writing encompasses many different kinds of writing and documents, which has helped me to expand the medical writing services I offer as a freelancer. My focus is still on regulatory writing, but I now take on other types of documents, for example, conference reports, manuscripts, white papers and advisory board reports.

The art of freelancing can be tricky, and the possibility to discuss business matters with other freelancers and get advice at the biannual Freelance Business Forum is definitely helpful. The Freelance

Resource Centre on the EMWA website also provides lots of useful information on all aspects of freelancing, and the Freelance Directory is an important marketing tool.

As an employed medical writer, I would most likely have worked on a smaller range of documents, and I would probably not have had the same possibilities to attend EMWA conferences due to financial constraints on training budgets in many companies. What I particularly like about being self-employed is that you have the power to make your own decisions, for example, about educational activities, which is something I prioritise in my company.

MEW: You've been a member of EMWA for eight years. You have attended so many different workshops and obtained several certificates (foundation and advanced). You have so much experience and a great client portfolio. So what keeps you returning to EMWA conferences?

IE: Learning is lifelong, and EMWA has training tailored to the needs of medical writers. I still learn a lot from workshops on topics that are new and interesting to me, but I welcome the new EMWA initiatives with one-day symposia and expert seminar series. The previous symposia have provided some interesting perspectives on writing for health economics and market access and on transparency in clinical trial data. The expert seminars, aimed at more experienced medical writers, have an exciting programme for the inaugural event in Dublin 2015, and I will definitely attend several of these seminars. In the future, I believe that a balanced mix of workshops, symposia and expert seminars will keep me coming back to the EMWA conferences.

Another major reason for returning is, of course, meeting and networking with colleagues. It is good to catch up with the many friends I have made over the years and to make new ones. Networking at conferences is primarily social, but has resulted in professional engagements on some occasions. Even though my conference schedule usually is filled with workshops, seminars and social events – making the conferences quite hectic – I find the conferences to be relaxing and pleasant breaks from everyday work. Last, but not least, I enjoy going to all the beautiful places where the EMWA conferences are held. As a Sweden-based

advocate of EMWA, may I suggest that a future conference city location would be Stockholm, also called Venice of the North.

MEW: What do the EMWA workshops offer to you as an experienced medical writer?

IE: Knowledge is perishable and needs constant ‘refilling’. It is important to keep up to date with what is happening in the field of medical writing – both the medical/science part and the writing part – so training is essential. When you are employed, you are updated in-house through company training, discussions with colleagues, etc. As a freelancer working alone at the home office, you need to go out and find your own training. There are professional organisations in Sweden offering courses in life sciences, but I think EMWA is the best option with the ambitious Professional Development Programme.

Because EMWA continually adds workshops on hot topics, I always find something that interests me. If I am familiar with the subject, it is valuable

to gauge my experience with others. If the subject is unfamiliar to me, it is stimulating to learn new things and skills, and afterwards I feel more confident about taking on assignments in that particular area. The learning experience is even better if I put in the extra time for the pre- and post-workshop assignments, which I usually do. Feedback on the assignment from the workshop leader, preferably personalised, is also a vital component in the learning process; most, but not all, workshop leaders provide that. The certificates that follow on completed assignments are a bonus and look good on my CV.

Ingrid has given us a broad view of what EMWA means to her, and it really seems that this professional association can make a difference both in your professional and in your private life. She has indeed met many of her professional contacts and made a bunch of friends at the EMWA conferences. I cannot imagine a better reason to keep coming back!

Ingrid Edsman can be contacted at ingrid.edsman@edmedica.se; www.edmedica.se

Plagiarism: No longer grounds for retraction or correction?

The marvelous if depressing Retraction Watch blog¹ welcomed the new year by reporting contentious decisions of two journal editors not to retract or correct published articles containing substantial plagiarism.²

The case relates to Marios Sophocleous, formerly of Kansas University, and four articles he published in *Hydrogeology Journal* and *Journal of Hydrology* (two per journal). Kansas University found convincing evidence of plagiarism in these articles and contacted the journals to request their retraction. Nope, said the journals.

To explain their decisions, the editors of both journals published editorial notes.^{3,4} The *Hydrogeology Journal* note in particular makes remarkable reading. In it, Executive Editor Clifford Voss:

- Plays down the copying of substantial amounts of text without using quotation marks as ‘strictly’ plagiarism (while acknowledging that it is unacceptable)
- Explains that he rejected the idea of correcting the articles by adding the missing quotation marks because no-one would believe that his peer reviewers had accepted papers that were ‘composed of largely quoted material’³

- Argues that the articles shouldn’t be retracted as they are highly cited and thus valuable to researchers in his field

The message seems to be this: There’s no need to retract or correct papers that shouldn’t ever have made it through peer review because of extensive plagiarism if they’ve contributed to the visibility of your journal. Let’s hope other journals don’t adopt this position.

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Risk management

‘A ship is safe in a harbor – but this is not what ships are made for’.

(William G.T. Shedd, American theologian, 1820–1894)

Risky scenarios are something many people try to avoid. But you will find yourself in situations when you have to face risks, especially in business. To better control these kinds of scenarios, large organisations began to implement a new kind of operation: risk management.

To figure out what this term actually means, a first step might be to check Wikipedia:

http://en.wikipedia.org/wiki/Risk_management.

Here you will find useful information and a definition based on an article by Douglas Hubbard (2009): ‘Risk management is the identification, assessment, and prioritization of risks (defined in ISO 31000 as the effect of uncertainty on objectives) followed by coordinated and economical application of resources to minimize, monitor, and control the probability and/or impact of unfortunate events or to maximize the realization of opportunities.’

Searching the internet is not only about reading texts. A presentation with animated slides – quality-gurus’ 18-minute ‘Introduction to Risk Management’ video – can be viewed at

www.youtube.com/watch?v=Cp_XEhexcDw.

The homepage of the Professional Risk Managers’ International Association (PRMIA) can be found at

<http://www.prmia.org/>.

Founded in 2002, PRMIA is a non-profit organisation focused on ‘the promotion of sound risk management standards and practices globally’ and ‘the integration of practice and theory’. Its website offers different kinds of news and information, including blogs written by the organisation’s members.

The Accenture 2013 Global Risk Management Study canvassed the views of executives at over 400 companies covering eight industry groups and three major geographic regions. Information on the study can be found on the company’s website:

<http://www.accenture.com/Microsites/risk-management-research/2013/Pages/home.aspx>.

In a short video, Steve Culp, Accenture’s Global Managing Director, tells some facts about the study. The full report can be downloaded as a PDF free of charge.

What risk management means in medical environments is defined at

<http://medical-dictionary.thefreedictionary.com/risk+management>

as ‘a function of administration of a hospital or other health facility directed toward identification, evaluation, and correction of potential risks that could lead to injury to patients, staff members, or visitors and result in property loss or damage’.

Focussing on risk management in the pharmaceutical and life science industry, you will find a useful presentation at

[http://www.economistinsights.com/sites/default/files/Risk management in the pharmaceuticals and life sciences industry.pdf](http://www.economistinsights.com/sites/default/files/Risk%20management%20in%20the%20pharmaceuticals%20and%20life%20sciences%20industry.pdf).

A definition and overview of a risk management plan are available as a PDF from Pfizer’s company website:

http://www.pfizer.com/files/health/medicine_safety/2-2_What_is_a_Risk_Management_Plan.pdf.

On November 11, 2011, Ann O’Mahony, a quality assurance specialist at Pfizer, held a presentation titled ‘Quality Risk Management – The Pharmaceutical Experience’. Her slides can be found at

<http://www.pda.org/docs/default-source/website-document-library/chapters/presentations/ireland/quality-risk-management---the-pharmaceutical-experience.pdf?sforsn=6>.

Finally, the U.S. Food and Drug Administration (FDA) provides Quality Risk Management guidance

for industry, which was developed by the Expert Working Group (Quality) of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The PDF of the guidance (ICH Q9) is available at

<http://www.fda.gov/downloads/Drugs/.../Guidances/ucm073511.pdf>.

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Inflating journal impact factors

Some journals are shameless in their efforts to boost their impact factors. Below is part of a decision letter relating to a manuscript I worked on 4 years ago:

... we would like to emphasize that we attach great importance to cross referencing very recent material on the same topic in [our journal]. Therefore, it would be highly appreciated if you would check the last 2 years of [our journal] [...] and add all material relevant to your article to the reference list.

The reference to '2 years' is pertinent, because a journal's impact factor for a given year is calculated based on the number of citations for articles published in the two preceding years.

Anecdotal evidence suggests that this kind of abuse is not uncommon. Indeed, it partly explains a recent amendment to the References section of the ICMJE *Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals*¹ (see the *Manuscript Writing* section of this issue of *Medical Writing*). The journal behind the above request has since signed up to these recommendations. We can only hope that it has modified its editorial policy accordingly.

Fishing for citations through private correspondence is seemingly too subtle for some. The Thai

journal *Thammasat International Journal of Science and Technology* (TIJSAT) went a step further by including the following in its Instruction for Author (sic):

'Please kindly give some citations related to your written article from any articles published in TIJSAT in order that the TIJSAT's impact factor can be raised to a higher level.'

Following derision and scorn on the Retraction Watch blog,² TIJSAT removed this instruction from its website. Unsurprisingly, TIJSAT is not included in the ICMJE's list of journals that follow the ICMJE recommendations.³

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Stephen Gilliver

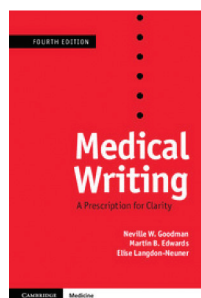
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Medical Writing: A Prescription for Clarity (fourth edition)

By Neville W. Goodman, Martin B. Edwards, Elise Langdon-Neuner (Editor), and Andy Black (Illustrator);

Cambridge University Press, 2014.

ISBN-13: 978-1-10762815-1.

37.50 GBP. 380 pages.

Do you know the difference between compliment and complement? Do you know your breeches from your breaches? Do you know why the word 'Ghoti' should be pronounced 'fish'? Answers to these questions and many other interesting facts regarding the English language can be found in the fourth edition of *Medical Writing: A Prescription for Clarity* by Neville Goodman, Martin Edwards, and Elise Langdon-Neuner. This book caters for writers at all stages of their careers and from different fields of medical writing; whether you are a physician, a professional medical writer, or a student, this book provides an array of practical information to help improve the clarity of your writing. Those writers for whom English is an additional language will find this book particularly useful as a guide to ensuring effective and coherent writing.

The book is divided into three main parts. Part 1 (chapters 1–3) introduces the reader to key problems which have arisen through decades of unchanged medical writing practice, in particular the level of unnecessary complexity, redundant jargon, and phrasing seen in medical journals, and the problems facing writers for whom English is not their first language.

Part 2 (chapters 4–22) attempts to address these problems by highlighting some of the common errors made with spelling and offers useful tips on choosing the appropriate wording. Furthermore, this section questions the choice of vocabulary used in medical literature and offers simpler and clearer alternatives to avoid the key messages being lost in the 'polysyllabic fog' of the writing. In chapter 4, the authors describe how the advent

of computers and the internet has shaped the way we write about, reference, and research topics of interest. Searching databases such as Google Scholar and PubMed has shown an increased prevalence of unnecessarily complex words such as *ameliorate*, *novel*, *myriad*, and *elucidate*, and our dependence on such aids as the Microsoft spell-checker can result in common spelling mistakes if we do not truly consider what we are writing.

The most extensive chapter of Part 2 is chapter 7, which provides simpler, clearer alternatives to over 100 words that are commonly used in medical writing, but that are either often incorrectly used or unnecessarily complex. This chapter is complemented nicely by chapters 8 to 10, which focus on superfluous and imprecise words and phrases that have become ingrained in everyday medical writing.

The authors often refer to the writing of James Watson and Francis Crick, who are complimented on the short and simple statements in their seminal work on the structure of DNA, which get straight to point of what they are proposing. To some extent, I agree with the authors' viewpoint: clarity is paramount in scientific reporting. But clarity is not always achieved by using simple words. A writer must gauge his or her audience when writing a scientific document. Although certain types of scientific communication, such as medical journalism, require the utmost simplicity to communicate a difficult subject matter to a lay audience, intricate medical documents such as clinical study reports will inevitably require a level of complex terminology, especially when describing adverse events. A writer cannot simply say this subject *had the flu*; the writer must document a detailed description of the event (including specific symptoms, diagnostic tests, and possible causality) that often necessitates the use of a complex medical vocabulary.

Chapters 11 to 20 in Part 2 explore further aspects of the English language, including word order, punctuation, prepositions, tenses, and the use of clichés. These chapters cater more for writers with English as an alternative language. However, native English speakers would also benefit, as

these aspects are often overlooked in everyday writing. I disagree, somewhat, with the authors' views on circumlocution (chapter 16), the process by which a writer deliberately uses more words than are necessary to get their point across. I agree that sentences should be succinct; however, removal of too many words, as shown in the examples in this chapter, could perhaps lead to misinterpretation. In chapter 21 the authors apply their philosophy of simplicity and clarity to graphs as well as text and give some fine examples to follow.

In Part 3 of this book (chapter 23), the authors conclude with a selection of 43 exercises to test the reader's knowledge of what he or she has learnt throughout the course of Parts 1 and 2. The exercises consist of excerpts from medical books and journals which the authors have rewritten to reduce the use of redundant phrases. The authors also provide uncorrected versions of the 43 exercises which allow the reader to attempt their own corrections.

Valuable changes to this fourth edition when compared to previous versions include a shorter introduction, an updated suggested reading list, and an updated list of 'abused' words. In addition, exercises from previous editions are now incorporated into the main body of the text and PubMed is used to highlight key wording and phrases in medical literature that need addressing to ensure that the correct message is delivered and to avoid confusing readers.

If English is not your first language then this book is a useful introduction to some of the pitfalls of medical English. If English is your native tongue, then this book will not dramatically change the habits of a lifetime. But I would imagine that if 10 medical writers read it they would each take from it a different piece of information that would improve their writing in some small way, and that can only be a positive thing. My main criticism of this book is that the authors could apply their own techniques more thoroughly in certain chapters, in order to maintain the reader's engagement; however, they should be credited for representing their points with amusing illustrations, which enhance the text in an entertaining way. This is certainly not a book to read cover to cover in one sitting, but instead is to be used as a resource to refer back to every so often. Furthermore, this book is unlikely to provoke a fundamental change in the way that medical documents are written, but it does effectively highlight key issues and solutions that all writers should be conscious of. I would recommend this book as a necessary addition to any medical writer's bookshelf.

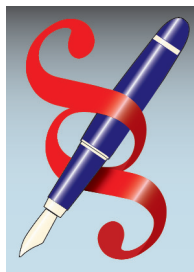
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Regulatory Writing

Review process in regulatory writing

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Recently, Phil Leventhal posed the question 'What does it take to go from being a good medical writer to an excellent one?' on EMWA's LinkedIn Discussion Group. My impression is that the responses were written largely with medical communications (that is, texts for publication) in

mind rather than regulatory writing per se. Posters made plenty of useful suggestions such as a focus on the target audience and forward planning. Given the involved debate about ghost writing, I was perhaps a little surprised though that there was no mention of ensuring that the thoughts and opinions of (all) named authors are included. According to my understanding, medical writers are channels through which the intellectual authors can express themselves appropriately. This presumably involves interacting and negotiating with authors during review rounds to ensure that the text is representative of the desires of the headline authors.

In the case of regulatory writers, management of review cycles is an essential component of being an excellent regulatory writer. Most regulatory documents necessarily follow a process of 'design by committee'. Thus, many different departments within a pharmaceutical company, and different levels of management within a department, might have a stake in a document, and often, reviewers may have different goals and different priorities. With input from so many sources, review cycles can become chaotic with the result that the final document lacks coherence and vision. A skilful and experienced medical writer should aim to navigate the sometimes bumpy review rounds and come out with a document that is both readable and well-structured while also representing the positions and opinions of the different contributors.

While it is easy to recognize the importance of having effective review rounds, in practice this is harder to achieve. There is no right way and no magic formula. What might work for one writer might not work for another (we are all different). It may even be that what might have been a

successful approach for a writer in a past project might not work for a current one because of differences in the nature of the project and also differences in team. There are however, certain tips and suggestions that can perhaps be applied universally.

Fostering goodwill in the team

It may be an obvious point, but it is important to foster goodwill within a team. There are many different details that can help you win over the team and build a rapport. For example, in cases where the responsibility for a relatively trivial task is not clear, you can show yourself willing (German has the pithy expression '*nicht meine aufgabe*' used by those who refuse to budge a millimeter from their job remit). Over-willingness though has its own dangers, as you may find you begin to get lumbered with tasks that should be nothing to do with you (and the time spent may not be billable if you are a freelancer or your line manager may consider that you are wasting your time if you are an employee). The gains in terms of goodwill, however, can be great (and difficult to quantify).

Kick-off meetings

Related to the above point about building rapport, many writers will advocate the usefulness of face-to-face meetings, where you can get everyone in the same room and talking to one another. In a multinational company this will often not be possible, and a video conference or conference call (with some sort of screen sharing technology such as Webex) can be the next best thing. Such meetings are of greatest importance at the beginning of a project to decide on who is responsible for which content and agree on timelines and other project details. These kick-off meetings also generally set the tone and enable you to get a feel for the team members and the team dynamic, who is going to be cooperative, and who is going to be problematic. Leading such meetings is a bit of a black art, and different writers may have different preferred approaches. I do believe, however, that it is important to prepare conscientiously. Make sure you have read the background information and are

familiar with the project. There is nothing more annoying for a busy person to attend a meeting and think that they are wasting their time.

Adjudication meetings for review comments

As the project progresses, review comments will need to be adjudicated and a consensus reached. Sometimes (but by no means always) a meeting or a conference call is an efficient way of doing this, especially if the meeting enters a kind of brainstorming dynamic. On other occasions, prolonged arguments about minor points will lead to an unproductive meeting. To avoid such situations, a well-prepared hierarchical agenda can help ensure that points are addressed in descending order of importance.

When two headstrong participants do have differing opinions, reaching a successful outcome often involves compromise and negotiation. Hopefully, we will have already formed an idea of who is going to be stubborn, who is going to be reasonable, and so on. To move things forward, you often have to make a concession to some of the participants. Finding an appropriate concession may require certain creativity and perhaps a certain Machiavellian streak.

If some important decisions or agreements have been made, then it is often helpful to send out a summary of these to the participants soon after the meeting while it is fresh in their minds (these will usually not have to be formal minutes). This will also ensure that your understanding of what was said is aligned with that of the others as interpretations of the same meeting can vary greatly. It will also provide a record of these decisions or agreements should a blame game begin later down the line after problems emerge in a project (not necessarily the fault of anyone, circumstances may

simply have conspired, but the urge to find scapegoat can be strong).

Further miscellaneous thoughts about review cycles

For the comments themselves, the higher up the management chain you get, you should remember that reviewers are less and less likely to be fully familiar with the project (and also probably spend less time on the actual review). Patience may therefore be required if the reviewers simply don't seem to get it. When this happens, you should also ask yourself whether this lack of comprehension is an indication that the explanation could be improved. Finally, on the Linked-In thread I mentioned in the opening paragraph, one contributor mentioned the need for a thick skin. This is an important point, I think. You should try not to take review comments personally (though reviewers can be rather tactless). First drafts in particular are often just a question of getting something down on paper to get the authors thinking about how to approach the project. This initial act of creation is often the hardest and not always well appreciated.

Conclusion

Although we are often labelled medical writers, or regulatory writers, the writing itself is only one aspect of what we do (albeit an important one). Good writers also need to be facilitators, deal brokers, and negotiators. Even though the actual texts we produce are not always interesting and engaging (though they can be), these additional facets contribute to making our job interesting.

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Lingua Franca and Beyond

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Welcome to Lingua Franca and Beyond



It is my real pleasure to welcome you to the second issue of *Lingua Franca and Beyond*, a regular feature of *Medical Writing* for non-native English speaking medical writers.

As soon as I'd written those words, I realised that this section should not be exclusively for non-native English-speaking medical writers; but should be valuable for all medical writers. So, we would like to hear the voice of native English-speaking medical writers, as well. In my welcome message in the previous *Medical Writing* issue, I wrote that although I believe that being a non-native English-speaking medical writer has certain advantages, 'it does not mean, that we can manage to make it all happen on our own'. We need help from our native English-speaking colleagues; we need to work in teams. The next issue of *Medical Writing* is about Business Models. What better theme to

discuss the idea of collaborating, team working, and sharing complementary skills with both groups of medical writers! In the next issue, we will outline some business models for working together across different native languages.

This issue is more about '*Beyond*' as Laura Collada Ali from Spain, but based in the Italian Alps shares her story about going *beyond* in her short journey from a non-EMWA-member to a very active EMWA Executive Committee (EC) Officer. Laura served as Public Relations Officer for two years where she implemented initiatives such as the EMWA webinars and the Conference App. As her term finished last May, I'd like to thank Laura for her contribution, and invite you to read how she sees the role of non-native English-speaking medical writers at the EC – the role that extends far *Beyond* writing in English.

Acknowledgements

I thank Amy Whereat for helping to edit this text.

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A non-native English speaker in the Executive Committee!

The European Medical Writers Association (EMWA) is, a truly 'European' organisation that includes medical writers, editors and translators who speak twenty-four official languages (Table 1). The European Union is in favour of linguistic diversity and even has a special role for securing linguistic diversity, namely – the European Commissioner for Multilingualism.

English, the *lingua franca* at EMWA, unites professionals from many different linguistic cultures, who represent a diverse heritage. Despite having a common language, some members still feel uneasy about getting involved in the organisation precisely for their 'non native English' background.

To get the most from a professional organisation, it is important to get involved, either as a volunteer or through an elected role on the Executive

Committee (EC). Getting involved means understanding the importance of professional networking, following current affairs in the field, continuing education, defending and promoting medical communications professions, improving working conditions, and other important professional issues. It is also an investment in your chosen career area.²

Table 1: Languages of the European Union¹

Languages of the European Union	
Official languages	Bulgarian, Croatian, Czech, Danish, Dutch, English, Estonian, Finnish, French, German, Greek, Hungarian, Irish, Italian, Latvian, Lithuanian, Maltese, Polish, Portuguese, Romanian, Slovak Slovenian, Spanish and Swedish
Semi-official languages	Basque, Catalan, Galician, Scottish Gaelic and Welsh

Source: Wikipedia.

Although I think all this might seem quite obvious to all of us, there is nevertheless a certain tendency, particularly among members who have recently joined EMWA, to consider oneself an inappropriate candidate either as: (a) a young member – having been part of EMWA for less than a year; or (b) a non-English native speaker, as our *lingua franca* is English.

Now, here is how I became involved in the EMWA EC!

I first attended an EMWA fall conference in 2011, in London. Before then, I had not realised that apart from translating, writing texts for my clients had an official name: ‘medical writing’. Indeed, ‘medical writers’ are not well recognised in the Mediterranean area so joining a professional association and promoting it in the area became even more important to me! After that, during a dinner table conversation at the Cyprus conference, I was rather critical about some aspects of the organisation and, the comment I got back was: ‘It’s great you are so judgmental. We need people like you. Get involved!’ As a result, I immediately joined the Social Media Team and at the end of that same year I sent a candidate statement for the Public Relations Officer position and got elected in May 2013.

Well, having been part of the EC for the last two years, I have come to three main conclusions. Firstly, recently joined members often have a fresh, external view and can critically spot areas where input is needed – in my case, this has always been very much appreciated. Secondly, enthusiasm and

proactivity are more useful than experience, when proposing new initiatives. And thirdly, language really is not a barrier; we all speak – up to a certain level – the language of science, even if we may use a different one at a professional level. I do not work in English, but from English. That said, EMWA business is conducted in English and native speakers within the EC are always very helpful reviewing text. After all, we are medical writers, we love writing, reviewing and helping colleagues!

During the last three EC mandates, we have had two non-English native speakers out of the 9 members that form the committee. Thus, as you can see, language is not a barrier to get involved in the association.

If you are one of those fortunate professionals who is passionate about what you do, committing to your professional association will be most rewarding. Do not think twice about it and get involved!

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Gained in Translation

Editorial



We often write articles to satisfy two states of mind: pleasure and curiosity. In my case, this means the curiosity to delve into some of the intricacies of translation on the one hand, and, on the other, the desire to work together with colleagues with whom I share a passion for the transfer of knowl-

edge through culture and time. Translation is involved in every level of knowledge production and distribution in medicine. It presents a wealth of opportunities to combine the insights of literary, historical, and cultural studies of science. Scott L Montgomery says in his 'Science in Translation'¹ that 'As the second oldest profession on the streets of authorship, it is generally conceived in fairly obvious terms, as a matter of rendering the words of one language into those of another, hopefully with little or no spillage of meaning'. Yet, this is more a description than a definition and it does not deal with the enormous complexity of the inevitable sharing of knowledge in this global and multi-lingual world we now live in.

The chance to run this section is a real opportunity and I am grateful to Gabrielle Berghammer who produced it for several years. This means that I am not starting from scratch – although it will not be easy to keep up with the quality of the articles

Gaby published; my thanks are also due to Medical Writing's Editor-in-Chief, Phil Leventhal, who kindly accepted my proposal to follow in Gaby's footsteps, and whose patience is a model of the editorial art.

My aim is to make this section a medium for open discussion among translators and writers interested in this field, as well as those using translation services, but I also envisage a written agora where we can exchange different and, maybe, amusing experiences. If you have anything you would like to contribute, please contact me at laura.collada@ontranslation.it. You are warmly invited to share your knowledge and thoughts.

Our first article deals with a frequent dilemma we need to solve when addressing medical translations: whether to retain euphemisms in the original text or not. The issue is not that simple, because euphemisms are highly influenced by culture and, yes, we transfer culture through language and not only words. Enjoy the article!

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'Safe', 'safety', and 'potential risk': Examples of euphemisms used by the pharma industry

Euphemisms and political correctness

What is a 'euphemism'? In this paper we have specifically avoided expressions such as 'politically correct' and 'political correctness' as these are, in our opinion too vague to be useful: for example, what does politics have to do with the fact that some writers may now use – or recommend the use of – the term 'differently-abled-people' instead of 'disabled', 'disabled people' or 'the handicapped'? These one-word or compound terms, labelled as politically correct, are

actually euphemisms. In all scientific or specific jargon and languages there are words that – by implicit or explicit agreement among speakers – are not spoken or written. We refer to these as taboo words, and any spokesperson – not always voluntarily – substitutes them with other words: words that form euphemisms.

The Merriam-Webster Dictionary¹ defines 'euphemism' as follows:

1. the substitution of a mild or indirect expression for one thought to be offensive or blunt.
2. the expression so substituted.

Collins Dictionary,² as follows:

1. an inoffensive word or phrase substituted for one considered offensive or hurtful, esp one concerned with religion, sex, death, or excreta. Examples of euphemisms are *sleep with* for *have sexual intercourse with*; *departed for dead*; *relieve oneself* for *urinate*
2. the use of such inoffensive words or phrases

And the *Diccionario de la lengua española*, issued by the Royal Spanish Academy (RAE) (22nd edition)³ defines ‘euphemism’ in its first meaning as:

1. Manifestación suave o decorosa de ideas cuya recta y franca expresión sería dura o malsonante. (Use of a gentle and polite expression of ideas instead of direct and rude wording).

What do we mean with the euphemisms ‘safe’ and ‘safety’?

Many medical writers and translators may have noticed the increasingly frequent use of the words ‘safe’ and ‘safety’, either as words on their own or as part of compounds (such as ‘safety evaluation’, ‘safe procedure’, ‘safety data’), particularly in texts written by pharma companies for investigators (clinical trial protocols, investigator’s brochure), health authorities (Summary of Product Characteristics) or subjects and patients (patient information sheet and leaflet).

Unfortunately, in Spanish texts – in both original language texts and translations from English – we read the words ‘seguro’ and ‘seguridad’ too often. This is mainly because there is a tendency to translate in a mechanical and uncritical way, or in its worst form, to write in what some call ‘Spanglish’ when dealing with medical content. It is obviously one of the bad influences of having a universal and vehicular language for science.

That said, what does ‘safe’ mean exactly in the context of drug development? Does it mean it does not have any adverse effects? (Note we use the wording ‘adverse effect’ as a superordinate of ‘side effect’ or ‘adverse reaction’). Does it mean that it has adverse effects, but that they are not frequent, or that they are also only minor? As is usual with euphemisms, ‘safe’ and ‘safety’ are vague, imprecise words that therefore act against clarity and precision, which should always be the principal objective of scientific language.

Using the word safe to describe any drug might therefore suggest that it does not have any side effects. Thus, not only have we used an imprecise word – this is also tantamount to deceptive

advertising if used when advertising the product to consumers.

There is no ‘zero’ risk in clinical medicine, which means that all diagnostic and therapeutic procedures entail risk. Thus, how can we speak of ‘safe drugs’? Does this mean that the drug does not cause any risk for patients?

The *Diccionario de la lengua española* (22nd edition)³ issued by the RAE states that the first meaning of ‘safe’ is (bolding from authors):

‘Libre y exento de **todo peligro**, daño o riesgo’.
(Free from danger, harm or risk).

The Merriam-Webster Dictionary¹ defines ‘safe’ in its first meaning as (bolding from authors):

‘Not able or likely to be **hurt or harmed** in any way: not in danger’.

And Collins Dictionary,² defines it as follows:

1. ‘affording security or protection from harm
2. (postpositive) free from danger
3. secure from risk; certain; sound’

In our opinion, the health authorities responsible for regulating the production, distribution and marketing of drugs, such as the Food and Drug Administration, the European Medicines Agency and the Spanish Agency of Medicines and Medical Devices should forbid the use of the terms ‘safe’ and ‘safety’ in texts targeting clinical trial subjects, investigators, patients, media, and their own staff, as, even in the best case scenario, their meaning is vague and inaccurate, and in the worst-case scenario, they constitute deceptive information.

‘Potential risk’: Euphemism by softening of meaning

Another euphemism very often used by the pharmaceutical industry is ‘potential risk’ – and its synonym, ‘potential threat or danger’. In this case, it is a subtle euphemism, and therefore, difficult to detect: we consider it to be a euphemism because the adjective ‘potential’ softens the clearly negative meaning of the noun ‘risk’.

We need to consider that the concept of ‘risk’ – and the same applies to ‘threat’ – already contains the idea of possibility or probability, and thus ‘potential’ is redundant. Something entails risk or not: it is not possible to have a ‘potential’ risk or a ‘non-potential’ risk. Furthermore, something may constitute a risk independent of the final outcome of the risk situation: someone driving while drunk may usually arrive at their destination safe and

sound, but this certainly does not mean that drinking and driving does not entail risk. In the same way, if sudden death has been associated with a drug in some patients, even if its incidence is very low, the risk of sudden death exists and may affect all patients who receive the drug. To talk about a potential risk of sudden death is therefore euphemistic. Additional use of the word 'potential' has the sole aim of reducing the absolute negative meaning of 'sudden death'. This lack of accuracy and clarity in the choice of words in a scientific text actually leads to deceptive information and deceptive advertising, which is even worse.

Other redundant and euphemistic wordings are 'This may be a risk', or 'It may be harmful' and, in general, all statements in which the verb 'may' is combined with words such as 'risk' or 'threat' – indeed, any statement where the 'blow' dealt by the main noun is softened by adjectival modification thus generating a euphemism. The most outstanding redundant and euphemistic statement in our type of text is 'There may be a potential risk of ...', which contains a triple redundancy. The most popular and completely uncritical Spanish translation '*Puede existir el riesgo potencial de (...)*' is just as bad, and often it even appears in Spanish original texts (not translated from English).

Far more frequent in Spanish is to use the adjective '*posible*' before the noun and not the anglicism '*potencial*' after the noun.⁴ Thus, '*posibles efectos secundarios*', '*posibles secuelas de la enfermedad*', '*posibles complicaciones del posoperatorio*' are idiomatic, that is natural, Spanish wordings, and '*efectos secundarios potenciales*', '*secuelas potenciales de la enfermedad*' and '*complicaciones potenciales del posoperatorio*' are not. Note that in the same way, the Spanish equivalent of the English wording 'may be potential' –also redundant or euphemistic– obviously translates as '*poder*': '*A dosis elevadas, el fármaco puede producir* (or *produce en algunos casos*) *náuseas, vómitos y diarrea*', instead of '*A dosis elevadas, el fármaco tiene el potencial de producir náuseas, vómitos*

Table 1: Spanish translation of some English complex forms

English expressions	Spanish translation ⁴
Safe drug	Medicamento inocuo; sin efectos adversos importantes
Food safety	Inocuidad de los alimentos
Preclinical safety	Toxicidad en animales; en voluntarios sanos
Safety event	Efecto secundario; reacción adversa
Safety profile	Toxicidad del medicamento; tolerabilidad del medicamento
Safety evaluation or assessment	Evaluación de la toxicidad; de la tolerabilidad
Safety studies	Estudios de toxicidad

Table 2: Legally imposed terminology

English term	Standard translation	Comment
Ethics Committee	Comité Ético	'Comité de Ética' is, no doubt, the correct wording in Spanish, as 'ético' is an adjective. In the same way, we say 'libro de ética' (ethics book), 'profesor de ética' (ethics teacher).
Informed consent	Consentimiento informado	A person can be 'informado', not a 'consent', that is a legal procedure and, as such, it cannot be informed or non-informed.
Adverse event	Acontecimiento adverso	'Acontecimiento' means 'fact', 'happening' or 'contest', but does not refer to a given actual or final outcome.

These terms are cited, for example in the 'REAL DECRETO 223/2004, de 6 de febrero, por el que se regulan los ensayos clínicos con medicamentos'.⁵

y diarrea', which is clearly a translation from English where due care has not been taken.

What should Spanish writers and translators do?

We believe that ideally professionals should follow the wording and translations recommended in the 'safe' and 'safety' definitions of the *Diccionario crítico de dudas inglés-español de medicina* (2nd edition)⁴ by Fernando A Navarro. However, many compounds including these words are so well established through usage that changing them means risking that readers may no longer know what is meant.

Examples of these complex forms are presented in Table 1.

On other occasions, health authorities force translation from English in one way or another by legally imposing words, and there is nothing the translator or writer can do about this.^{5,6} There are, however, still many complex terms where translators and writers may vary the standard wording, as they are not collocations or required by the health authorities. From the dictionary of Fernando A Navarro⁴ (words 'safe' and 'safety'):

Table 3: Spanish translation of the words 'safe' and 'safety'

English expressions	Spanish translation ⁴
Safe blood	Sangre que no está contaminada, ni infectada
Safe disposal	Evacuación higiénica
Safe food	Alimento salubre
Safe maternity	Maternidad sin riesgo
Safe sex	Relaciones sexuales sin riesgo; con protección
Safe water	Agua salubre
Drug safety monitoring	Farmacovigilancia

For 'potential risk', we advise that simple '*riesgo*' be used, without adding anything else, but if an author wants us to keep the redundancy in Spanish, we believe it is better to write '*posible riesgo*' than the calque '*riesgo potencial*'. We generally advise not to translate 'potential' when it modifies nouns such as 'risk' and 'threat'. 'Potentially' can be omitted in most cases, and, if it is translated, '*posiblemente*' and not '*potencialmente*' should be used. It is also advisable to omit the verb 'may' if it is unnecessary. For example, 'The drug may cause skin rash in about 34% of patients' should be translated as follows: '*El medicamento produce sarpullido en aproximadamente el 34 % de los pacientes*', rather than '*El medicamento puede producir sarpullido en aproximadamente el 34 % de los pacientes*'. Indeed, authors and translators should strive to avoid such imprecise terminology when writing English.

It is advisable to avoid the redundancy of '*Puede existir el riesgo potencial ...*' in Spanish which is a calque from the English 'There may be the potential risk ...'. And the unnatural and stiff '*Tiene el potencial de causar ...*' should also be avoided in Spanish. It is enough to say '*Puede causar*' or omit the English wording, as in the example: 'Selective serotonin reuptake inhibitors have the potential to cause erectile dysfunction', '*Los inhibidores selectivos de la recaptación de serotonina producen (or causan) disfunción eréctil*'.

Last, it is important that the writer and translator are aware that the best equivalent of the English adjective 'safe' is not always '*seguro*'. For example, in our opinion, '*Este producto es apto para diabéticos*' is a better translation of 'This product is safe for diabetic persons' than '*Este producto es seguro para diabéticos*', and '*El procedimiento conlleva cierto riesgo*' is a better translation of 'The procedure is not safe' than the calque '*El procedimiento no es*

seguro'. In general, the words 'safe' and 'safety' are used much less frequently in Spanish than in English – except in the case of texts translated from English – which means that we need to look for more accurate and idiomatic equivalents when translating or writing texts for the biomedical sciences.

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Manuscript Writing

1. Learn more about the author's background and the journal's requirements. 2. Write a clear, concise summary of the study's objectives and findings. 3. Discuss the implications of the results and how they relate to the existing literature. 4. Conclude with a strong recommendation for future research.

A guideline for manuscript flow. Part 4 – The discussion

Medical writers with little experience of writing manuscripts can struggle to organise their thoughts. Linking the information within the different sections of a manuscript

can be referred to as 'manuscript flow'. This article is the last of a series of four articles on manuscript flow. Article one focused on the introduction,¹ article two on the methods,² and article three on the results.³ The focus here is the discussion, the manuscript section that many find most challenging.

Where to start

A recommended flow for the discussion is shown in Figure 1. Begin by outlining what the study showed, making sure that you explain how the data collected address the study objective(s). It is fine to restate the main objectives as they were presented in the introduction to remind the reader what they were.⁴

What the study showed (provide context)



Interpretation of findings
Comparison with the literature
(explain any differences)



Limitations & strengths
(may be combined with other sections)



Conclusions & recommendations

Figure 1: Summary of flow of the discussion.

While it is okay to highlight key findings at the beginning of the discussion, do not simply repeat all the results. The results section is where you should present and describe the results; in the discussion you should interpret them and discuss their implications. A sentence in the results section might read as follows:

Child-related stressors were the strongest predictor of membership in the high-stress group (odds ratio = 2.16).

In the discussion you might interpret this result thus:

In this study, we showed that childhood stress is one of the strongest predictors of stress in adulthood.

The middle part: Comparing your results with the literature

Compare your findings with the literature. Be sure to include references to articles by key people in the research field. This will show that you know the field, and won't do any harm if these key people end up refereeing your manuscript. Report any discrepancies with related studies, and try to provide explanations for them; don't pretend they don't exist.⁴ Provide also alternative explanations for your findings.⁴ This will again help show that you know your field, and that you have carefully considered the meaning of your results.

Be sure to explain the study's strengths and limitations. Don't forget the strengths! For example:

This initial study, which included 37 patients, did not allow us to draw formal conclusions about the efficacy of the malaria treatment. However, it is highly relevant for understanding malaria treatment because it was performed in a region of high transmission.

Importantly, if particular study limitations didn't affect the results, make this clear. Explain also any steps you took to limit the influence of potential biases and other limitations.

End strongly by presenting your conclusions and recommendations

Finally, present your conclusions and recommendations. Mention unanswered questions and future research by all means, but don't just write 'Further studies are needed.' Be specific: if you think future studies are needed, indicate what it is they should aim to do and how. But make sure future research isn't the very last thing you mention; instead, leave

your readers with a punchy statement about the importance and implications of your findings.⁴

What do official guidelines say?

This flow is also recommended by the ICMJE (International Committee of Medical Journal Editors) *Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals*.⁵ The ICMJE recommendations, which were recently updated (see page 107), include the following for the discussion section:

'Emphasize the new and important aspects of the study and the conclusions that follow from them in the context of [...] the best available evidence. Do not repeat in detail data or other information given in other parts of the manuscript [...] briefly summariz[e] the main findings, then explore possible mechanisms or explanations for these findings, compare and contrast the results with other relevant studies, state the limitations of the study, and explore the implications of the findings for future research and for clinical practice.'

'Link the conclusions with the goals of the study but avoid unqualified statements and conclusions not adequately supported by the data. In particular, distinguish between clinical and statistical significance, and avoid making statements on economic benefits and costs unless the manuscript includes the appropriate economic data and analyses. Avoid [...] alluding to work that has not been completed. State new hypotheses when warranted [...].'

The guidance on distinguishing between clinical and statistical significance, in the second paragraph above, is particularly important. For example, in an epidemiological study of 4 million people, an odds ratio of 1.05 could easily be statistically significant. But is it necessarily clinically meaningful?

Some information on essential content is included in the CONSORT 2010 Checklist,⁶ which has the following specific items for the discussion section:

- Item 20: Trial limitations; addressing sources of potential bias; imprecision; and, if relevant, multiplicity of analyses
- Item 21: Generalizability (external validity, applicability) of the trial findings
- Item 22: Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence

Item 21 is especially noteworthy. *Generalisability* is a relatively young word, first documented only 100

years ago,⁷ but it has become a key concept for clinical studies. How generalisable a study's results are to the wider population will help to determine how broadly the tested treatment can be applied. Be realistic when describing the generalisability of your results. Don't make unwarranted claims – journal editors, referees, and readers won't accept them.

Additional points to consider

Use transition words and phrases such as *therefore*, *however*, *thus*, *conversely*, *consistent with*, and *in contrast to*,⁴ but make sure you use them appropriately. Don't, for example, start consecutive sentences with *However*.

Do not introduce new data or refer to 'data not shown' in the discussion. Any references to data not shown belong in the results section. Moreover, if the data are important enough to bring up in the discussion, they should be presented in the results section!

A final point

Making sure that the discussion flows logically from one element to another so that it tells a story can be difficult. The flow described in this article is a good place to start, but feel free to adapt these recommendations to your specific needs and writing style.

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ICMJE Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals: December 2014 update

In December 2014, the ICMJE¹ updated its *Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals*.² The material changes are listed below. No explanatory notes are provided. This forces users to infer the precise intended meanings of terms such as 'self-interest' (section IV A 3 g) and 'concerns' (IV B). The reasons for the changes are also unclear. However, a number of them seem to reflect ethical issues and dubious practices that journal editors and authors have engaged in or faced in recent years. Indeed, I can confirm that the amendment to section IV A 3 g was introduced to discourage journal editors, peer reviewers, and authors from choosing references in a manner aimed at increasing citations of their own (journal's) papers (Darren Taichman, personal communication, 2015 Feb 3). Elsewhere, the new section on fees (III F) would appear to be a response to hidden charges levied by predatory journals. Sadly, such journals are hardly likely to adopt the ICMJE recommendations.

Section II E. Protection of Research Participants.
New guidance:

'Approval by a responsible review committee does not preclude editors from forming their own judgment whether the conduct of the research was appropriate.'

Section III D 2. Duplicate Publication. Change in policy:

Registration of clinical trial results (not more than 500 words) in an acceptable registry other than the primary trial registry will no longer be considered prior publication.

Section III E. Correspondence. New guidance:

'Responsible debate, critique and disagreement are important features of science, and journal editors should encourage such discourse ideally within their own journals about the material they have published.'

Section III F. Fees. New section:

'Journals should be transparent about their types of revenue streams. Any fees or charges that are required for manuscript processing and/or publishing materials in the journal shall be clearly stated in

a place that is easy for potential authors to find prior to submitting their manuscripts for review or explained to authors before they begin preparing their manuscript for submission.'

Section IV A 3 Manuscript Sections. b. Abstract.
New guidance:

'If the data have been deposited in a public repository, authors should state at the end of the abstract the data set name, repository name and number.'

Section IV A 3 Manuscript Sections. d. Methods.
New guidance:

'The Methods section should aim to be sufficiently detailed such that others with access to the data would be able to reproduce the results.'

'If an organization was paid or otherwise contracted to help conduct the research (examples include data collection and management), then this should be detailed in the methods.'

The Methods section should include a statement indicating that the research was approved or exempted from the need for review by the responsible review committee (institutional or national). If no formal ethics committee is available, a statement indicating that the research was conducted according to the principles of the Declaration of Helsinki should be included.'

Section IV A 3 Manuscript Sections. g. References.
New guidance:

'References should not be used by authors, editors, or peer reviewers to promote self-interests.' They should instead be chosen according to relevance and usefulness for the reader (Darren Taichman, personal communication, 2015 Feb 4).

Section IV B. Sending the Manuscript to the Journal.
New guidance:

'The [cover] letter or [completed journal submission] form should inform editors if concerns have been raised (e.g., via institutional and/or regulatory bodies) regarding the conduct of the research or if corrective action has been recommended.'

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GPP3 on the way

In January 2015, an article describing GPP3 (the third iteration of the Good Publication Practice guidelines) was submitted to *Annals of Internal Medicine*.¹ GPP3 builds on GPP2, described in a *BMJ* article from 2009.² The original GPP guidelines were published in 2003.³ GPP2 and GPP3 are the work of members of the International Society for Medical Publication Professionals (ISMPP). New to GPP3 are sections devoted to core publication principles and data sharing. In addition, the persistent problems of plagiarism and self-plagiarism are addressed for the first time. As ISMPP points out, peer reviewers will have some influence as to the final content of the GPP3 paper. Expect a fuller description of GPP3 in *Medical Writing* when the GPP3 paper is published.

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New authorship framework for industry-sponsored publications

Are ICMJE guidelines on authorship¹ too broad to allow valid and consistent assignment of authorship of publications based on clinical trials? Yes, according to members of the Medical Publishing Insights and Practices (MPIP) Initiative, which brings together representatives of pharmaceutical companies and ISMPP.

One of MPIP's 10 recommendations for improving the credibility of industry-sponsored publications is to 'Improve disclosure of authorship contributions and writing assistance and continue education on best publication practices to end ghostwriting and guest authorship'.² To address this recommendation and perceived shortcomings in the application of ICMJE and other guidelines, MPIP members worked with other stakeholders to develop a five-point framework for determining authorship.³

Key steps in developing the authorship framework were:

- (1) Creation of seven case scenarios illustrating difficult decisions regarding assignment of authorship
- (2) Creation of an online survey based on these scenarios

(3) Emailing of this survey to four groups of stakeholders: clinical investigators involved in industry-sponsored trials, journal editors, medical writers, and industry-paid publication professionals

(4) Discussion of survey results in two roundtable meetings to identify key themes³

498 people completed the survey. Their responses reveal some interesting trends:

- (i) A majority of respondents felt that trial site management and a considerable contribution to patient recruitment were sufficient grounds for authorship.
- (ii) A majority of respondents felt that a statistician who contributed to data analysis and interpretation, but not trial design or manuscript drafting, should be added as an author of the final manuscript.
- (iii) A quarter of journal editors and clinical investigators felt that medical writers should be listed as authors.³

The opinions expressed in (i) and (ii) above are potentially valid according to ICMJE guidelines, but only if the potential author fulfills additional authorship criteria. By contrast, medical writers do

not normally qualify for authorship. Several respondents highlighted what they considered to be the conflict between what is permitted by the guidelines and what is fair.

The five-step authorship framework

Based on the survey and their discussions, MPIP suggests the following five steps as a framework for determining authorship in clinical trial publications:⁴

- (1) Establish a working group responsible for steps (2) to (5) below. Members of the working group need not be authors and should not be guaranteed authorship.
- (2) Identify trial-related activities that are to be considered 'substantial'.
- (3) Track and record substantial trial-related activities.
- (4) Assess the recorded substantial activities and invite those responsible for them to be authors.
- (5) Ensure those invited to be authors fulfill all ICMJE criteria.¹ Authors can be added or removed, at the consent of all authors. In the interests of internal transparency, authorship changes and the reasons for them should be documented.

To me, this all seems very sensible. Importantly, it is suggested that the framework be backed up by a

'publication agreement', which defines the procedures in steps (2) and (5) and which should be approved by all trial contributors.⁴ The framework has the potential to increase consistency in authorship decisions and reduce disputes over authorship. However, people invited to be authors in step (4) and then removed from the author list in step (5) are unlikely to be overjoyed, irrespective of any publication agreement they might have signed.

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English Grammar and Style

Revising medical writing

Reasons not rules:

Backtracking, pronoun-induced

Part 3 - Double syntactic unit revision and syntactic position revision

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Introduction

This is the last of this series of three articles on pronouns that cause distraction by making the reader backtrack. In the first part of this article, we examine a technique for eliminating backtracking by making two changes to the construction of the sentence. The technique is to eliminate the pronoun that is causing the distraction by sentence syntax reduction.

Example 1: 'It' in the subject position of the dependent clause in a complex sentence

The example, from an Introduction section, conveys a description of the research problem context, consisting of a descriptive and an assertive statement:

Timely accurate screening and diagnosis is important because it can reduce the progression of the malignancy.

The reader is led to backtrack because of the ambiguity whether 'it' refers to screening, diagnosis, or both. The question is whether the pronoun 'it' can be eliminated by syntactic reduction of both clauses. The answer is yes, because the independent clause is reduced into a noun phrase; the dependent clause reduced into a predicate.

The suggested revision is:

Timely accurate screening and diagnosis can reduce the progression of the malignancy.

Notes

- (a) In the example, 'it' refers to the pair 'screening and diagnosis' considered as a singular collective.

- (b) In the revision, 'is important' is unnecessary because of self-evidency.

Example 2: 'It' in the subject position in the second independent clause of a compound sentence

This example, also from an Introduction section, conveys a description of the research problem context, consisting of a descriptive and assertive statement:

Lysine is an abundant muscle constituent, and it decreases in amount during starvation.

The reader backtracks because 'it' could refer to lysine, or to constituent. This 'it' can also be deleted by double syntax unit revision. The predicate of the first independent clause is transformed into the appositive 'an abundant muscle constituent', enabling elimination of the 'it' of the second clause, which is reduced to a verb phrase 'decreases in amount during starvation'. The suggested revision is:

Lysine, an abundant muscle constituent, decreases in amount during starvation.

Notes

- (a) In the revision, the appositive 'an abundant muscle constituent' is short enough to not interfere with the flow of the sentence.
- (b) In the example, the backtracking may be a cue that the compound sentence pattern is not matched to rhetorical intent. Additional cues to this mismatch are the following: (1) the first independent clause is descriptive and the second is assertive, (2) the verbs are non-parallel, namely, the linking verb 'is' and the intransitive verb 'decrease'.

A second technique for eliminating backtracking is by syntactic position revision. The technique is to

eliminate the pronoun that is causing the distraction by appropriate positioning of compared entities.

Example 3: 'Those' in the prepositional phrase of an intra-sentence comparison

This example, from a Results section, describes a data-interrelative comparison:

The absolute values for fracture toughness of primary teeth were similar to those for permanent teeth.

The suggestion here is to avoid repeating 'values' in the form of 'those' by using a sentence-end compared entities pattern. By coordinating the noun phrases 'primary teeth' and 'permanent teeth' in an end-of-sentence comparison, the pronoun 'those' can be deleted. A further advantage is avoiding the repetition of 'teeth' in the coordinated pair.

The absolute values for fracture toughness were similar between primary and permanent teeth.

Note: Instead of the addition of explicit textual markers to avoid backtracking or pronoun elimination by clause-to-phrase reduction, a positional revision is applied.

Summary

Pronoun-induced backtracking can be eliminated by (1) syntactically reducing both clauses or (2) repositioning the coordinated noun phrases.

In the next series of articles, we will examine techniques for eliminating backtracking induced by non-pronouns.

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Out On Our Own

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Editorial

All of us are aware by now that we can't live without technology and not only at work. With advice, aids, appliances and apps in abundance, we are at the point where we can't see the wood for the trees. Thank goodness we have advice from Michelle Storm Lane of the Association of Independent Professionals and the Self Employed (IPSE). In this issue, Michelle continues her series of articles introducing us to a raft of technologies there to help us. She is convinced that those who use selected technologies effectively are able to increase productivity, reduce stress, and free up spare time to earn (more?) money – or simply to enjoy life. She even recommends having a robot vacuum cleaner, which at least one of the editors of this section (AR) also fully recommends.

Amy Whereat has been looking at reference management software, and also points out that one way for those working on publications to work more effectively is to use systems that automate low-value tasks. These include keeping track of and

correctly citing and formatting references and bibliographies. She provides us with an interesting overview of the pros and cons of different reference management systems.

As well as working efficiently as a self-employed person, you have to be able to market yourself and your services effectively using personal branding. Channels for these days are your CV and your LinkedIn profile, and perhaps an executive biography or website – where you describe 'brand You', your value proposition, your abilities and your track record. Matt Craven is an expert in this and has an offer not to be missed for EMWA members: a FREE personal branding consultation. See Matt's article and don't miss this opportunity.

We also publish a question from Ruth Whittington in this issue about challenges when working with procurement agencies or outsourcing departments. This is a real problem we all face at some time in our careers, and we (and Ruth!) look forward to hearing about your experiences.

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Technology you can't live without

Why is it that some people have the magic touch when it comes to technology? Are there some strange magnetic forces within us that cause machines to spring to life in the hands of some, when in the hands of others they go into total meltdown? I have a very technophobic friend who certainly thinks so!

But if you can somehow master the miracle of technology, the rewards are significant. Freelancers who use technology effectively are able to increase productivity, reduce stress, and free up spare time to earn money – or simply to enjoy life.

Could you be making better use of all the amazing tools that are out there?

We asked a range of writers and medical translators for some ideas. This is what they came back with:

Call in the robots

One of the wonders of the modern world is the sheer volume of innovative solutions coming out that allow you to automate repetitive tasks.

Sean d'Souza says that one of his biggest time-saving tools is Text Expander¹. As a writer, he frequently has to type out very similar passages of text in articles or emails. Text expander allows him to programme shortcut keys for each passage – when he hits the shortcut key, the whole passage is automatically pasted into the document or email and he can tweak as necessary without retyping the whole thing. So if you frequently use the same phrases, paragraphs or even pictures, this is one 'robot' that could really speed up your work rate.

Another area that lends itself to automation is bookkeeping – there really is no need to do it all manually when you could quicken the process using online software. Tools like www.getharvest.com allow you to keep track of time spent on projects and to generate invoices automatically. If you're in France, then www.itool.com offers online solutions tailored to the French auto-entrepreneur and small business regimes. For other languages, try www.zoho.com/books, available in Dutch, German, Italian, Portuguese, Spanish and Swedish. You can find a range of other accountancy software solutions at www.ipse.co.uk/supplier-directory.

Oh, and while you are busy working, a robot could be cleaning your house as well. Heard of the Roomba? This robotic vacuum cleaner zooms around the house hunting for dirt. Its special sensors prevent it from crashing into your furniture or falling down the stairs!² (Editor's note: these robotic vacuum cleaners really do work and save loads of time!)

Cloud control

Whereas in the past we had all our software and data stored on our hard drives, the current trend is for more and more things to be done via the cloud. This means that everything is available simultaneously on your computer, your phone, and online, so that you can access what you need anytime, anywhere – even if you don't have your own computer or mobile device with you.

For example, Frederique David³, a freelance writer and technical adviser, takes advantage of a wide range of cloud-based tools provided by Google. Google Drive allows her to back-up files and share documents as required. Using Google Keep, she takes notes on the go, uploads voice and video memos, produces checklists and assigns colour codes to different types of information. Google Mail provides her with email, which she can check on any of her devices. If her computer breaks, or she loses her phones, all her emails are still available online. She can also share calendars, which is great for team working.

To link these all together she uses Google Apps, for which she pays a monthly subscription fee. This enables her to send emails using her own company domain name, which she feels is more professional than using a generic extension such as @gmail.com. However, if you don't need this, you can still use all of Google's cloud services for free just by creating a Google account.

Frederique also uses www.hubic.com to back up data online and synchronise it between her devices. As she is based in France, she prefers the

fact that Hubic is subject to French law, which gives her greater protection over the privacy of her data, unlike some of the other services such as Dropbox, which are based in the US. Hubic is available in most European countries.

Finally, if you have ever tried to set-up your own email using Outlook or a similar email programme, it probably asked you if you wanted to use POP3 or IMAP. In case you are wondering what the difference is: IMAP is the option that allows you to keep everything on the cloud as described above. Select this option to have a mirror image of your email available online, automatically synchronising with all your devices. Just be sure to keep an eye on the storage space provided by the company that hosts your email – if this runs out, you will stop receiving emails. However, these days it is usually very economical to contract unlimited storage.

A world of information

As early as 1984, at the first ever 'Hackers' Conference', Stewart Brand told Steve Wozniak, the co-founder of Apple: 'On the one hand information wants to be expensive, because it's so valuable. The right information in the right place just changes your life. On the other hand, information wants to be free, because the cost of getting it out is getting lower and lower all the time.'

This is good news for freelancers – if your client doesn't provide you with all the reference sources you need, the internet offers a wealth of robust information that you can access for free.

One of the medical writers we spoke to mentioned www.globalhealthfacts.org as very useful for researching health trends. For example, if you needed to build some 'scene-setting' slides to illustrate disease prevalence rates, this website allows you to download the data for each country in a convenient .csv file that you can use to create your own graphs. Other sources are www.biomedcentral.com and www.pubmed.gov, provided by the US National Library of Medicine.

For academic references, www.google.com/scholar is one of the best ways to search through journal articles. Not everything you find through that will be free to download, but you can set up a free account with <http://about.jstor.org/rr>, which gives you access to a huge range of journals, primary sources and books. The free account allows you to read up to three articles every two weeks. You can subscribe to the paid service if you need more.

Finally, for all the fantastic new inventions that appear in our professional lives every year, Noelia Corte, a freelance medical translator, urges us not

to forget the value of time-honoured technologies: 'To be able to tap into a colleague's knowledge is priceless. I have a group of good professionals and friends who I can turn to.'

Michelle Storm Lane is Business Development Manager at IPSE, the UK Association of Independent Professionals and the Self Employed.

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References

1. You can find out more about this tool at <http://www.smilesoftware.com/TextExpander>. You can also listen to Sean d'Souza's strategies for running a freelance business at <http://www.nationalfreelancersday.com/podcasts>.
2. Read about the Roomba at <http://www.wikipedia.org/wiki/Roomba>. A great place to find other time-saving tools is <http://www.lifehack.org/articles/technology/30-essential-tools-and-web-apps-for-freelancers.html>.
3. Frederique David helps French-speaking freelancers to promote themselves on the internet. You can find out more at <http://www.creizic.com>.

The Toolbox

Managing your references saves time and money

Software automates reference management

Freelance medical writing, like any business, is more profitable when efficiently run. One way to improve efficiency is to use systems that help automate low value tasks. A particularly time consuming job during manuscript writing is keeping track of and correctly citing and formatting references and bibliographies.

What does the software do?

Reference management software is very useful for automating this process and some programs include plug-ins that give you direct access from some word-processing programs (e.g. MSWord, Open Office, Pages).

The basic function of reference management software is to create formatted bibliographies, in-text citations, and footnotes suitable for journal publications. However, modern programs offer various different useful features, so it's worth surveying the market before purchasing.

Here are 5 straightforward things you can do with reference management software:

1. Create an electronic library for an article or research topic. This allows you to keep all research documents, websites, and articles in one place. Some programs allow you to send the library to a client or team member, otherwise it can be shared online via a cloud or other online shared facilities. You can even copy references from one library to another.

2. Search online databases, import existing PDF collections or upload websites to the library. Some programs also allow PDF file access so you can highlight and annotate key phrases or sections in references that you might want to include in your article or refer to later.
3. Automatically upload reference information when the reference you have is incomplete or you just need to check a reference either exists or is correctly cited.
4. Choose the exact citation and bibliographic style required by your target journal. Most software packages contain typical journal style guides and additional ones can be obtained from an internet database, and saved for further use.
5. Change the citation and bibliography style with one click, if you need to change journals. No more retyping or reformatting.

Longer term, using a reference management system can save you time *and* money. It helps you to keep your references organised and ensures they are correctly cited. While the software can be purchased by individuals, some universities provide continued alumni access, so this is worth exploring. Some software programs also provide free tutorials and after-sales assistance. For freelancers on the go, several packages now provide telephone and tablet access. Table 1 summarises the main pros and cons from referenced websites for several different programs.

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Table 1: Pros and cons of reference management software

Reference management software	Pros					Cons		
RefWorks®	Internet-based solution	Mobile device access	Large number of citation styles	Easy to edit citation styles	Free access with Bodleian Libraries subscription for students and alumni	Cannot extract metadata from PDFs	WP plug-in only compatible with MS Word	Very limited offline access
EndNote®	Desktop-based solution with plug-in for Pages, MS Word, Open Office	Copes well with a very large library. Large number of citation styles	Journal abbreviation recognition	Can search & upload references from online databases or PDFs e.g; Pubmed	Can highlight and annotate PDFs	Incompatible with Linux	For advanced features need to buy the software	
EndNote® online	Online collaboration	Mobile device access	Direct ref download button in: Web of Science database™	Free with Endnote®		Word processor plug-in not compatible with Linux	Limited citation styles and storage	
Reference manager®	Desktop-based solution with plug-ins, MS Word	Can share references		Can search and upload online databases		Incompatible with Mac	Limited citation styles	Limited organizational facility
Zotero™	Can make separate collections from one source library	iPhone/ android apps	Useful tools for creating references from websites	Can make notes on the go and store in a library collection	Free access	Compatible Mac, windows, Linux	Limited free storage space (300 MB)	
Mendeley™	Collaborative pdf annotation / notes	iPhone/iPad interface	Showcase your work. Share reading lists with a social network	Free Access	Can search for keywords in references	Manual syncing of desktop application to web account	Limited free storage space	
ColWiz™	Nested folders	iPhone/iPad and android apps	Collaborative research management tools	Can share reading lists with a social network	Access available if with some university libraries	Direct export of refs only with desktop application.		
Papers™	PDF annotation	Social network	iPhone/iPad apps	Large number of citation styles		Need to buy software	Not compatible with Linux	Not able to sync across several computers

The information in the above table is summarised from the following websites:

- <http://ox.libguides.com>
- https://workspace.imperial.ac.uk/library/Public/Reference_management_software_comparison.pdf

The truth about personal branding

It seems that there has been a wave of curiosity since Bianca Miller (finalist in the UK's TV reality business show 'The Apprentice') mentioned that she runs a personal branding business – perhaps some folks think it might be a new concept that she invented along with her hosiery business. The truth is that personal branding has been around for many years and the savvy freelancers, job seekers and contractors realised the importance of developing 'brand You' long ago. What is positive is that Bianca's foray into primetime TV has created some awareness around personal branding, and the more people who start to embrace the subject, the more people will be moving forward with their career.

So let's start with a quick overview! Personal branding is really no different from marketing any

product, service or company – companies have a 'brand' and their products and services follow suit. The same can be said of individual professionals – whether you are seeking permanent employment or self-employed opportunities, you are still selling your services to that organisation, so before you are hired, they will want to explore your brand (i.e. what do you stand for, what is your ethos, or what is your philosophy?). They will also want to explore your value proposition, your abilities, and your track record. These are exactly the same points that consumers consider before buying from companies.

The point of all this is that your externally facing marketing materials need to incorporate these exact same points, and of course, your externally facing marketing materials are your CV and

LinkedIn profile (and perhaps an executive biography or website). By capturing 'brand You', your value proposition, your abilities and your track record, you will be much more likely to convince a potential employer or client that you can add value to their organisation. The key is to think of your CV and LinkedIn profile as a business case and through that business case, demonstrate how you can deliver return on investment on the remuneration that you are seeking.

For more information, The CV & Interview Advisors are offering a FREE Personal Branding

Consultation to all EMWA members; just email your CV to info@cvandinterviewadvisors.co.uk quoting EMWAAFPBC and one of their team will provide a detailed critique of your CV, LinkedIn profile and any other collateral that you might have.

Matt Craven

Managing Director

The CV & Interview Advisors

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www.cvandinterviewadvisors.co.uk

Question: Challenges when working with procurement agencies or outsourcing departments

This question was posed during the Freelance Business Forum at the EMWA conference in Florence: 'What can freelancers do if the procurement agency working on behalf of a pharmaceutical company, or the procurement department of a pharmaceutical company won't employ freelancers because they have a policy in place only to employ companies on their preferred supplier list?'. Thank you to Ruth Whittington for asking this question.

We would love to hear your thoughts on this, what your experiences are, and how you have overcome this challenge. We plan to write an article on this topic and, as always, please get in touch with us if you would like to volunteer as the lead author. Please contact either Kathryn or Alistair at the email addresses provided.

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Freelance foraging

Lake Bled, Slovenia

The Slovene and German (not perfect) here say:



Crossing to the island, with a half-hour stay, other arrangements on request.

The Italian version promises you half an hour of expectation, and in the English version, whatever 'the rest' is, you won't get it until you wait half an hour, and then only if you ask for it. We opted to hire our own rowing boat to get to the island.

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