Medical Writing

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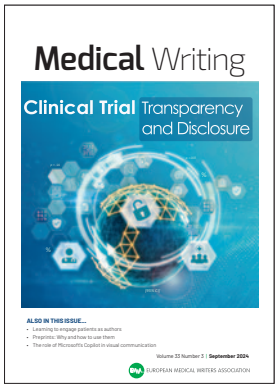
Volume 33 Number 3 | **September 2024**

EMWA EUROPEAN MEDICAL WRITERS ASSOCIATION

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

Medical Writing



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Clinical trial transparency and disclosure from the medical writing perspective

doi: 10.56012/gkvo3717

It's been more than six years since our last *Medical Writing* edition dedicated to clinical trial transparency and disclosure.[1] Since then, we have seen the full implementation of the long-awaited EU Clinical Trials Regulation (CTR)[2], the pause and restart of EMA Policy 0070[3], and of course a global pandemic which resulted in a worldwide surge in freedom of information requests for Covid-19 vaccine clinical trial data. Although many of the regulations and policies governing public disclosure of clinical trial data and documents remain unchanged, we have seen significant changes in the way these are implemented. As those of us who work in this field know all too well, the landscape is ever changing, and it is essential to keep up to date with those changes. Resources such as the Drug Information Association Clinical Trial Disclosure Community,[4] PHUSE Data Transparency Working Group,[5] and Clarity and Openness in Reporting-E3 based (CORE) Reference[6] provide invaluable updates and insights. This issue of *Medical Writing* touches on a number of different aspects of clinical trial transparency and disclosure, all of which involve medical writers as key stakeholders

Following a public consultation on the rules for the operation of the EU CTR and its Clinical Trials Information System (CTIS), the EMA Management Board adopted revised CTIS transparency rules[7] in October 2023. In this issue **Merete Jørgensen, Kathy Thomas, Matthias Zerm,** and **Robert Paarlberg** describe the impact of these revised rules on the protection of personal data and commercially confidential information within CTIS and the key role medical writers play in preparing disclosure-ready clinical documents. They also discuss interrelated requirements of other regulations applicable for public disclosure of clinical trial information within the EU/EEA.

Following the application of the EU CTR with the go-live of CTIS on January 31, 2022, a three-year transition period started where clinical trials originally authorised under the Clinical Trials Directive 2001/20/EC[8] and are expected to continue in the EU/EEA after January 2025 must meet the requirements of the EU CTR. In their article on transitioning trials from EudraCT to CTIS, **Mirjana Miric** and **Sarah Bly** describe this process. They highlight the very short turn-around times for addressing requests for information and how medical writers play a critical role in meeting

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these deadlines if clinical documents need updating. Mirjana and Sarah also stress that the work is not done once transition is completed as there is a substantial amount of work required in preparation of the first substantial modification, especially if a minimum dossier was submitted for transition.

Pooja Phogat and **Stuart Donald** provide an excellent summary of the different clinical trial transparency requirements, highlighting how medical writers can take a lead in ensuring these are met while maintaining data privacy, confidentiality, and the integrity of data. Their article also underlines the increasing complexity of clinical trial transparency by highlighting the regional differences in transparency requirements which present challenges for global studies.

Although only recently mandatory with the application of the EU CTR in January 2022, many clinical trial sponsors have long recognised the value in producing summaries of clinical trial results in lay language. In her article on plain language summaries of clinical trial results, **Lisa Chamberlain James** explores the significance of these highly specialised documents. She describes the importance of involving patients in the development of these results summaries and discusses how artificial intelligence provides the opportunity to streamline the process – but emphasises that medical writers still play a crucial role in ensuring quality results.

As already mentioned, CORE reference provides invaluable guidance on best practice in the preparation of clinical study reports with disclosure and transparency in mind. **Zuo Yen Lee, Alison McIntosh, Vivien Fagan**, and **Sam Hamilton** present the findings of the 2023 CORE Reference Utility Survey aimed at measuring awareness and perceived usefulness of these resources by the regulatory medical writing community. They compare results of this survey with the previous survey in 2017 and report an increased use of the CORE Reference open-access manual and confirm that the manual remains a useful tool when preparing disclosure-ready clinical study reports (CSRs). Positive responses were also received on the usefulness of the bi-monthly "News Summaries" to provide subscribers with updates on major changes in regulatory reporting and public disclosure requirements from around the world, including Asia.

The Covid-19 pandemic perfectly demonstrated the importance of accessible and understandable information being made available to the public in a timely manner to empower patients and foster trust. **Devaki Thavarajah, Sylvia Baedorf Kassis, Alyssa Panton, Barbara Bierer**, and **Trishna Bharadia** describes PHUSE and MRCT Centre's experiences creating an informational video series and complementary infographics aimed at explaining clinical trials to patients and the general public, focusing on how data are collected, used, shared and protected.

In addition to the EU CTR requirement for plain language summaries of clinical trial results, some journals also now publish plain language summaries alongside scientific publications. In their article **Slávka Barónková, Adeline Rosenberg, Christopher Winchester,**

EUROPEAN MEDICAL WRITERS ASSOCIATION

Submissions:
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All manuscripts should be submitted to mew@emwa.org.

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Valérie Philippon, **Jo Gordon**, and **Joana Osório** report on findings from a survey conducted in 2022/23 by the multi-sponsor collaboration Open Pharma. The survey indicate journals are not routinely supporting submission of a plain language summary, and where they do there is significant variability in the content, format, and accessibility.

As well as the "Clinical Trial Transparency and Disclosure" edition feature articles, we also have the regular "Regulatory Public Disclosure" section supplied by **Sam Hamilton** and the **CORE Reference Team**. The team present a selection of key regulatory information to support the continuing professional development needs of medical and regulatory writers, including links to information related to the EMA CTIS re-launch on June 18, 2024, and the accompanying EMA Guidance document describing how to approach the protection of personal data and commercially confidential information while using CTIS. Alongside this, they have prepared a handy, "bitesize" comparison between Policy 0070 and EU CTR.

Regulatory medical writers have an important role to play in the process of preparing clinical documents suitable for public disclosure, and separately can have a role in preparing clinical trial datasets suitable for data sharing. The methods used to manage the risk of de-identification of individuals in both processes have commonality. In the regular "In the Bookstore" section **Alison McIntosh** reviews *Guide to the De-Identification of Personal Health Information* and advises that this book provides useful background to the topic alongside details of the statistical concepts applied to de-identify clinical datasets.

We will continue our exploration of different aspects of clinical trial transparency and disclosure by publishing two further articles in the December issue of MEW, and both should not be missed.

One will address the need for different transparency requirements globally and how this presents challenges in maintaining consistency with publicly disclosed information, particularly for multi-national trials. **Maren Anne Moehlmann**, **Zhen (Sophie) Yu**, **Yu (Julia) Zhou**, and **Qiang (Johnson) Liu** will give a detailed insight on the processes a global pharmaceutical company uses to manage and harmonise global and local clinical trial registration and results disclosure. They will describe how they operationalise "central disclosures" in Germany, EU, and US versus "local disclosures" using the example of China. Be sure to keep an eye out for this important article in the next edition of MEW.

The other will examine the growing complexity of disclosure and transparency by highlighting the need to balance the requirements of regulations aimed at ensuring transparency of clinical trials with those governing the protection of personal data. **Bina Mehta**, **Sayanti Sau**, **Dhruv Patel**, and **Akanksha Rai** will look at transparency requirements from a data protection and privacy perspective. Their article will raise the crucial topic of GDPR[9] and the importance of understanding the roles of Data Controller and Data Processor, and the need for Data Processing Agreements. They will describe their experiences supporting both EMA Policy 0070 and CTIS submissions, highlighting keys to success, the impact of medical writers, and lessons learned. Please look out for this interesting article in the December edition of MEW.

The guest editors would like to thank all authors for their valuable contributions and for openly sharing their knowledge and expertise on clinical trial transparency and disclosure. We would also like to thank the MEW editorial team for their help and support in producing this issue. Finally, we hope you find this themed issue of *Medical Writing* interesting as well as informative and beneficial.

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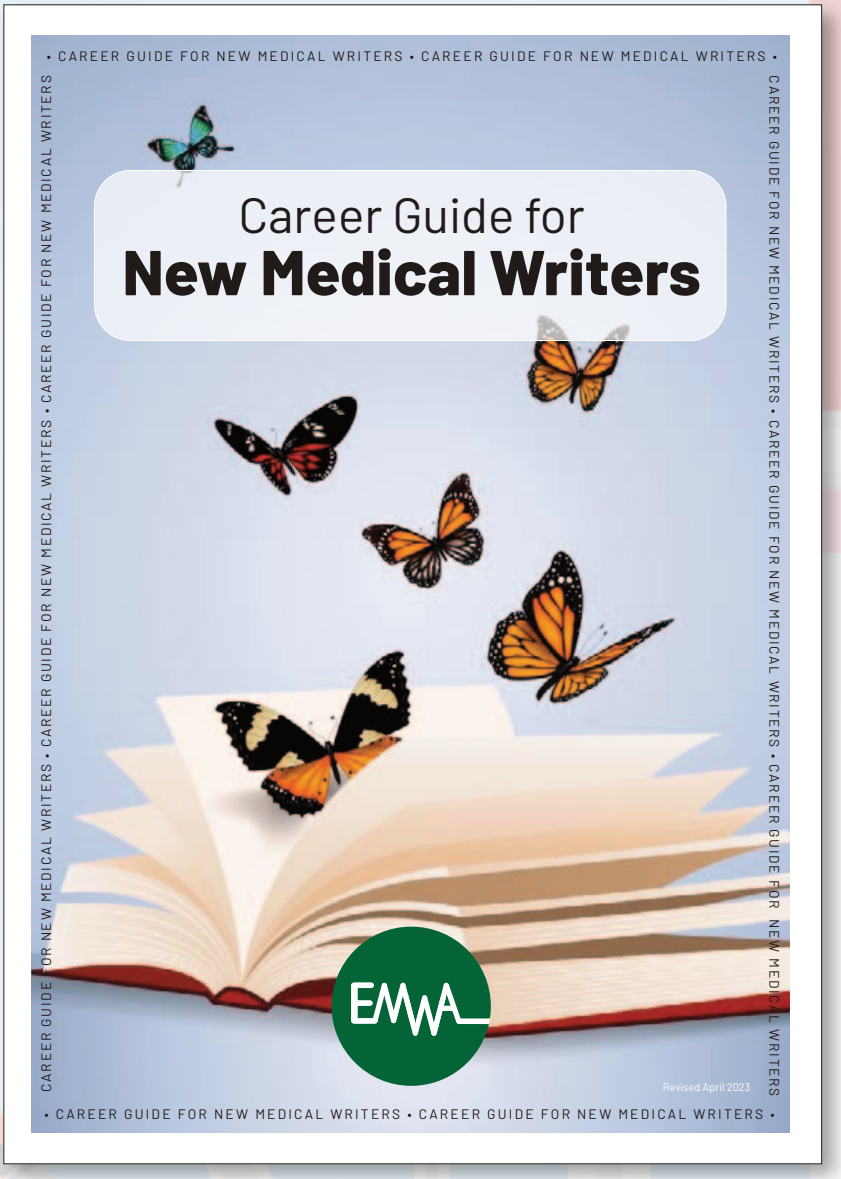
Author information

Holly Hanson began her career in clinical research as a pharmacokineticist in 2001, transitioning to medical writing in 2007. Holly has been a subject matter expert for clinical trial disclosure since 2015 and was co-chair of the EMWA Regulatory Public Disclosure Special Interest Group from June 2020 to May 2023.

Alison McIntosh, PhD, became a medical writer after completing five years of postdoctoral research in molecular virology. She has been an EMWA workshop leader for over 20 years, currently serves as a member of the CORE Reference Project Team, and is a section editor for MEW. Alison has provided medical writing, education, and consulting services to the pharmaceutical industry for over 25 years and has a particular interest in regulatory public disclosure.



Career Guide for New Medical Writers

EMWA's Getting into Medical Writing group has created an updated *Career Guide for New Medical Writers*, which is available on the EMWA website. If you're new to medical writing, it's a useful resource that will help you take your first steps on this rewarding career path. You can email us at gettingintoMW@emwa.org with comments.

From the Editor

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doi: 10.56012/djjd9152

The clinical research transparency journey

It has been a long road to get here. Figure 1 shows my humble attempts in documenting the data transparency journey in clinical research.

The 2000 version of the Declaration of Helsinki was first to highlight the need for publicly sharing research results.

"Authors have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. Negative and inconclusive as well as positive results should be published or otherwise made publicly available".[1]

The US was at the forefront, with the creation of ClinicalTrials.gov registry, primarily driven by the FDA Modernization Act of 1997.[2]

In Europe, the driver legislation was already in place in 2001. Regulation (EC) No 1049/2001 stipulates the fundamental right of EU citizens to information access and governs public access to documents of the European Parliament, Council and all other institutions, including the EMA.[3]

Once the wheels started turning, there was no holding back Europe. The so-called "access to information" law was the foundation of the EMA Policy 0043 (2010),[4] the EU Clinical Trials Register (2011),[5] EU CTR (2014),[6] and EMA Policy 0070 (2016).[7]

It was in the autumn of 2016 when the EMA clinical data site went live.[8] It was a landmark event in the field of data transparency and public disclosure, when clinical study reports, for the first time, saw the light of day. The bar was set. Health Canada quickly followed suit in 2019, with the launch of the Public Release of Clinical Information (PRCI) initiative.[9]

Here we are in 2024. There have been hitches and glitches, snags and setbacks. But we have made a lot of progress!

There are currently over half a million studies registered on ClinicalTrials.gov,[2] and over 4000 on the recently launched EU Clinical Trials Information System (CTIS).[10] There are approximately 430 marketing authorisation procedures on the EMA clinical data website[11] and over 650 records on the Health Canada PRCI.[9] For each entry in these public databases, there is at least one document that a medical writer has worked on – a study protocol, a study report, a safety narrative, a clinical summary.

Today, medical writers stand proud to see their documents in the public domain.

EMWA has accompanied us on this journey right from the start – and just to name a few initiatives:

- Intensive discourse between the regulators and the industry at the full day symposium

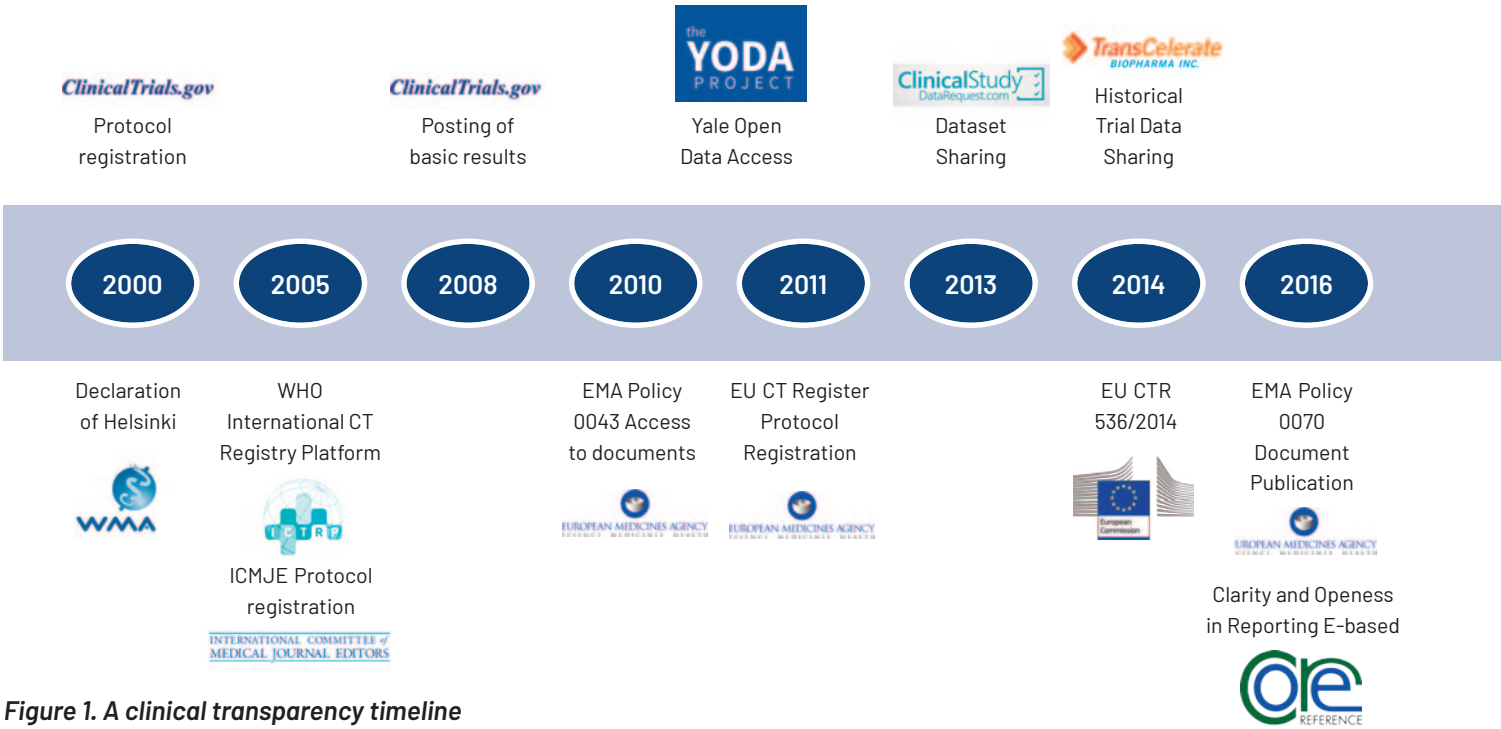

Figure 1. A clinical transparency timeline

"Transparency of clinical data – where does medical writing fit in?" at the 2014 Spring Conference in Budapest;

- Rollout of several EMWA workshops on data transparency at the November 2016 go-live date conference, in sync with the go-live date of the EMA clinical data website;
- Also in 2016, launch of CORE Reference (Clarity and Openness in Reporting E3 based), a collaborative work of EMWA and AMWA, now designated as an EMWA special project;
- Several symposia since 2014 that focused on this topic, e.g., "Transparency and Disclosure of Clinical Regulatory Documentation" (2017), "Plain Language Summaries for Scientific Publications" (2022), and the "EU CTR and CTIS" (2023);
- Several issues of the EMWA journal related to data transparency, e.g., "Public Disclosure" June 2018, "The Data Economy", June 2020, "Open Science and Open Pharma", Dec 2022, and of course, this issue. Our sincere thanks to Alison McIntosh and Holly Hanson and our contributors for the great work in putting together this edition.

The journey continues – transparency and disclosure are still nascent in other fields of research. Clinical research in medical devices and in vitro diagnostics is still awaiting a fully functional European Database for Medical Devices (EUDAMED) to be on par with medicinal products.

Our roles and responsibilities as medical writers have evolved with the new disclosure requirements. We used to be bound to trade secrecy and data confidentiality. We now have become protectors of patient personal data, stewards of data and document utility, and advocates of plain language communications. Our texts have become leaner and more focused, written with public disclosure in mind.

Medical writers are the proud champions of data transparency and public disclosure in health care. And this issue stands witness to this. Happy reading.

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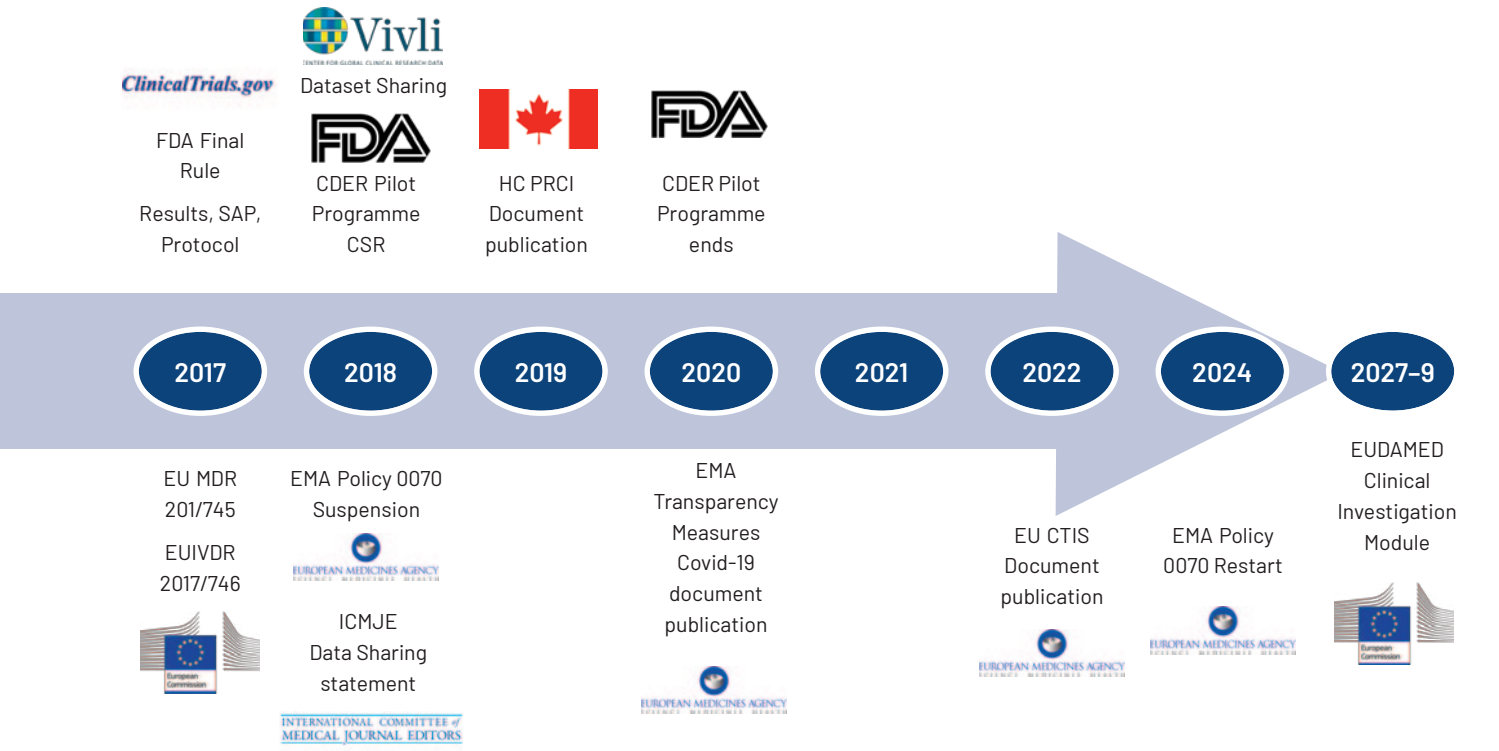

President's Message

Navigating the new era of clinical trial transparency

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doi: 10.56012/gkvo3717

Dear EMWA Colleagues,

This September's issue of *Medical Writing* comes at a time when the summer holidays are behind us. Here's hoping it has been a relaxing and rejuvenating time for all. As we get back to our day-to-day work, our fellow EMWA colleagues bring us an expert insight into the latest requirements in clinical trial transparency and disclosure. As medical writers, this has been on our agenda for many years now, but as we look to the future, transparency in clinical research is emerging as more than just a regulatory requirement – it is a cornerstone of public trust and ethical responsibility. Yet navigating this terrain is not always straightforward. With new regulations, evolving expectations, and the ever-present need to protect sensitive information, it can feel like we must add yet another string to our bow.

In force since January 2022, the European Union's Clinical Trials Regulation (EU No 536/2014) has been a significant and long needed evolution, designed to increase transparency. But as with any regulation, it comes with its share of challenges. The recent revisions to the EMA's Clinical Trials Information System (CTIS) transparency rules remind us that our work was never about ticking boxes; it is about finding that delicate balance between openness and protection. We are expected to make clinical trial data available to the public while safeguarding personal data (PD), of the people who participate in a trial, and the commercially confidential information (CCI).

For those of us dealing with trials transitioning from EudraCT to CTIS, the pressure is on. Not only do we need to ensure a smooth transfer of data, but we also must be meticulous about how we present this information. What exactly constitutes PD or CCI can sometimes be a grey area, and it is our job to navigate these decisions with care. The goal is transparency, but never at the expense of privacy or commercial sensitivity. It is a challenge and we, as medical writers, are uniquely placed to drive forward best practice.

One such document that has been gaining momentum is the plain language summary (PLS). I am sure you are already familiar with the push to make clinical trial results more accessible to the public, especially to patients. Again, this is not just a regulatory requirement; it is a genuine effort to engage and empower those who stand to benefit from clinical research. Should patients have a say in how these summaries are written? Absolutely. They can provide insights that we, as professionals, might miss. And what about AI? It is a tool, as any other, but one that may help us craft clearer, more concise summaries that resonate with a broader audience.

As we work globally, the challenge of transparency grows even more complex. Each region has its own set of rules and expectations, and it is our job to ensure that we are not only compliant but also consistent across borders. Certain companies have shown that it is possible to meet these challenges head-on, maintaining a commitment to transparency while navigating a web of global regulations.

In this digital age, we have more tools than ever to reach people where they are, but with that comes an increased dimension to our responsibility to ensure that the information we provide is accurate, accessible, and meaningful.

Staying up to date requires continuous learning. The results of the 2023 CORE Reference Utility Survey are presented in this issue (see pages 38). We need to keep evolving, refining our skills, and staying informed about best practices. This is a task for our EMWA specialists and volunteers and is a timely reminder to keep coming to our EMWA conferences and attending our very professional educational workshops and seminars. Do not forget to register for the November online conference when registration opens and do think about joining one of the local hubs to participate in the face-to-face networking activities.

We have a journey ahead of us. It is complex, sometimes challenging, but undeniably crucial. Let us continue to work together to uphold the highest standards of transparency, all while protecting the privacy and integrity that our work demands.

Continually learning,
Sarah

Don't miss!

The December 2024 edition

Medical Writing Around the World

Medical writing transcends geography, demography, language, and culture. To date, EMWA has over 1400 members from 48 countries on 6 continents, and we want to celebrate the diversity and global presence of the medical writing community. In this issue, we will focus on medical writing activities around the world and will delve into topics like the benefits of having geographically diverse teams, translation and language-specific challenges, the landscape of global freelance medical writing, etc. We hope that these insights will assist the medical writing community in strengthening interactions and collaboration with teams and freelancers spread across the world.

Guest Editors: Asha Liju and Evguenia Alechine

EMWA News

SECTION EDITOR

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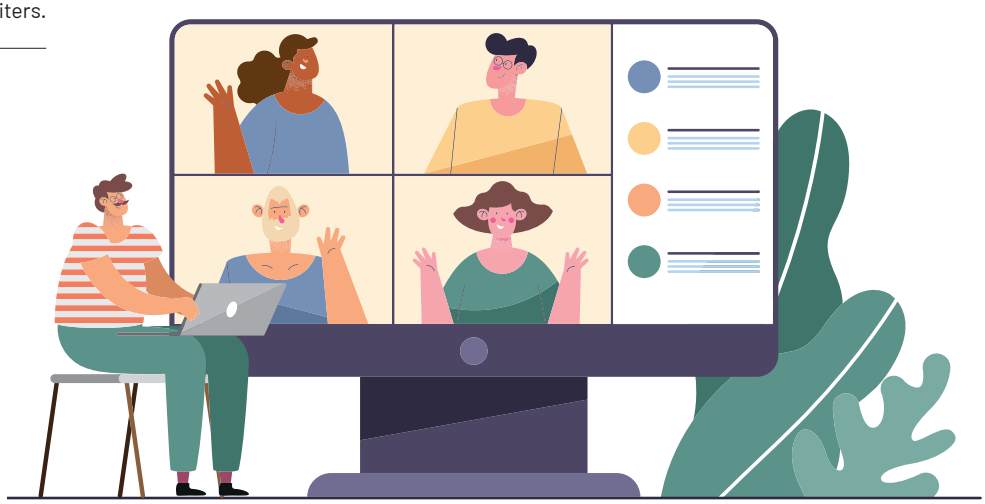
doi: 10.56012/imbl5235

Local hubs for the virtual November conference

We are pleased to announce EMWA's support for local groups and independent local associations of medical writers.

These can be local groups of EMWA members or independent national associations established as separate legal entities. Both are designed to facilitate local networking, discussions, information sharing, and the dissemination of best practices in a given European country or geographic area.

If your local group or association is interested in finding out more about how the local hub initiative works, or learning whether one is taking place in your area, please contact info@emwa.org.



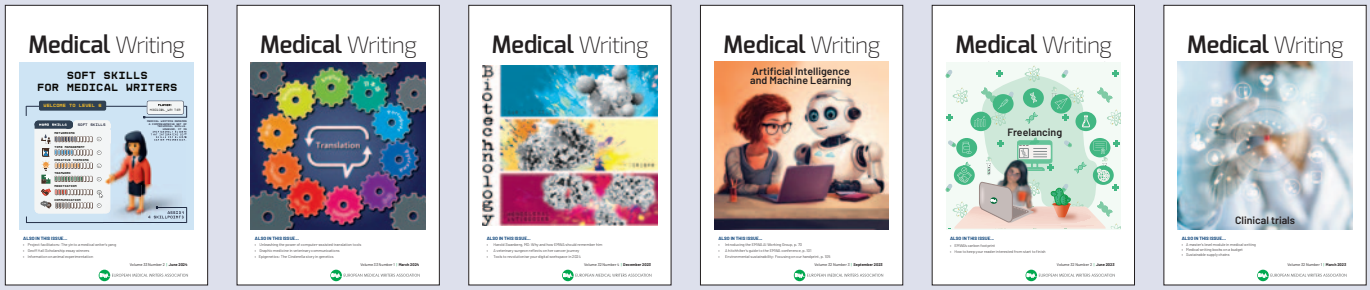
Journal errata

In the June 2024 issue of *Medical Writing*, a production error resulted in an erroneous description of the article by Asha Liju, Diana Daniel, and Girshma Kanchan, titled The 3 C's of medical writing: Communication, conflict management, and critical thinking. The erroneous text, in the editorial by the Guest Editors Clare Chang and Nicole Bezuidenhout, incorrectly stated that the Liju et al. article included observations from a related survey the authors had conducted. The text has been corrected in the online edition of the article, available at: https://doi.org/10.56012/tblo2282.

Also in the June 2024 print issue, an incorrect doi was indicated for the "From the Editor" column by Raquel Billiones. The correct doi is: 10.56012/prvw9168. The online version of the article has the correct doi and is available at: https://doi.org/10.56012/prvw9168.

Did you know?

Existing EMWA members can receive a 10% discount off their next year's subscription for referring a new member to EMWA. For more information, please contact Head Office at info@emwa.org



Check out the back issues of EMWA's journal *Medical Writing* at https://journal.emwa.org!

EMWA Professional Development Committee (EPDC) news

The EPDC is thrilled to announce the successful completion of our pilot QR code feedback questionnaire project for workshops conducted at our May 2024 conference in Valencia, Spain.

We ran 49 workshops and had 694 participants attending them. Thanks to the commitment of the workshop leaders and the participants' collaboration, we achieved an impressive 80% response rate. This innovative approach provided valuable insights and proved to be an environmentally friendly solution by drastically reducing paper use. The EPDC uses this feedback in its ongoing quality assurance process in workshops.

We extend our heartfelt thanks to everyone who took the time to provide their feedback. Your contributions are crucial in helping us improve and evolve our programmes. Let us continue to support and embrace this environment-friendly initiative to ensure our association remains at the forefront of sustainable practices.

Nick Thompson Fellowship Award

Established in 2001, The Nick Thompson Fellowship Award recognises service to EMWA above and beyond what would normally be expected of members or those who hold or have held elected offices (https://www.emwa.org/about-us/emwa-awards/nick-thompson-award/).

Nick Thompson, for whom this award is named, was a member of EMWA who embodied the collegial spirit, bonhomie, and professional dedication representing the organisation's core persona. He died tragically young. EMWA wishes to recognise and preserve those values that were so important to Nick.

Present holders of the Award are Julia Cooper, Stephen de Looze, Barry Drees, Art Gertel (Chair), Barbara Grossman, Sam Hamilton, Marian Hodges, Wendy Kingdom, Julia Forjanic Klapproth, Elise Langdon-Neuner, Phil Leventhal, Alistair Reeves, James Visanji, Raquel Billiones, and John Carpenter. The late Geoff Hall was an inaugural Nick Thompson Fellow.

The award confers lifetime EMWA membership and registration at association conferences on the elected Fellow. Fellows serve informally as advisors to the organisation, given their length of service, knowledge of the history of EMWA, and their involvement in the profession.

Nominations of candidates can be made by any EMWA member except a Nick Thompson Fellow or a sitting member of EMWA's Executive Committee (EC). Members of the EC may be nominated.

Nominations must be received by the EMWA Head Office by October 1, 2024. They must be accompanied by a statement of qualification, including details of the candidate's unique contributions to EMWA and justification for the nomination (not less than 200 words). The Fellows will consider all nominations and advise the EC via the President of the results of their deliberations.

If you know an EMWA member who would deserve this award, please submit your nomination to EMWA Head Office: secretariat@emwa.org (please do not inform the candidate that you have nominated them).

webinar

EMWA Professional Development Committee webinar

The next webinar will take place in October and the topic is European Clinical Trials Regulation 536/2014.
(Please see EMWA.org for additional details.)

Protection of personal data and commercially confidential information under the Clinical Trials Regulation (EU) No 536/2014

EMA "Revised CTIS Transparency Rules"

Merete Jørgensen[1], **Kathy B. Thomas**[2], **Matthias Zerm**[3], **Robert A. Paarlberg**[4]

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doi: 10.56012/frkj6889

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Abstract

The Clinical Trials Regulation (EU) No 536/2014 (CTR) came in force on January 31, 2022, specifying requirements for performing clinical trials in the EU and the European Economic Area (EEA). The CTR and the Clinical Trials Information System (CTIS) harmonise the approval process of clinical trials across the EU/EEA, provide a transparent process, and increase public access to information from clinical trials. Such transparency efforts must assure protection of personal data and commercially confidential information. The CTIS transparency rules were revised and recently implemented. The revised CTIS transparency rules focus on easier and earlier access by the public to documents of primary focus for patients and researchers. This article highlights the protection of personal data and commercially confidential information in public clinical trial documents according to the revised rules and also the EMA Policy 0070, which have overlapping transparency requirements. Medical writers and other functions involved in the preparation of regulatory documents during the clinical drug development play an integral role in applying transparency principles.

Clinical trial disclosure

The efforts to increase transparency of clinical trial information in the EU and the European Economic Area (EEA) are again in focus. Implementation of the revised Clinical Trials Information System (CTIS) transparency rules (RTR)[1] was triggered by feedback from the stakeholders after the initial launch of CTIS.

The RTR were adopted by the European Medicines Agency (EMA) Management Board on October 5, 2023, and implemented on June 18, 2024, with the launch of a new version of the CTIS public portal.[2] The RTR changes the previous requirements by reducing the amount of information submitted to EMA for public disclosure, simplifying processes for sponsors, striking a balance for protecting personal data (PD) and commercially confidential information (CCI), and focusing on simpler and earlier disclosure of information to patients and researchers. Information included in the clinical trial application (CTA) and marketing authorisation application (MAA) is made public via the CTIS public database. Public documents must comply with legislations that protect the PD of clinical trial participants and personnel involved. Information that qualifies as CCI may also be protected.

This article focuses on the protection of PD and CCI in public clinical trial documents, according to the requirements of the RTR of the CTR and also according to the revised EMA Policy 0070 (Policy 0070),[3] because of interrelated disclosure requirements. The EU legal terms, the hierarchy of laws, rank in authority and scope are summarised in Table 1.

CTR and CTIS

The CTR[4] was adopted in 2014 and entered into application on January 31, 2022, with the launch of the CTIS.[5] CTIS is a single point entry (portal and database) for the online system of regulatory submission, authorisation, and supervision of interventional clinical trials in the EU/EEA. CTR repealed the Directive 2001/20/EC Clinical Trials Directive[6] from 2004 that used the EU Drug Regulating Authorities Clinical Trials Database (EudraCT).[7] The CTR harmonises processes for assessment and supervision of CTAs throughout the EU/EEA and contains a set of requirements for performing an interventional clinical trial in the EU/EEA. Public disclosure of clinical trial information is just one of the aspects addressed.

CTIS[5] has been mandatory for all new interventional CTAs with medicinal products for human use in EU/EEA since January 31, 2023. Any EU/EEA trial initiated under the CTD with a foreseen completion in EU/EEA after January 30, 2025, is required to transition to the CTR and use CTIS ahead of the January 30, 2025, cutoff date.[8]

CTIS is the tool through which the CTR requirements are implemented, including the clinical trial disclosure activities. CTIS supports the flow of information between clinical trial

Table 1. Summary of legal terms for the EU/EEA

Term	Definition
Regulation	In the EU legal hierarchy, a *regulation* is directly applicable under EC law and automatically becomes part of national law of the 27 EU member states (plus the 3 EEA states Iceland, Norway, Lichtenstein). A regulation is likely to achieve the intended purpose of the law in a fast and harmonised way among all the EU/EEA member states.
Directive	A *directive* is not directly applicable under the EC law; EU member states are required to implement directives, but they can choose the form and methods of how to do that at a national level. This can lead to a protracted process that is often imbalanced in interpretation and realisation of the law among the EU/EEA states.
Policy	A *policy* may or may not have a legal basis. It is a set of instructions and processes prepared by the organization/agency entrusted with fulfilling certain requirements. In the context of clinical trial disclosure and transparency legal requirements, EMA has created relevant policies.

Abbreviations: EC, European Commission; EEA, European Economic Area; EMA, European Medicines Agency; MS, member state

sponsors, member state (MS) authorities, and the European Commission (EC). As shown in Figure 1, CTIS consists of two main domains: secure and open access. Sponsors and authorities use two separate workspaces in the secure domain. The open access domain of the CTIS database content is accessible to the public.

The RTR define which part of the information and documents in CTIS are destined for public disclosure and also the timeline when these are publicly disclosed. Documents in scope for public access may still contain elements of PD/CCI that should be protected:

- PD, according to Regulation (EU) 2018/1725[9] and Regulation (EU) 2016/679.[10]
- CCI, by taking into account the status of the MA for the medicinal product, unless there is an overriding public interest in disclosure.[11]

Additional laws for clinical trial disclosure

In addition to the CTR,[4] two other laws (both regulations) are applicable for disclosure and public accessibility of clinical trial information in the EU/EEA. Moreover, Policy 0070[3] for MAAs also affects documents for public disclosure. The interaction of the requirements is summarised below and depicted in Figure 2.

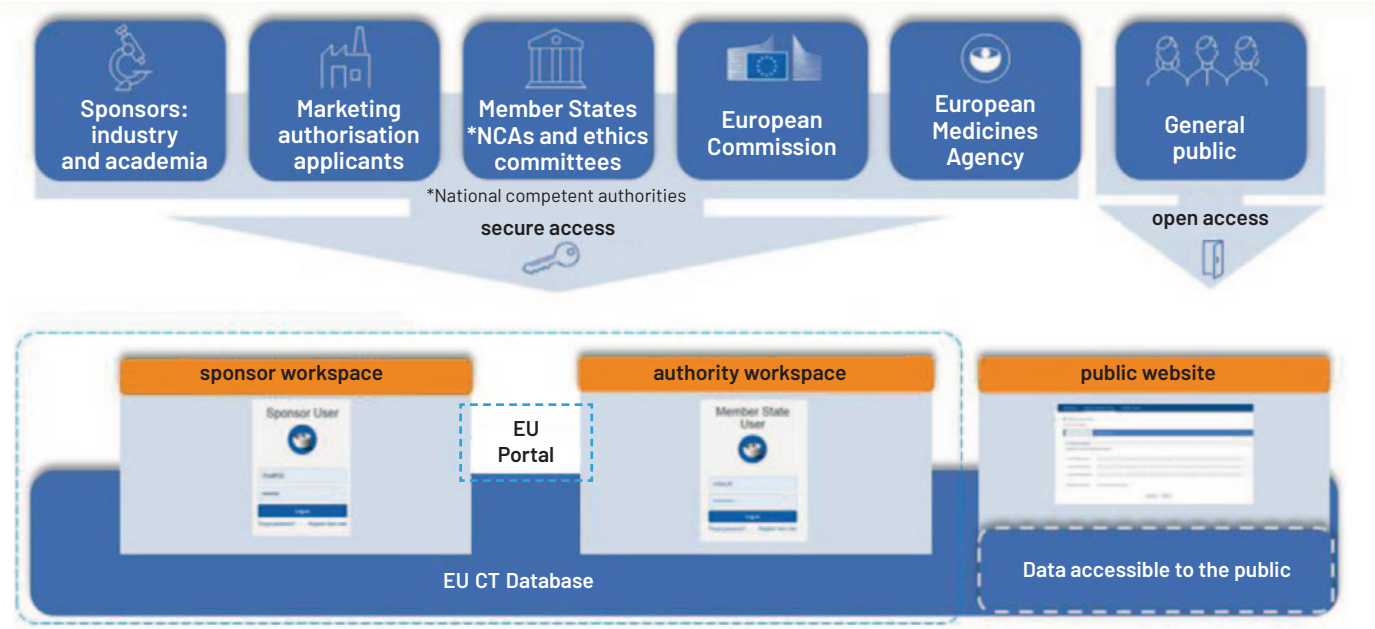

Figure 1. CTIS structure: domains, workspaces, databases

Figure is reproduced from the public EMA document Guidance document on how to approach the protection of personal data and commercially confidential information while using the Clinical Trials Information System (CTIS) Version 2.[11]

- **Paediatric Regulation No 1901/2006**[12] deals with medicinal products for paediatric use and drugs that have a potential use in the paediatric population within the EU/EEA. This regulation specifies shorter timelines i.e., 6 months after end of trial (EoT) for disclosure of results from paediatric trials and also for non-paediatric trials that are included in a Paediatric Investigational Plan (PIP).
- **General Data Protection Regulation No 679/2016 (GDPR)**[10] is an essential component of EU privacy and human rights laws. CTR (Article 93) references the GDPR regarding PD, available in the Guidance on protection of PD and CCI.[11,13]
- **Policy 0070**[3] deals with proactive disclosure of documents for products approved as part of an MAA in the EU/EEA through a centralised procedure.

Personal data and commercially confidential information

While the CTR sets aims for transparency through publicly accessible information, it also limits disclosure of PD and CCI. PD is not allowed in documents submitted to the public domain of CTIS unless specifically required by law. Clinical trial participants must be assured (through the informed consent process) that their PD and rights are protected against misuse. The overall rules for protection of PD are governed by the GDPR. Sponsors *may* need to protect CCI. Both PD and CCI should be redacted from the documents that are in scope for public accessibility *before* submitting them to CTIS.

> Both PD and CCI should be redacted from the documents that are in scope for public accessibility *before* submitting them to CTIS.

Responsibilities for PD by clinical trial sponsors and marketing authorisation applicant/holder

As defined by the EC,[14] PD is any information that relates to an identified or identifiable living individual. Separate pieces of information (direct or indirect identifiers), which when collected or combined can lead to the identification of a particular person, also constitute PD. For data to be truly anonymised, the anonymisation must be irreversible.

The processes and requirements governing the handling of PD in CTIS are described in the Joint Controllership Arrangement for CTIS,[15] the guidance on protection of PD and CCI,[11] Annex I,[16] and Question and Answer document.[13] Representatives from the sponsor, marketing authorisation applicant/holder (MAA/MAH) organisation(s) who use CTIS must adhere to the data protection rules and are responsible for protecting PD in publicly accessible documents.[13] As summarised below, four types of PD can arise in CTIS.

- **CTIS registered users:** These users are registered in the database "Identity Access Management" with their name, surname, and email address. This information is only for administrative purposes but is not published.
- **Clinical trial participants:** PD of trial participants may be contained in CTA documents submitted to CTIS, but it should be avoided in documents in scope for publication. PD of trial participants contained in clinical study reports (CSRs) must be protected by redactions and/or other anonymisation techniques.
- **Principal investigator (PI):** Names and professional contact details for the PI are submitted into CTIS and are published. The PI's curriculum vitae is submitted to CTIS but is not published.[1]
- **Sponsor/clinical staff:** Details on the sponsor/MAA/MAH contact point in EU and the legal representative in EU are required in CTIS but are not published.[1] Scientific and public contact points are required and are published;[11] use of generic functional mail addresses and phone numbers is recommended.

Protection principles for CCI

The EMA describes what is considered as CCI along with examples:

Any information which is not in the public domain or publicly available. When its disclosure may undermine the legitimate economic interest or competitive position of the concerned entities, e.g., clinical trial sponsors, MAA/MAH, or service providers.[11]

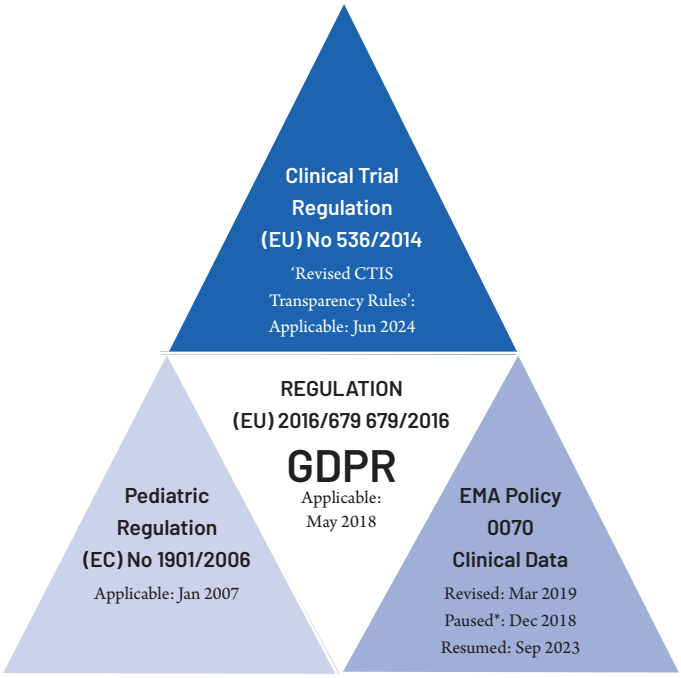

Figure 2. Legal and other requirements for disclosure of clinical trial information

*Activities were paused for all procedures except for clinical trials dealing with COVID-19; paused due to EMA office move from London to Amsterdam.

Table 2. Disclosure requirements* up to *and* after *June 18, 2024

Requirements *up to* June 18, 2024	Requirements *after* June 18, 2024
• All documents publicly accessible *except* for quality-related documents.	• Documents with key relevance for researchers and patients are publicly accessible.
• All versions of documents publicly accessible.	• Only the most recently approved versions of documents are publicly accessible.
• Deferral of document disclosure available to protect CCI.	• Deferral of document is not available. • Redaction of documents is recommended to protect PD and CCI.
• Almost all CTA data fields publicly accessible.	• Fewer CTA structured data fields publicly accessible.
• Historical trials (CTAs submitted *before* June 18, 2024) - publicly accessible for a large number of documents at a timeline that depends on the requested deferral by the sponsor and granted by MS.	• Historical trials (CTAs submitted before June 18, 2024) only structured data from CTIS are made publicly accessible for all trial categories. None of the documents submitted "for publication" before June 18, 2024 will be publicly accessible. • **Note:** Certain updates to a CTA will trigger public accessibility of documents that are in scope of the RTR.

Revised CTIS transparency rules' were adopted by the EMA Management Board on October 5, 2023, and implemented on June 18, 2024.

Abbreviations: CCI, commercially confidential information; CTA, clinical trial application; PD, personal data; RTR, revised CTIS transparency rules

Sources: RTR[1], Guidance on protection of PD and CCI, version 2,[11] and Annex I.[16]

CCI may be protected by redaction in the "for publication" version of documents while the "not for publication" version remains unredacted. It is assumed that as the drug development progresses, less information qualifies as CCI. After a decision on an MAA has been made (i.e., MA approved, rejected, or withdrawn), no information in the CSR should be considered as CCI.[11]

Revised CTIS transparency rules

The recent implementation of the RTR was accompanied by a release of the Guidance document,[11] its Annex I,[16] and other relevant documents,[1] based on the requirements of the CTR.[4] Further specifications are given in documents from the EMA: *CTIS application* fields[17] and *Notifications and results,*[18] which can be used to assess structured data fields and documents for each clinical trial category that incorporates the trial phase of clinical drug development.[19] The main changes in the RTR[1] and their implications as compared with the previous disclosure requirements are described in Table 2.

Structured data fields in CTIS

CTIS contains more structured data fields than the EudraCT database under the CTD. Details on publicly accessible information are available.[17,18] Information entered into the structured data fields in CTIS cannot be redacted and it is important to pay attention to the timing when

Abbreviations

CCI	Commercially confidential information
CHMP	Committee for Medicinal Products for Human Use
CSR	Clinical study report (synonymous for Clinical trial report)
CTA	Clinical trial application
CTIS	Clinical Trials Information System
CTR	Clinical Trials Regulation (Regulation (EU) 536/214)
EC	European Commission
EEA	European Economic Area (all EU countries plus Iceland, Norway, Lichtenstein)
EMA	European Medicines Agency
EoT	End of trial
EU	European Union
EudraCT	European Union Drug Regulatory Authorities Clinical Trials Database
FDAAA	Food and Drug Administration Amendments Act
GDPR	General Data Protection Regulation
ID	Identification (Subject ID)
MA/MAA/MAH	Marketing authorisation/Marketing authorisation application/Marketing authorisation holder
MS/MSC	Member State/Member State Concerned
PI	Principal investigator
PIP	Paediatric investigation plan
PD	Personal data
Policy 0070	Clinical Data Publication/EMA Policy 0070
RTR	Revised CTIS transparency rules
SmPC	Summary of product characteristics

Table 3. CTIS Documents **"for publication"** *and relevant disclosure timelines*

Documents To be submitted in two versions "for publication" and "not for publication"	**Publication timelines** Category 1 Paediatrics and/or PIP	Category 1 Adults	Category 2 and 3 including integrated ph1 & 2
Protocol, *including patients facing documents*	Upon results' submission	30 months after EU/EEA EoT	First MSC decision
Protocol synopsis			
SmPC, *if available*	Never		That MSC decision
Recruitment arrangements, *including procedures for inclusion and copy of advertising material*			
Subject information and **informed consent form**			
Lay person summary of results	As soon as submitted	30 months after EU/EEA EoT	As soon as submitted
Final summary of results			
Clinical study report, *if available*	As soon as submitted		

Abbreviations: EoT, end of trial; EU/EEA, European Union/ European Economic Area; PIP, paediatric investigation plan; SmPC, summary of product characteristics.

Source: This table is reproduced and slightly modified from the public EMA document Annex I, Table II.[16]

these will become publicly accessible. The timing depends on the category of the clinical trial,[19] the type of information, and whether the trial is in scope for the Paediatric Regulation.[12]

Documents in scope for public disclosure in CTIS

Documents designated as "for publication" and relevant disclosure timelines according to the RTR (see Table 3). Documents must be submitted to CTIS as "disclosure-ready". If redaction is needed to protect PD and CCI, the documents must be submitted as two versions by the sponsor – "for publication" (publicly accessible) and unredacted "not for publication" (for regulatory assessments). To guarantee the correct channelling of the documents, their electronic upload into CTIS must be made in the correct order.

Documents in scope for publication that are expected to contain PD should be checked and redacted, as described below and in Table 4.

- **Clinical trial protocol, protocol synopsis**, and **patients facing documents related to trial endpoints** (such as patient informed consent forms and recruitment arrangements) will be publicly accessible for all trials. For Category 1 trials in paediatrics or trials included in a PIP, the public disclosure will be at the time of summary results submission; for trials in adults, at 30 months after the end of trial (EoT) in the EU/EEA. For Category 2 and 3 trials, public disclosure will occur at the first member state concerned (MSC) decision on the CTA submission.
- **Subject information, informed consent form, recruitment arrangements,** and **SmPC** will be publicly accessible *only* for Category 2 and 3 trials, upon MSC decision on the CTA submission.
- **Lay person summary of results, summary of results,** and **CSR** (if applicable) will be made public as soon as submitted to CTIS; exception to this are Category 1 trials in adults, which will be made public 30 months after EoT in the EU/EEA (Table 3).

Timelines for clinical trial results-related documents

The information in Table 3 shows when the various clinical trial documents become *publicly accessible*. However, the timelines for when the documents are *due for submission* to the regulatory authorities via CTIS are defined in the CTR[4] and in the Paediatric Regulation[11] (Table 5). It is important to distinguish between the two sets of timelines and understand their implications. For example – results summaries for a Category 1 trial in adults will be *publicly accessible* 30 months after EoT; however, for regulatory purposes, such documents need to be *submitted* to CTIS 12 months after EoT.

> Special considerations are noteworthy for CSRs used in an MAA.

Structured data fields and documents *not* destined for public access

A list of structured data fields and documents that are *not* intended for public access is shown in Table VI in Annex I,[16] which specifies documents that are required for *submission* to CTIS and indicates the expectations of the EMA regarding the presence of PD.[17,18]

Special considerations are noteworthy for CSRs used in an MAA. This is because CSRs are in scope for public disclosure according to both the CTR, at a single clinical trial level[4] – and according to the Policy 0070, at a MA dossier level (Table 6). In the CTR, reference is made to Policy 0070 regarding the disclosure of CSRs. A comparison between the two sets of requirements, specifically regarding the CSR, is shown in Table 7. Thus, the earliest public access to CSRs will most likely be in CTIS through the CTR. How such an early public access to the CSR will affect the Policy 0070 process remains

Table 4. Documents* "for publication"*; templates and personal data usually included

Documents **To be submitted in two versions "for publication" and "not for publication"**	**Personal data** **To be anonymised in the doc version "for publication"**	**Websites on the standard templates**
Protocol, including patients facing documents	Personal details of sponsor staff, including signatures	https://www.ema.europa.eu/en/ich-m11-guideline-clinical-study-protocol-template-and-technical-specifications-scientific-guideline
Protocol synopsis		
SmPC, *if available*	Not expected	https://www.ema.europa.eu/en/human-regulatory-overview/marketing-authorisation/product-information-requirements/product-information-templates-human and, for Nationally Authorised Products: https://www.hma.eu/human-medicines/cmdh/templates/qrd.html
Recruitment arrangements, *including procedures for inclusion and copy of advertising material*	Name, surname or identifying element of PI (to be disclosed) or of other individual(s) including trial site personnel	https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-authorised-under-regulation-eu-no-5362014
Subject information and informed consent form		
Lay person summary of results	Not expected	https://health.ec.europa.eu/document/download/8a42b8f5-4ec3-4667-969c-3dd89ea8b270_en?filename=glsp_en.pdf
Final summary of results	Personal details of sponsor staff, including signatures	
Clinical study report, *if available*	Pseudonymised data of trial participants	https://database.ich.org/sites/default/files/E3_Guideline.pdf

Abbreviations: CTIS, Clinical Trials Information System; CTR, clinical trial report; PI, principal investigator; EoT, end of trial; SmPC, summary of product characteristics.
Source: This table is reproduced from the public EMA document Annex I, Table III.[16]

Table 5.* Submission *timelines for final clinical trial summary results and for lay persons summary of results to MSC via CTIS

Trials with *only adult subjects*

- The timeline for submission of summary documents to CTIS is 12 months after EoT in the EU/EEA.*
- Information on study centre(s) outside the EU/EEA must be captured in the trial protocol and the definition of the global EoT specified, in case the timeline for submission is required to be relative to the global end of trial.
- Documents will be publicly accessible immediately upon submission to CTIS (trial Category 2 and 3 in adults).
- Documents will be publicly accessible at 30 months after the end of the trials in EU/EEA (Category 1 trials in adults).

Trials with *paediatric subjects* and *trials included in a PIP*

- The timeline for submission of summary documents to CTIS is 6 months after trials completion in the EU/EEA.*
- Information on study centre(s) outside the EU/EEA must be captured in the trial protocol and the definition of the global end of the trial specified in case the deadline for submission is required to be relative to the global end of trial.
- The documents will become public immediately upon submission.
- **Note:** The paediatric requirements apply not only to paediatric trials performed in the EU/EEA but also to non-paediatric trials (i.e., adult trials) that are included in a PIP, and under special circumstances, also paediatric trials performed in 'third countries' (outside EU/EEA), as described in Table 6.

Intermediate/Interim (terms used synonymously) trial results summaries

- Intermediate/interim trial results summaries (if specified in the trial protocol) must be submitted to MSC via CTIS when available but will not be publicly accessible.

Abbreviations: EoT, end of trial; EU/EEA, European Union/ European Economic Area; PIP, paediatric investigation plan. Sources: CTR,[4] Paediatric Regulation No 1901/2006,[12] and Annex I, (Table II).[16]
*If a trial has sites outside of EU/EEA, and the global end is required to be considered for such countries, the expected EoT must be described in the trial protocol. Otherwise, the trial results are required 12 months after EoT in EU/EEA.

Table 6. Overall requirements of CTR[4] and EMA Policy 0070[3]

Clinical Trials Regulation (EU) No 536/2014 Clinical Trials Level	EMA Policy 0070 Clinical Data Dossier Level
• All clinical trials performed in EU/EEA.Trials performed outside EU/EEA that are part of PIP. *Note: requirements apply to non-paediatric included in a PIP (i.e. trials in adults).* • Paediatric trials using IMP with EU marketing authorisation and sponsored by MAH, whether or not included in a PIP or whether performed in or outside EU/EEA. • Channel for publication of documents: CTIS Portal applicable: January 31, 2022; Revised: June 18, 2024. Clinical Trials website	• All clinical reports submitted in the regulatory marketing authorisation to EMA. Applies to centrally authorised products only. • Clinical trials performed in EU/EEA or outside EU/EEA ('third countries'). • Channel for publication of documents: EMA Clinical Data publication website. Applicable 2015/Revised 2019. Paused* December 2019; Resumed September 2023. EMA Clinical Data website

*Paused for all procedures except for clinical trials dealing with COVID-19 (paused due to EMA office move from London to Amsterdam)

Abbreviations: CTIS, Clinical Trials Information System; EU/EEA, European Union/ European Economic Area; MAH, marketing authorisation holder; PIP, paediatric investigation plan

Source: Modified from a public EMA document Clinical Data Publication: Comparison with the Clinical Trials Regulation.[20]

to be clarified by the regulators, as summarised in Table 6 and Table 7.

Role of medical writers in clinical trial disclosure activities

Increasing transparency and disclosure of clinical documents has intensified the role of medical writers, from the primary focus of complying with regulatory requirements to also balancing transparency obligations by preparing documents suitable for the public while protecting PD and CCI. Typical documents such as CSR have to be disclosure-ready and disclosure-friendly at the time of creation, with minimal need for time-consuming redaction. Supporting documents regarding the clinical trial disclosure processes and activities are available from the EMA.[19,21]

Supporting documents regarding the clinical trial disclosure processes and activities are available from the EMA.

Minimisation of information and disclosure-ready documents

- Reduce PD and CCI to what is necessary by regulatory requirements. Consider the information that is provided in CTIS in both the structured data fields and the submitted documents. For redacted documents, retain sufficient level of data utility of the information.
- Avoid details of trial participants in patient narratives. Use: month and year for date of birth; relative number of days from trial start; world region instead of a specific country.
- Keep information on clinical trial sponsor and other staff involved to a minimum.
- For scientific and public contact points, use generic functional email and phone number.
- Avoid replicating paragraphs/statements *within* and *between* documents; use cross-references (including electronic links).
- Avoid (or redact) all authors' signatures in documents versions *'for publication'*.
- Use clear naming convention for files to ensure *submitting* documents into the correct electronic slot of CTIS.
- Keep an overview of the company's transparency policy; monitor information made publicly available not only via CTIS but also in the sponsor websites, conference presentations, and global public databases.

PD protection and legal requirements

- PD of trial participants is only allowed if needed for regulatory assessment in the "not for publication" version and must be redacted in the "for publication" version *before* uploading to CTIS.
- Principal investigator names and contact details are legally required and should not be redacted. Redact all signatures. For contact details, use functional non-personal phone numbers and email addresses.
- In documents not destined for publication,[11,16] some PD data may be required for the regulatory assessment; i.e. names and surnames of certain functions/roles are expected in the "not for publication" version, and must be redacted in the "for publication" version, e.g., person issuing the site suitability document and composition of the Data Safety Monitoring Board.[13]
- Remove PD from document metadata (within document properties) *before* submitting to CTIS.

CCI protection

- For CCI identification processes, sponsors should involve experts with relevant scientific and technical skills, including patent legal counsel and follow a consistent decision-making process.
- Follow the principles for CCI protection described for Policy 0070.[3]
- Study protocols become public in most cases immediately after the decision by the first MSC; this implies careful consideration of CCI protection.
- For Category 1 trials in adults, the protocol is disclosed at a later time than for other trials. Nevertheless, consider a situation when a trial ends earlier than planned and thus information is public earlier than anticipated.

Table 7. Specific requirements of CTR[4] and EMA Policy 0070[3] for Clinical Study Reports

Clinical Trials Regulation (EU) No 536/2014	EMA Policy 0070
Scope of MAA documents	
• CSR of trials performed under the CTR and used in an MAA in the EU/EEA.	• Clinical overview, clinical summaries and CSRs of trials globally used for a centralised MAA in the EU/EEA
Scope of content in individual clinical study report documents	
• CSR, as used in the MAA with appendices, except those listing individual patient data.[15]	• CSR body including specific appendices 16.1.1 (trial protocol), 16.1.2 (sample CRF), and 16.1.9 (Statistical Analysis Plan).
Timelines for *submission* and *disclosure* of documents	
• CSR to be *submitted* within 30 days after MAA decision, and made public immediately thereafter.	• Timeline for submission of MAA dossier package depends on the opinion of CHMP. • Package of documents (Clinical Data) is made publicly available after EMA review and approval. • For approved products, public disclosure is expected 60 days after Commission decision; for withdrawn applications 150 days after receipt of the withdrawal letter.
Procedure	
• MAA/MAH to *submit* the CSR appropriately redacted/anonymised for PD and CCI. • CSRs will be publicly accessible immediately upon upload to CTIS. • No Anonymisation Report should be submitted, unless specifically required.	• MAA/MAH to submit the package of documents in scope for Policy 0070, including Anonymisation Report and a set of justification tables (not for publication) for the proposed CCI redactions. • Pre-meeting and consultation contact and process are offered by EMA.
Public access to CSR	
EU Clinical Trials • Clinical Trials website	**Clinical Data** • EMA Clinical Data website

Abbreviations: CCI, commercially confidential information; CSR, clinical study report; CTA, clinical trial application; CTR, Clinical Trials Regulation (Regulation (EU) 536/214); CHMP, Committee for Medicinal Products for Human Use; EU/EEA: European Union/ European Economic Area; MAA, marketing authorisation application; PD, personal data.

CSR - additional considerations

- CSR is likely the document that contains most of the PD information that needs redaction/anonymisation. Details of process alignment for the public disclosure of CSR in scope of the CTR and Policy 0070 are not yet available from the regulators.
- For safety information in the Annual Safety Reports that is potentially also included in the CSR, the Worldwide Unique Case Identification (ID) Number (case ID) and the trial ID should be used for referencing a trial participant rather than the subject ID.[13,22]

Disclaimer

The views expressed in this article are the personal opinions of the authors and do not necessarily reflect the position of the authors' affiliated organisations.

Disclosures and conflicts of interest

The authors declare no conflicts of interest.

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Making the leap: Transparency requirements for clinical trials moving from one regulatory framework to another

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doi: 10.56012/ghkj9468

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Abstract
This article discusses the fast-approaching deadline for sponsors to transition ongoing clinical trials in the EU/European Economic Area from the Clinical Trials Directive 2001/20/EC to the Clinical Trials Regulation 536/2014. In particular, the authors discuss the medical writer's crucial role in ensuring that documentation meets the regulation harmonisation and transparency requirements; they also highlight challenges seen when redacting commercially confidential information in the preparation of transition applications.

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Transitional trials and the imminent deadline

From January 31, 2025, onwards, only the Clinical Trials Regulation (CTR: Regulation [EU] 536/2014)[1] and its delegated acts will apply to clinical trials in the EU. This deadline will mark the end of a 3-year transition period that started when the CTR became applicable in the EU on January 31, 2022. All ongoing clinical trials currently governed by the Clinical Trials Directive 2001/20/EC[2] and expected to continue in the EU/European Economic Area (EEA) after January 2025 must transition to the CTR regulatory framework, per the European Commission guidance for the transition of clinical trials.[3] If such clinical trials have not transitioned to the CTR by that date, they will be considered non-compliant and in breach of the CTR. Sponsors could, therefore, be subject to corrective measures and penalties by member states (MSs) and civil and criminal liability pursuant to Article 77 of the CTR.

Sponsors of those clinical trials expected to continue after this deadline must submit a transition application. It is strongly advised to submit the transition application promptly to ensure sufficient time is given for approval. To help streamline the process for multinational transition applications, MSs will implement, where possible, an expedited, harmonised evaluation procedure as agreed by the Clinical Trial Coordination Group (CTCG)[4] for transitioning trials to the CTR. This expedited procedure is open until October 16, 2024.

Transitional application preparation

Prior to proceeding with a transition application, the first step is to evaluate if the clinical trial is in line with the principles of the CTR. Early consideration must be given to any document harmonisation requirements for multinational clinical trials. Documents common to all MSs that are covered by the CTR Part I assessment report (e.g., protocol, investigator brochure and investigational medicinal product dossier) are to be either consolidated or harmonised. As per the CTCG guidance,[4] harmonisation means that the respective document(s) are identical and include the same trial procedures across all MSs. Consolidation is when there are substantial differences in the respective document(s) in different MSs but the document itself is identical, i.e., MS-specific issues are outlined within the document text or in an appendix to the respective document. If harmonisation is required, this must be first submitted as a substantial amendment under the Clinical Trials Directive prior to a transition application. The role of the medical writer is of importance here to support the regulatory submission team to ensure that documents meet these requirements prior to transition.

Transition of a minimum dossier

The transition application is an administrative process. The assessment by MSs is reduced to the minimum to ensure compliance with the CTR rules, including transparency requirements. When transitioning a minimum dossier, teams must prepare redacted versions of the protocol, subject information sheets and informed consent forms in addition to submission of the non-redacted documents already approved by the MS. Box 1 shows the minimum dossier documentation. This is applicable for all trial categories, except category 1 trials, where it is sufficient to provide a redacted version of the protocol only, in line with the revised Clinical Trial Information System (CTIS) transparency rules.[5]

After approval of a transition application, teams must ensure that at the time of the next substantial modification, redacted versions for publication of those documents that are within the scope of the revised CTIS transparency rules (as per Annex I) must replace these minimum dossier documents. Resources must, therefore, be considered not only for the transition application but also the next substantial modification.

What are the consequences of transitioning a study?

Clinical trials that transition have to comply with the obligations of the CTR. Documents submitted as part of a transition application fall under the transparency requirements and will be made publicly available. The public website[6] has a searchable function that can be used to find detailed information on clinical trials from January 31, 2022, based on the information contained within CTIS.

Practical consequences of CTIS on transitional studies

This transition has resulted in an increased burden of documentation for sponsors. Effectively managing this documentation presents several challenges. Clear communication and a well-defined understanding of responsibilities are crucial, particularly in strategising redactions and adhering to strict timelines. This is especially important when responding to requests for information, given the limited 12-day maximum response window. A rapid response team, including medical writers, should be available to update documentation to ensure timely translations and appropriate redaction within this strict timeline.

> The transparency rules introduced with CTIS have heightened awareness of the importance of appropriate timing in the disclosure of any full or segmented information related to an active clinical trial.

Although the regulations for the redaction of personally protected data are clear and anchored in the widely recognised General Data Protection Regulation[7] and CTR standards, the scope of commercially confidential information (CCI) redaction poses a significant challenge in the preparation of dossiers for CTIS publication. A collaborative approach involving teams from medical writing, regulatory, transparency, and often legal, is essential, as CCI is unique to each company and often to each product or study. A clear definition of CCI, provided early, enables the medical writing team to draft documents that minimise CCI content. However, protocols and subject information sheets or informed consent forms for active trials transitioning from EudraCT to CTIS are rarely composed proactively with CCI considerations. The most significant hurdle in transitional trials is balancing the risk of over-publication, which could reveal excessive CCI, against over-redaction, which frequently stems from a sponsor's limited comprehension of what constitutes CCI in their documents.

Short vs. long-term CCI

According to EMA guidance[8] the concept of CCI is time-dependent, with a particular focus on the development phase of the medicinal product used in a clinical trial. The revised CTIS transparency rules[5] have removed the deferral mechanism that allowed sponsors to delay the publication of key clinical trial documents for up to 7 years from the end of the trial in the EU/EEA. In the context of this change, for transitional trials, it is important to differentiate between CCI that is applicable in an earlier development phase at the time of submission of a clinical trial application and CCI during the trial life cycle.

Publicly available information

Information that is already in the public domain cannot be considered CCI. For this reason, conducting a literature search for publicly available information is a standard part of the redaction process. With transitional trials underway, there is an increased likelihood that data may be prematurely published, particularly on sponsor websites, through conference presentations, and in scientific articles they have published. If the information sponsors wish to redact is even partially available in the public

Box 1. Minimum dossier documentation

General documents: form section

- Cover letter
- Statement of compliance with regulation (EU) 2016/679
- Proof of payment (if applicable)
- EU application form (to be completed in the Clinical Trial Information System portal)

Part 1 documents

- Clinical trial protocol (latest harmonised or consolidated version)[a]
- Investigator brochure (latest harmonised or consolidated version)[a]
- Good manufacturing practice relevant documents, e.g., manufacturer's importation authorisation
- Investigational medicinal product dossier (latest harmonised or consolidated version)[a]
- Latest approved version of documents related to non-investigational medicinal products, if applicable

Part 2 documents

- Latest approved versions of the subject information sheet(s) and informed consent form(s)[a]

[a] Clinical documents written by medical writing teams that are affected.
Please refer to guidance for the transition of clinical trials, annex 1, for country-specific requirements.[3]

Photo: Unsplash Sammie-Chaffin

domain, it can impact the planned redaction strategy for information-dense documents such as the protocol. For example, a dose escalation scheme for one cohort that was presented at a scientific conference and made publicly available as a PowerPoint presentation could compromise the sponsor's intention to protect the overall dose escalation plan as CCI. The transparency rules introduced with CTIS have heightened awareness of the importance of appropriate timing in the disclosure of any full or segmented information related to an active clinical trial.

Licence-protected material

The protection that should be applied to service providers (for example vendors for scales and questionnaires) does not fall under CCI, but it is a highly sensitive matter for transitional trials. The EMA recognised the issue[9] and introduced the option for sponsors to upload a placeholder for licence-protected material where the sponsor and the third-party service provider have written agreements in place that expressly establish that patient-facing documents cannot be disclosed publicly. Standard contractual clauses between sponsors and vendor companies usually provide approval for using copies of the vendor's intellectual property for regulatory submissions. Some of the clinical trials transitioning to CTIS signed their contracts with vendor companies before they were aware that all patient-facing material related to study endpoints would become publicly available when the clinical trial was posted on CTIS; considering this, it is unlikely that this provision was included as a standard contractual clause. In essence, vendors agreed that their intellectual property would be reviewed by regulatory authorities, but they may not have been informed or consented to the same material being available to the public. Public disclosure could undermine their economic interest or competitive position; hence, reassessing the vendors standing under these new circumstances is necessary

> With the revised CTIS transparency rules, site-level documents are no longer subject to publication, which has significantly decreased the workload for transparency teams.

National requirements

The industry has noted that MSs continue to impose national requirements on submission documentation. This practice has not spared the CTIS transparency rules for transitional trials, even now when a minimum dossier requires a minimum number of documents. For instance, for reimbursement and insurance amounts provided in subject information sheets and informed consent forms, the majority of MSs approve the redaction of such details, while some states require the disclosure of these types of financial agreements. Applying different redaction strategies to the same document types that will all eventually be available on the public CTIS portal as part of the same package cannot be an example of good transparency practice.

Improvement

Before the revised CTIS transparency rules became effective, the greatest challenge in protecting personally protected data lay in managing site-level documents, primarily due to the sheer volume of such documentation. These included investigator curricula vitae and site suitability forms that were created using non-standardised templates, and which varied by country or site. The information in these documents often contained unnecessary personal details of investigators and third parties, such as nationality, family status, home addresses, names of mentors and supervisors, personal photographs, and names of site personnel, necessitating extensive redaction. Although a slight improve-

ment was made with the introduction of standardised Part II application document templates,[10] ensuring that sites actually used the EMA template was nearly impossible. With the revised CTIS transparency rules, site-level documents are no longer subject to publication, which has significantly decreased the workload for transparency teams.

Conclusion

For clinical trials that are expected to continue in the EU/EEA after January 30, 2025, it is advisable that transition applications be submitted at the earliest date to ensure sufficient time for approval. Study teams, including medical writers and transparency specialists, must collaborate to assess the time required to prepare this package, ensure appropriate documentation consolidation and harmonisation, and apply the necessary redactions to comply with the CTR transparency requirements.

Disclaimers

The opinions expressed in this article are the authors' own and not necessarily shared by their employer or EMWA.

Disclosures and conflicts of interest

The author declares no conflicts of interest.

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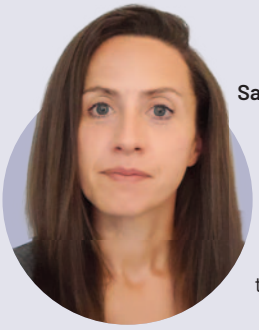

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Navigating the complex landscape of clinical trial transparency: What medical writers need to know

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doi: 10.56012/timm8993

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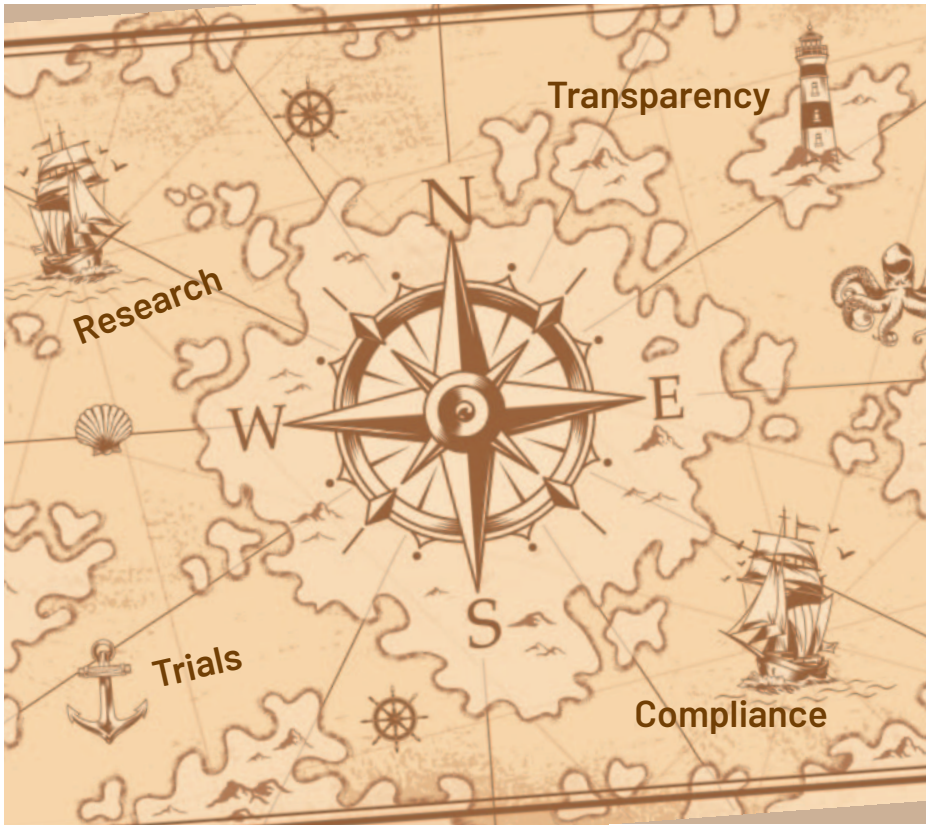
Abstract

Clinical trial transparency is beneficial for patients, researchers, and the general public. However, rapidly evolving regulatory requirements for transparency have increased the information that will be published. Medical writers can play a key role in driving compliance with applicable regulations. This paper provides an overview of transparency regulations and provides some points for medical writers to consider in this rapidly evolving area.



Introduction

The transparency of clinical research has been increased through voluntary initiatives and regulations. This has helped inform patients about clinical trials, reduced reporting bias and selective publication of data, provided information for secondary research, and fostered greater public trust in clinical research (Figure 1).[1]

A multitude of transparency-related regulations now applies from the start of clinical trials through to marketing authorisation applications.[2] Consequently, the regulatory framework governing transparency is ever more challenging to navigate. The scope of transparency is increasing and there is little harmonisation across regional regulations or transparency platforms.

Medical writers play an important role in the generation of information required for transparency and therefore need to be familiar with

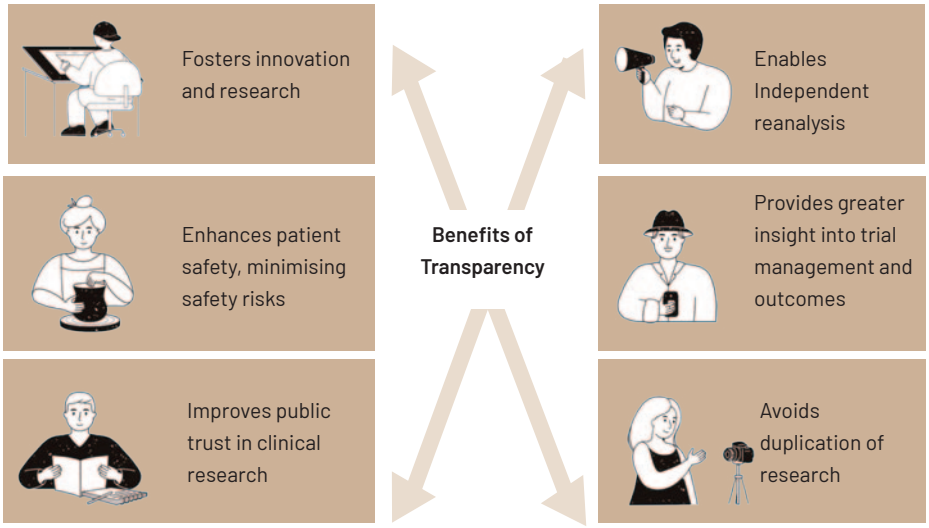


Figure 1. Benefits of transparency

relevant requirements. This article provides an overview of the main transparency regulations and offers some key points to consider for medical writers involved in transparency activities.

Types of transparency requirements

Transparency requirements can be broadly considered in 3 categories (Figure 2):

1. **Clinical trial registries:** Providing information on planned, on-going, and completed clinical trials, usually through a searchable interface
2. **Data and document sharing:** Publishing of clinical trial documents and data that have been suitably anonymised to protect personally protected and company confidential information
3. **Plain language writing:** Presenting clinical research information in language that is accessible to those without a scientific or medical background.

Clinical trial registries

Prospective trial registration on a public registry has been an obligation for medical researchers since the FDA Amendments Act of 2007 (known as FDAAA)[3] and the World Medical Association's 2008 revision of the Declaration of Helsinki (WMA, 2013).[4] Various clinical trial registries have been established across the globe and compliance with these is often mandatory. Trial sponsors must upload protocol information to registries prior to recruiting trial participants, maintain this information during the trial, and post summaries of trial results after trial completion.[5,6] There are similarities between registries, but differences include the studies in scope, the information required, and timelines. The section below highlights some of the main differences between the largest registries.

In addition to regulations, a significant incentive for researchers is that since 2004, the International Committee of Medical Journal Editors (ICMJE) has stipulated that registration of trials in a public database is a precondition for publication of trial results.[7]

Penalties for not adhering to registry requirements include monetary fines, but perhaps the greatest incentive is the risk to reputation as lists of organisations that are not compliant are frequently published.[8]

US

The ClinicalTrials.gov registry provided by the US National Library of Medicine (NLM) was launched in February 2000. It is the largest global registry with approximately 500,000 studies from over 200 countries.[9] This website provides patients and their advocates, health care practitioners, researchers, and the general public access to information on publicly and privately funded clinical research trials for a wide range of diseases and medical conditions. In June 2024, the NLM launched a modernised ClinicalTrials.gov website which enhances the user experience and provides greater functionality for searching, viewing, and downloading clinical trial information.[10] ClinicalTrials.gov registry requirements are presented in Table 1.

European Union/European Economic Area

The European Union (EU) clinical trials registry, the EU Drug Regulating Authorities Clinical Trials database (EudraCT), was launched in 2004. This currently contains almost 44,000 clinical trials with a EudraCT protocol.[11] The EMA has, over the last 2 years, introduced EU Clinical Trials Regulation 536/2014 (EU-CTR) that has increased the amount of clinical trial related information required for publication.[12] This information is submitted during the clinical trial application (CTA) process through a portal called the EU Clinical Trial Information System (CTIS). CTIS will replace EudraCT as the EMA's clinical trial registry from January 2025.

The EMA implemented in June 2024 a new version of the CTIS portal and revised the transparency rules.[13] The revised rules reduced the scope of publication to key documents of interest. The deferral mechanism was also revoked, meaning that sponsors must rely on redaction as the method to protect personally protected data (PPD) and company confidential information (CCI) within published documents.[14]

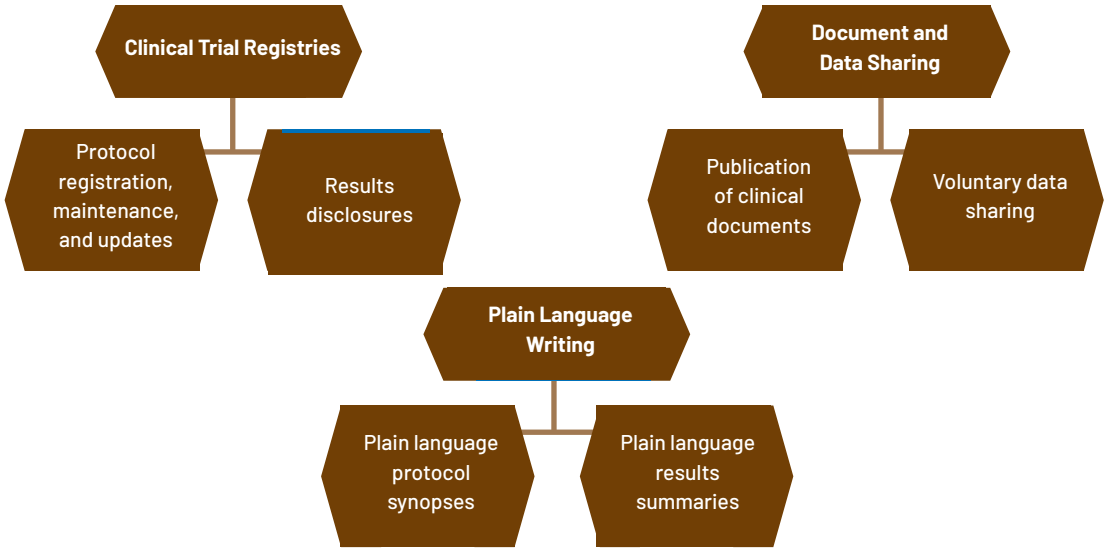


Figure 2. Categories of transparency

Table 1. Clinical trial registry requirements in the US and EU/EEA

Requirements	USA	EU/EEA
Applicable regulation	Created under the FDAMA of 1997 and expanded in the FDAAA of 2007	Initially governed by EU Clinical Trial Directive 2001/20/EC (EU-CTD); from January 31,2022, EU Clinical Trial Regulation No. 536/2014 (EU-CTR) applied
Scope	Controlled clinical investigations of drugs, biologics or medical devices (excluding Phase I studies) with at least 1 of the following: ● At least one US site ● Conducted under an FDA IND or IDE ● Involves a drug, biologic, or device manufactured in the US and exported for research	● All interventional trials on medicinal products submitted to National Competent Authorities of the EU/EEA ● All trials conducted outside of the EEA that are part of a PIP or are conducted under Article 45 or 46 of Regulation (EC) No 1901/2006
Information included	● Trial information ● Summary results (with some adverse event information) ● Redacted protocol and statistical analysis plan ● Indication of plans to make IPD and data dictionaries available	● Structured data fields containing trial information ● Documents including but not limited to protocol, protocol synopsis, plain language protocol synopsis (optional), patient facing documents, subject information sheets, informed consent forms ● Scientific summary of results, plain language summary of results, CSRs
Timelines	● Trials should be registered within 21 days of the first participant enrolled ● Summary results should be provided within 12 months of the trial's primary completion date	● Timelines for documents publication is based on the trial category*, defined in the revised transparency rules

Abbreviations: CSR, Clinical Study Report; EEA, European Economic Area; EU, European Union; FDA, Food and Drug Administration; FDAAA, FDA Amendments Act; FDAMA, FDA Modernisation Act; IDE, Investigational Device Exemption; IND, investigational new drug; IPD, individual participant data; PIP, paediatric investigation plan.

*Category 1 Trials: Phase 0 and Phase I clinical trials in healthy volunteers or patients, bioequivalence and bioavailability trials, biosimilarity trials

Category 2: Phase I and Phase II integrated clinical trials, Phase II and III clinical trials

Category 3: Phase III and Phase IV integrated clinical trials, Phase IV clinical trials and low interventional clinical trials

A comparison of the clinical trial registry requirements in the US and European Union/European Economic Area (EU/EEA) are presented in Table 1.

Other countries and regions

By creating their own clinical trial registries, countries can gather data to support local policy-making and healthcare decisions. Consequently, dozens of national clinical trial registries now exist.

The WHO operates the International Clinical Trials Registry Platform (ICTRP). This is not a clinical trials registry, but it facilitates access to trial information from various primary registries within its network, including ClinicalTrials.gov.[15]

In the UK, the Health Research Authority requires sponsors to register clinical trials in a publicly accessible database before they begin, report results within 12 months of trial completion, and make lay summaries of trial results available to the public.[16]

Other countries also mandate registration of trials either in a national registry or on a globally recognised registry or platform such as WHO ICTRP. Currently, this also applies, but is not limited to, Australia, Brazil, China, India, Iran, Israel, Japan, South Africa, South Korea, Sri Lanka, Taiwan, and Thailand.

Data and document sharing

Clinical trial registries initially provided limited information. The transparency domain has now evolved to provide direct access to certain clinical study documents and datasets. This adds complexity as these documents and datasets may contain PPD and/or CCI that must be appropriately redacted before documents are published. This section describes current key data and document sharing initiatives.

US

- **Freedom of Information Act (FOIA):** Allows any individual or organisation to request access to US federal agency documents. The FDA shares these documents unless they fall within one of nine exemptions or the information has been lawfully disclosed to the public.[2] The FDA received over 11,000 FOIA requests in 2022.[17] These requests cover a variety of topics including 510(k) submissions for medical devices, inspection reports, and compliance documentation such as Form 483 observations. The processing time for these requests varies based on their complexity and sensitivity.
- **NIH Final Rule:** The NIH mandates the publication of redacted versions of protocols and SAPs on ClinicalTrials.gov.[18]
- **FDA's Pilot Programme for Redacted Clinical Study Reports (CSRs):** In 2018, FDA initiated a pilot programme to make

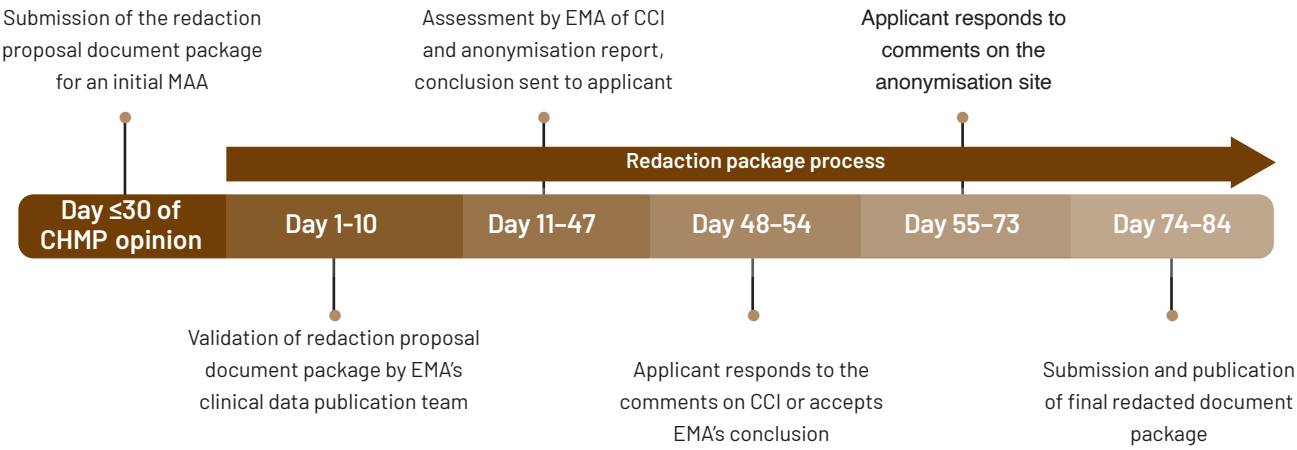


Figure 3. EMA Policy 0070 timeframe

Abbreviations: MAA, marketing authorisation application; CCI, company confidential information

CSRs more accessible to the public. However, on its conclusion in 2020, no additional steps were taken, with the FDA citing concerns about "inefficiencies in having multiregional disclosure requirements relating to often identical clinical data summaries".[19]

European Union/European Economic Area

EMA Policy 0043

EMA Policy 0043, developed in accordance with EU Regulation 049/2001/EC and effective since 2010, outlines the rules for requesting access to documents held by the EMA.[20] Requests can be made for clinical and certain non-clinical documents subject to certain conditions. The EMA can refuse access to a document if disclosure would undermine public interest, an individual's privacy, commercial interest, or court proceedings unless there is an overriding public interest in disclosure. The EMA redacts PPD and CCI from these documents and sponsors can request additional redactions.

EMA Policy 0070

EMA Policy 0070 mandates the publication of clinical trial data within 30 days of a CHMP opinion (Figure 3).[21] The scope of the policy currently includes disclosure of clinical documents only; Phase 2, to be introduced at a date yet to be specified, will require the publishing of individual participant data. Applicants must demonstrate that they have suitably anonymised PPD in documents and can also redact certain CCI if a robust justification is provided. Failure to comply with the policy results in the issuance of a non-compliance notice; financial penalties are not currently imposed. The details of the scope of EMA Policy 0070 are presented in Table 2.

EU-CTR: Requires sponsors to publicly share, through CTIS, redacted versions of Part I documents (scientific and medicinal product related) and Part II documents (national and patient-level) as part of the CTA process.[12] Further details on EU-CTR have been discussed in the previous section.

Canada

Health Canada's Public Release of Clinical Information (PRCI) policy, effective since 2019, makes anonymised clinical data from drug submissions and medical device applications available to the public.[22] It includes mandatory disclosure of new marketing approval submissions with final regulatory decisions made after March 2019, and, on request, prior to this date. (See Figure 4 for a timeline of Canada's PRCI timeline.) The documents in scope and the need to redact personal and confidential business

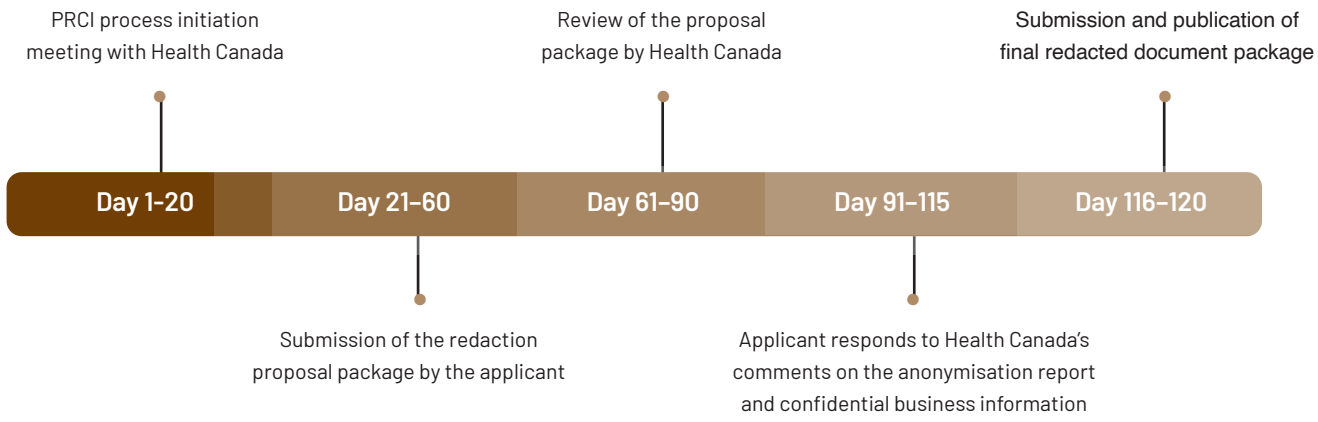


Figure 4. Health Canada PRCI timeframe

Abbreviations: PRCI, Public Release of Clinical Information

Table 2. Clinical trial documents and data sharing requirements in the EU/EEA, Canada, and Japan

Requirements	EU/EEA	Canada	Japan
Applicable regulation/ policy	EMA Policy 0070	Health Canada PRCI	Act for Access to Information Held by Administrative Organs (Act No. 42 of 1999)
Scope	• New marketing authorisation applications (MAAs) • Third-party submissions related to MAAs, procedures under Article 58 of Regulation (EC) No 726/2004 • Line extension applications • Extensions of indications for centrally authorised products	• New drug submissions (NDS) • Supplemental NDS (SNDS) • Abbreviated NDS (ANDS) • Supplemental abbreviated (SANDS) • Extraordinary use NDS (EUNDS) • Supplemental extraordinary use NDS (SEUNDS) • Medical device applications (Class III and IV)	• Japanese new drug applications (JNDAs) • Supplemental new drug applications (SNDAs)
Information included	A redaction proposal document package includes: • A cover letter • Documents marked for redaction (clinical overview [Module 2.5], clinical summaries [Module 2.7], CSRs [Module 5] with appendices [protocol and amendments, sample CRF, SAP]) • A justification table for CCI redactions • An anonymisation report detailing the methodology for re-identification risk management	For drug submissions, Health Canada requires the same documents as EMA Policy 0070. The justification table in Health Canada is known as the "Proposed Redaction Control Sheet" For device applications, documents include: • Device description • Performance study reports (CSR, trial plan, protocol, analytical evaluation), clinical trial summary • Operational information • Applicants must also submit a redaction control sheet • An anonymisation report • A certification letter	The package contains: • CTD Module 1 (review report, Module 1.15-1.10, and 1.12) a • CTD Module 2 (all documents, plus Module 2.7.6 synopses of individual studies) • Justifications for redactions • PMDA's review reports
Timelines	EMA validates the redaction package within 10 calendar days of submission and reviews this within a further 60 calendar days, after this, applicants have 30 calendar days to submit final redacted documents. Documents are published on approval (see Figure 3)	Time from process initiation to publication of redacted submission is 120 days. In addition, Health Canada gives an additional 30 days in case of notice of deficiency-withdrawal (NOD) or notice of non-compliance (NON), to allow for a reconsideration appeal (See Figure 4)	Final redaction document package submitted within 3 months of receiving marketing approval

Abbreviations: CCI, commercially confidential information; CRF, case report form; CSR, clinical study report; CTD, Common Technical Document; EEA, European Economic Area; EMA, European Medicines Agency; EU, European Union; PMDA, Pharmaceuticals and Medical Devices Agency; PRCI, public release of clinical information; SAP, statistical analysis plan.

information are the same as EMA Policy 0070. It is beneficial that packages approved by the EMA under Policy 0070 can subsequently be used for Health Canada submissions. Currently, there are no financial penalties for non-compliance with timelines.

Japan

Japan's Pharmaceuticals and Medical Devices Agency (PMDA) mandates public disclosure on its website of new drug development information. This requires the publication (primarily in Japanese) of appropriately redacted new drug approval information packages.[23] Non-compliance with timelines and other requirements is subject to penalties.

A comparison of clinical trial document and data sharing requirements in different regions is presented in Table 2.

Other data and document sharing initiatives

Other data sharing initiatives have been led by trade associations and other organisations. These

Table 3. Other data sharing initiatives

Organisation	Initiatives
• The European Federation of Pharmaceutical Industries and Associations (EFPIA) • International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) • Pharmaceutical Research and Manufacturers of America (PhRMA)	These organisations encourage members to share clinical data through disclosure of study results, provide access to IPD, and make CSRs available for secondary analyses, in a way that protects patient privacy and respects commercial confidentiality
• Vivli • clinicalstudydatarequest.com • Yale Open Data Access (YODA) Project	Independent platforms that provide access to clinical trial data from multiple sponsors, and make clinical trial data available to external investigators
• ICMJE	Requires authors to share de-identified IPD underlying research articles
• WHO	Endorses the timely release of clinical trial results and supports platforms that facilitate data sharing

Abbreviations: CSR, clinical study report; ICMJE, International Committee of Medical Journal Editors; IPD, individual participant data; WHO, World Health Organisation.

initiatives collectively aim to maximise the utility of clinical data, foster innovation, and improve health outcomes globally (Table 3).[24-27]

Plain language writing

Much of the published clinical research information can only be understood by those with scientific or medical training. In recognition of this, there is a groundswell of support for presenting clinical trial information in plain (or laypersons') language. This field is rapidly evolving and regulations are being introduced to encourage it.

European Union/European Economic Area

The EMA is taking the lead in requiring plain language summaries. Article 37 of EU-CTR requires sponsors to publish a plain language summary of clinical trial results (PLS).[28] The PLS is generally written to the literacy level of a 12-year-old. PLSs must be completed within 12 months of the end of the trial (6 months for paediatric trials or trials listed in a Paediatric Investigation Plan [PIP]). EU-CTR also includes a recommendation to include a plain language protocol synopsis in CTA submissions.

US and other countries

The FDA does not require PLSs, however in 2022, NIH produced a "Plain Language Checklist for Lay Brief Summaries". This guidance can be used to create content for two fields required in the ClinicalTrials.gov registry: the "Brief Title", a short title describing the trial, and the "Brief Summary", a short summary that provides a high-level overview of the study.[29]

In the UK, The Medicines and Healthcare Products Regulatory Agency, as part of their "Make it Public" strategy, requires research sponsors to publish a plain language summary of their findings no later than 12 months from the end of the study.[16]

The Netherlands' Medical Research Involving Human Subjects Act requires trials conducted in The Netherlands to disclose study results either as a scientific summary or PLS within 12 months of study completion on their Central Committee on Research Involving Human Subjects (CCMO) registry.[30]

Other countries, such as Ukraine and Türkiye, may be introducing requirements for plain language summaries of results.

Considerations for medical writers

Medical writers play a key role in preparing documents and information required to promote clinical data transparency (Figure 5). The considerations outlined below can help medical writers effectively prepare disclosure-ready clinical documents, meet regulatory requirements, and ensure transparency while maintaining data privacy, confidentiality and the integrity of data. Some of the key considerations are listed in Table 4.

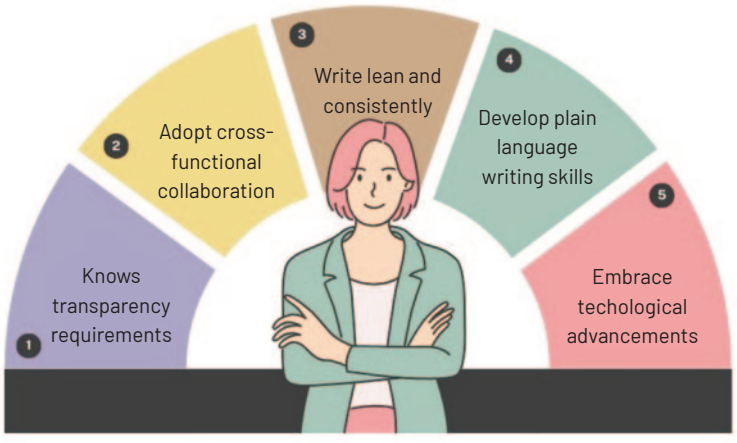


Figure 5. Considerations for medical writers

Table 4. Considerations for medical writers

Category	Practical application	Impact
Transparency requirements	• Understand what must and what must not be disclosed • Prepare documents with disclosure timelines in mind	Achieves compliance with regulations
Collaboration	Facilitate agreement between and train diverse stakeholders in transparency processes (e.g., legal, regulatory, and medical teams)	Greater consistency and reduced timelines
Lean writing and consistency	• Include CCI and PPD only when necessary • Create lean document templates • Maintain CCI glossaries for each product	Reduces the amount of redaction required and avoids cross-document variation
Plain language skills	Learn how to write in plain language, use infographics and engage patients directly in creating documents	More efficient and engaging plain language summaries
Technological advances	Be aware of how new tools (e.g., CORE reference secondary-use CSR, TransCelerate templates, generative AI) can support clinical trial transparency	More efficient writing processes

Abbreviations: AI, artificial intelligence; CCI, commercially confidential information; CORE, Clarity and Openness in Reporting; PPD, CSR, Clinical study report protection of personal data.

Conclusion

There are significant benefits of increasing transparency of clinical research, however the regulatory requirements in this area are becoming more widespread and more complex. Medical writers can be proud that they are often at the vanguard of making clinical information more widely available. Effective and compliant disclosure requires medical writers to stay informed about relevant regulations and to seek opportunities to improve the efficiency and consistency of transparency processes.

Acknowledgements

The authors would like to thank Shalini Dwivedi, Head of Medical Writing and Clinical Trial Transparency at Krystelis Limited, for her insights and helpful comments.

Disclosures and conflicts of interest

The authors declare no conflicts of interest.

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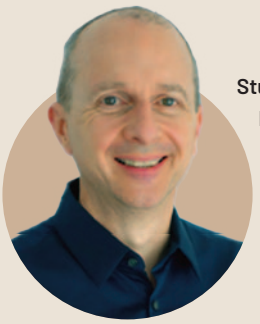

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Plain language summaries of clinical trial results: What is their role, and should patients and AI be involved?

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doi: 10.56012/yayy4394

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Abstract

Plain language summaries (PLSs) of clinical trial results are vital tools in the clinical development process for enhancing transparency and encouraging and facilitating patient engagement. The production of a PLS is now mandated in the EU for all interventional clinical trials by the European Medicines Agency under Regulation EU 536/2014 and became compulsory with the opening of the Clinical Trial Information System portal in January 2022. PLSs are intended to be accessible, comprehensible documents conveying complex trial findings to diverse audiences. This article explores the significance of PLSs, the importance of patient input in their production, and the role and concerns surrounding the use of artificial intelligence in generating them.

Introduction

Clinical trials are the cornerstone of evidence-based medicine. They are pivotal in advancing medical knowledge and shaping healthcare practices, and they rely on the participation of patients and healthy volunteers. Clinical trial participants and the general public should, and increasingly demand to, be informed about the results of clinical trials. This is crucial for them to be able to share and be involved in their healthcare decision making. However, traditional formats for reporting trial results, such as scientific manuscripts and regulatory documents, are often full of technical jargon and complex statistical analyses, which are extremely difficult for non-expert audiences to understand and interpret. To address these challenges, and as part of their transparency and inclusivity initiatives to promote patient engagement in clinical development, the European Medicines Agency (EMA) has mandated the production of plain language summaries (PLSs) of clinical trial results for all interventional trials in the EU.[1] Recently, two key legislations have pushed for plain language clinical trial lay summaries to be made available to the public – either via clinicaltrials.gov in the US or as part of the EMA's Lay Summary of Clinical Trial Results, which became mandatory with the opening of the Clinical Trial Information System (CTIS) in the EU.[2–4]

Complementing these efforts, some journal publishers are making available plain language summaries (PLSs) of journal articles to the general public.[5–8] Some industry sponsors of clinical trials have been doing this for some time, and others are starting similar initiatives,[9–11] with commitments to making these accessible to the public for all clinical trials.[12] Many national public health bodies, research hospitals, patient organisations, and non-profit bodies are now developing and making additional plain language materials such as videos, information brochures, or infographics freely available via their websites and social media channels.[13–15]

The aim of the PLS is to translate complex clinical information into clear, concise, and understandable documents aimed at the general public (non-expert audiences).

The aim of the PLS is to translate complex clinical information into clear, concise, and understandable documents aimed at the general public (non-expert audiences). This article explores the significance of PLSs, the importance of patient input in their production, the current use of artificial intelligence (AI) in generating them, and their role in enhancing transparency and patient engagement in the clinical development process.

Significance of plain language summaries

Clinical trial results are usually discussed and disseminated through scientific journals, regulatory documents, and conference presentations, which are all primarily targeted at healthcare professionals, the pharmaceutical industry, and researchers.[15] However, these formats use complex technical terminology and statistical analyses that are challenging for non-experts, such as patients and the general public, to understand. This knowledge gap not only hinders informed decision-making but limits patient engagement in healthcare decisions and the clinical development process.[16] PLSs serve as a bridge between the technical language of clinical research and the everyday language of patients and the general public. By distilling complex trial findings into plain language, PLSs help people make informed decisions about their healthcare and participate more actively in shared decision-making processes.[17] Moreover, PLSs play a crucial role in promoting transparency and accountability in clinical research by disseminating trial results in a format that is accessible and comprehensible to diverse audiences, which fosters trust between the general public and the pharmaceutical industry.[18] PLSs serve as a valuable resource for patients, caregivers, and patient advocacy groups seeking information about specific medical interventions or health conditions.[18]

Research has demonstrated the positive impact of personalised patient materials on patient understanding, satisfaction, and trust in the healthcare system. For example, a study by Bhattad et al. (2022) found that patients who received personalised patient education materials, in addition to verbal education by their doctors, had improved patient care via shared decision making and by improving patient satisfaction.[19]

Regulatory mandates for plain language summaries

The EMA requires the submission of a PLS for all interventional clinical trials conducted in the EU as part of EU Regulation 536/2014.[1] This regulatory mandate underscores the critical role of PLSs in promoting transparency and patient-centricity in the clinical development landscape.[20] By ensuring that trial results are communicated in a format that is accessible and comprehensible to diverse audiences, regulatory authorities empower patients to make informed decisions about their healthcare and encourage greater participation in clinical research.[18,21,22] However, despite the progressive movement towards clinical trial transparency, easily accessible PLSs on clinical trials are currently scarce.[23] It is hoped that this will change as the demand from, and awareness of, patients and the general public increases.

The importance of patient input in PLS production

Numerous studies have highlighted the benefits of incorporating patient input into the development of healthcare materials. This has even been echoed in the advice given by regulatory agencies and government bodies.[24] Furthermore, a systematic review by Davis et al. (2007) underscored the positive impact of patient engagement on healthcare communication and decision-making processes.[25]

These findings underscore the importance of integrating patient perspectives into the production of PLSs to enhance their effectiveness and utility for patients and caregivers. Incorporating patient input into the production of PLSs is essential for ensuring relevance and usability and for making sure that these summaries effectively address the informational needs and preferences of diverse patient populations.[26,27] Patients bring unique perspectives and insights that can enrich the content and readability of PLSs, making them more relatable and user-friendly. Engaging patients in the development process can help identify key concepts, terminology, and formatting preferences that resonate with the intended audience.[28]

Moreover, involving patients in reviewing and validating PLSs can enhance their accuracy, relevance, and overall impact on patient decision-making.[29] By prioritising patient input, stakeholders can foster a culture of patient-centred communication and help patients make informed choices about their healthcare.[28]

The current use of artificial intelligence in generating PLSs

By automating tedious tasks such as literature review, data extraction, and summarisation, AI tools enable researchers and medical writers to focus on higher-level tasks such as content curation and quality assurance.[30–32]

In terms of PLS production, advances in AI technology have revolutionised the generation of PLSs, offering innovative solutions to streamline the production process and enhance efficiency by automating labour-intensive tasks. AI-powered natural language processing algorithms can analyse and synthesise complex trial data into clear, concise summaries tailored to specific audience needs.[33]

AI-powered natural language processing algorithms can analyse and synthesise complex trial data into clear, concise summaries tailored to specific audience needs.

Recent studies have explored the use of AI-driven approaches to generate PLSs for clinical research. McMinn et al. (2023) demonstrated the feasibility of using AI to produce PLSs for clinical trials, highlighting the potential for AI to

accelerate the production of summaries.[34] However, while AI holds promise for enhancing the efficiency and scalability of PLS production, human oversight remains critical to ensure accuracy, relevance, and adherence to regulatory requirements.[33,34]

Conclusion

PLSs play a pivotal role in enhancing transparency and promoting patient engagement in the clinical development process. Regulatory mandates underscore the importance of accessible communication of trial results to allow patients to make informed decisions about their healthcare. By incorporating patient input into the production of PLSs, these summaries can effectively meet the informational needs and preferences of diverse patient populations. Moreover, advances in AI offer innovative solutions to streamline the generation of PLSs, although human oversight remains critical. Moving forward, continued collaboration among stakeholders, including patients, researchers, regulators, and the pharmaceutical industry, will be essential to optimise the utility and impact of PLSs in fostering a culture of transparency, accountability, and patient-centred communication in clinical research.

Disclosures and conflicts of interest

The author declares no conflicts of interest.

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The 2023 CORE Reference Utility Survey:

Perceptions on a best practice tool for globally applicable clinical study reporting and provision of continuing professional development resources for the regulatory medical writing community

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doi: 10.56012/rnqo6114

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Abstract

CORE Reference offers globally applicable resources for clinical study reporting, including a user manual and a mapping tool, and continuous professional development (CPD) resources. This report presents the results of the 2023 Utility Survey conducted by the CORE Reference Project Team to measure the awareness and perceived usefulness of these resources by the regulatory medical writing community. The survey found an increased use of the CORE Reference open-access manual, compared to results of the 2017 survey. Most respondents found the resources extremely, or somewhat, useful for preparing disclosure-ready clinical study reports. Over half of the respondents were aware of the CORE Reference CPD resources. Most respondents found the bi-monthly news summary extremely, or somewhat, useful. One-third of the respondents required knowledge of the reporting and public disclosure landscape in Asia and found the updates of Asia extremely, or somewhat, useful. The survey results indicate a positive reception of the CORE Reference Project amongst regulatory medical writers.

Introduction

CORE Reference (https://www.core-reference.org/core-reference/) was developed between May 2014 and May 2016 by the European Medical Writers Association (EMWA)/American Medical Writers Association (AMWA) Budapest Working Group (BWG), which comprised a group of experts from the regulatory medical writing community. Developed based on the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) E3 guidance and USA and EU regional guidance, CORE Reference integrates options to allow for the reporting of design elements common to today's complex clinical studies, as well as ensuring that public disclosure considerations are taken into account. Thus, it serves as a best practice tool for medical writers and regulatory professionals in developing globally applicable clinical study reports (CSRs) in the current regulatory reporting environment.[1]

The first CORE Reference Utility Survey was conducted in 2017 – one year after its launch – with a target audience of medical writing and regulatory communities. The 2017 questionnaire contained six questions that focused on utility of the user manual and its value to users; the results were presented at two conference meetings.[2,3] Since then, the CORE Reference website has evolved to not only house the established resources – the CORE Reference user manual, mapping tool, and related publications – but also provides self-directed continuing professional development (CPD) learning resources that support CSR authoring. CPD resources include an archive of monthly summaries of clinical study reporting and disclosure-related news and updates, as well as external links to public disclosure regulations, and portals of participating regulatory authorities.

The CORE Reference Project Team conducted a brief 2023 utility survey to rate both awareness of the 2016 original open-access resources and the perceived usefulness of the CORE Reference 2022 extended continuous professional development initiative.

In April 2022, the EMWA Special Project designation was conferred, with the aim of expanding the CPD offering to the medical writing community. Under the original Chair, the CORE Reference Project Team evolved and expanded to support the increased workload necessary for global surveillance of the regulatory reporting and public disclosure landscapes. The current CORE Reference Project Team provides subscribers with a free bi-monthly email in the form of a

news summary that includes updates on major changes in regulatory reporting and public disclosure requirements from around the world including the EU, Canada, USA, and Asia. In late 2023, the CORE Reference Project Team conducted a brief utility survey to rate both awareness of the 2016 original open-access resources, and the perceived usefulness of the CORE Reference 2022 extended CPD initiative. This article reports the results of this survey.

Methods

Questionnaire design and distribution

The CORE Reference 2023 Utility Survey contained 13 questions, building on the 2017 Utility Survey questionnaire. All questions were multiple-choice, fixed responses, with half of the questions containing an "other" response that provided a free-text option. The questionnaire was produced on Survey Monkey and was open for 6 weeks from October 25, 2023, to December 5, 2023. The questionnaire was designed to take less than 5 minutes to complete, and data were collected anonymously.

EMWA distributed the survey questionnaire with the access link to all its members via email and announced the survey on its social media platforms via newsletters and discussion groups. In addition, the CORE Reference Project Team distributed the survey to its subscribers via emails and announced it on the CORE Reference website. All announcements of the survey clearly outlined the survey's intention to collect information on the awareness and perceived usefulness of CORE Reference. The survey was open to all members of the medical writing community and was not restricted to EMWA or AMWA members or CORE Reference subscribers.

Data analysis

All responses were collected automatically and analysed on the Survey Monkey platform. The raw data and the survey results were exported into a Microsoft Excel spreadsheet and PDF documents. All results were presented using descriptive statistics only. For questions that allowed multiple responses, percentages of the different answers did not always add up to 100%. All percentages were rounded to full integers.

Results

Respondents

There were 154 respondents who participated in the 2023 survey, which was an increase of 75% compared with the 2017 survey (which had 88 respondents). Not all respondents in the 2023 survey answered all the questions in the survey.

The highest proportions of respondents worked in mid-sized contract research organisations (CROs) (19%; 29/154) and as freelancers (18%; 27/154). Ten percent (15/154) of the respondents worked in small CROs and 12% (18/154) worked in large CROs. Similarly, 10% (16/154) of the respondents represented small pharmaceutical companies, another 10% (16/154) represented mid-sized pharmaceutical companies, and 12% (19/154) represented large pharmaceutical companies. Among the 9 respondents who responded "other", 2 worked in the medical devices industry and 2 others in medical communications/writing agencies. Three respondents identified as writing medical devices documentation or worked for a medical device manufacturer. The overall distribution of the respondents' affiliations in the 2023 survey (41% CROs and 32% pharmaceutical companies) was similar to that of the 2017 survey (42% CROs and 38% pharmaceutical companies).

Just over half of the respondents were regulatory medical writers (52%; 79/153); 23% (35/153) of the respondents were in managerial roles; and < 10% were medical writers in medical communications (8%; 12/153) or transparency and disclosure (T&D) specialists (5%; 7/153). Of the 13% (20/153) of respondents who responded "other", most had cross-functional roles in clinical trial quality assurance (QA), project management, clinical operations, pharmacovigilance (PV), and T&D, as well as roles in medical communications.

Most respondents prepared documents for clients based in Europe (93%; 143/153) and the US (77%; 118/153), 34% (52/153) for Canada, 27% (42/153) for Asia-Pacific, and 8% (12/153) for clients based in other locations including

Latin America, South Africa, and the Middle East.

Utility of CORE Reference open-access manual

In the 2023 survey, most respondents found value in the CORE Reference open-access manual as an unofficial reference tool (52%; 78/150) and in authoring CSRs (47%; 71/150). Approximately one-third of the respondents used it to train others and had incorporated it into standard operating procedures, policies, or templates (Figure 1). Five of 8 respondents who responded "other" had never used the CORE Reference manual, and one respondent used it for CSR appendices collation for the European and USA regions. Compared with the 2017 survey in which 38% of the respondents used it as an unofficial reference tool and 28% used it to author CSRs, there was a notable increase in the use of the manual.

The CORE Reference mapping tool is a 4-page overview of the granularity within each main section in the CORE Reference manual, compared with the sections in the ICH E3 guideline. Users may download it to keep as a sectional reference while the manual itself contains a complete content description of these sections and subsections. Almost half of the respondents (45%; 63/139) had only downloaded the CORE Reference mapping tool. There were nevertheless respondents who found value in this overview document in that 41% (57/139) of the respondents had used it as an unofficial reference tool, and approximately one-fifth had used it to author CSRs and to train others (Figure 2), most likely as a supplementary tool to the manual. Of the 14 respondents who responded "other", 12 had not used or heard about the mapping tool.

When asked about the usefulness of the CORE Reference resources for preparing disclosure-ready CSRs, the majority of the respondents found it either extremely useful (50%; 74/148), or somewhat useful (21%; 31/148), most of the remaining respondents did

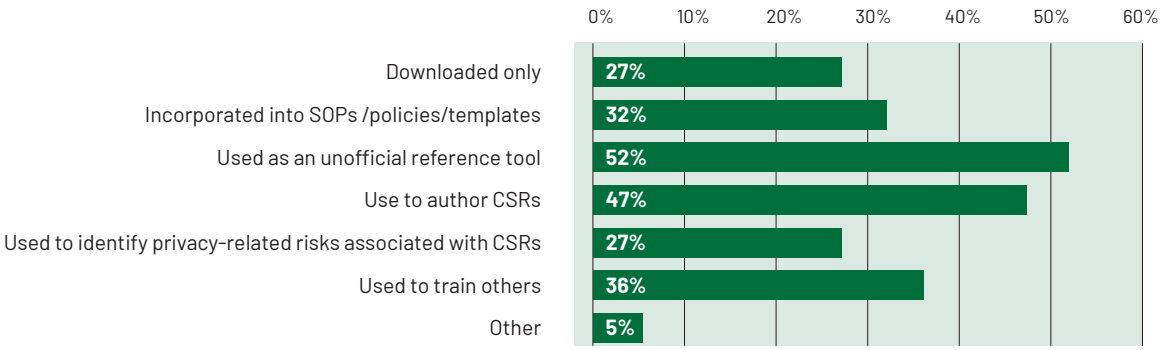

Figure 1. Use of the CORE Reference open-access manual

Abbreviations: SOPs, standard operating procedures; CSRs, clinical study reports

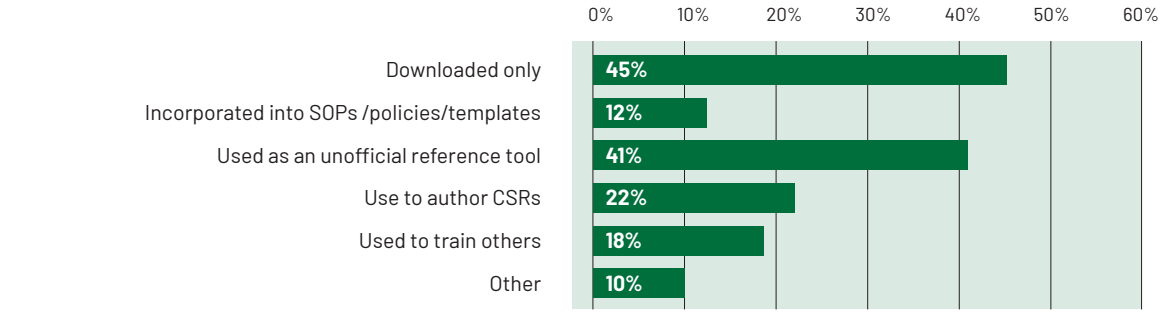

Figure 2. Use of the CORE Reference mapping tool

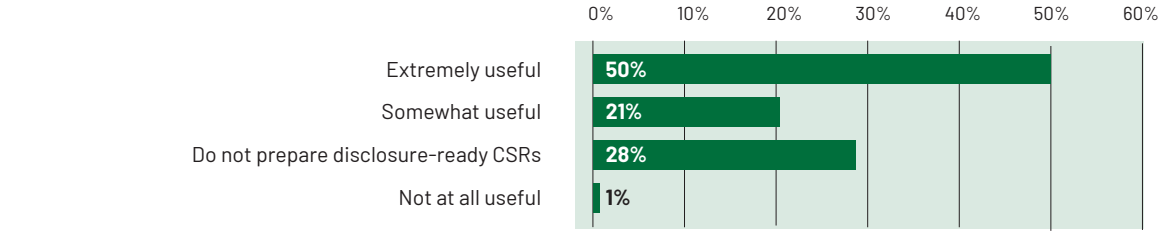

Figure 3. Usefulness of the CORE Reference resources for preparing disclosure-ready clinical study reports

not prepare disclosure-ready CSRs (28%; 41/148) (Figure 3). Notably, two respondents commented that they did not find the CORE Reference resources useful. One respondent – employed in a medical writing managerial role at a writing agency – commented on the redundancy of the CORE Reference resources with the availability of other open-access resources such as those from TransCelerate. This same respondent confirmed they used/had used CORE Reference open-access manual as both an unofficial reference tool and to train others. The second respondent was a freelance regulatory medical writer who prepared documents for medical devices and confirmed that they had only downloaded both the CORE Reference open-access manual and the mapping tool.

Utility of continuous professional development resources

Over half of the respondents (55%; 84/152) were aware that the CORE Reference Project also provides regulatory reporting and public disclosure updates as CPD. Interestingly, 73% (112/153) of the respondents had subscribed to the free CORE Reference bi-monthly news summary, which was not in line with the lower proportion of respondents who indicated their awareness of the CPD resources. The majority of the respondents found the news summary either extremely useful (47%; 69/148), or somewhat useful (32%; 47/148) (Figure 4).

Only 28% (43/152) of the respondents had accessed the archive of news summaries on the CORE Reference website (https://www.core-reference.org/news-summaries/). Respondents might find the "real-time" bi-monthly news summary sufficient to keep abreast of the fast-evolving regulatory reporting and public disclosure landscapes. Importantly, the bi-monthly news summary is shared with all EMWA members and the wider medical writing community via social media platforms and discussion groups. Once deposited in the archive it is a one-stop portal to view all updates within any given month.

With increasing demands of cross-regional regulatory submissions of clinical and regulatory documents, since mid-2022, the CORE Reference Project provides CPD on the T&D landscape in Asia to provide relevant information and updates to medical writers who may need to prepare clinical and regulatory documents for Asian health authorities. Approximately one-third of the respondents (35%; 54/153) confirmed that their roles required them to know about the regulatory reporting and public disclosure landscapes in Asia. However, only 27% (42/153) of the respondents had previously confirmed that they prepared documents for clients based in Asia-Pacific. Of the 20 respondents who did not confirm they prepared documents for clients based in Asia-Pacific, but did confirm that their roles required them to know about the regulatory reporting landscapes in Asia-Pacific, 4 respondents confirmed their role as T&D specialists who did not prepare disclosure-ready CSRs; 10 as regulatory medical writers; 3 as having a regulatory medical writing managerial role; and 3 as having "other" roles (namely: medical writer – clinical documents; scientist, also running clinical trials; and clinical trials project management).

Of the 10% (15/148) of respondents who found the regulatory public disclosure (RPD) updates from Asia extremely useful (Figure 5), 11 respondents reported preparing documents for the Asia-Pacific region; of the 29% (43/148) of respondents who reported the updates somewhat useful (Figure 5), 21 respondents were preparing documents for Asia-Pacific. The respondents who replied "Not at all useful" (5%; 7/148) were either not aware of the resources, did not need the resources, or did not currently find them useful, but may need them in the future.

Overall, there were positive responses about the usefulness of the CORE Reference Project amongst regulatory medical writers – 63% (95/151) of the respondents found the CORE Reference Project extremely useful and 24% (36/151) found it somewhat useful (Figure 6). Among the 11% (17/151) of the respondents who confirmed that they were not a regulatory medical writer (Figure 6), 4 were T&D specialists, 6 were medical communications

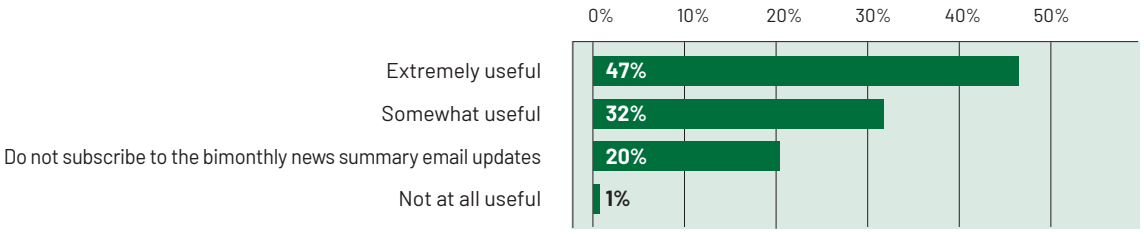

Figure 4. Usefulness of real-time CORE Reference bi-monthly news summary email updates for continuous professional development

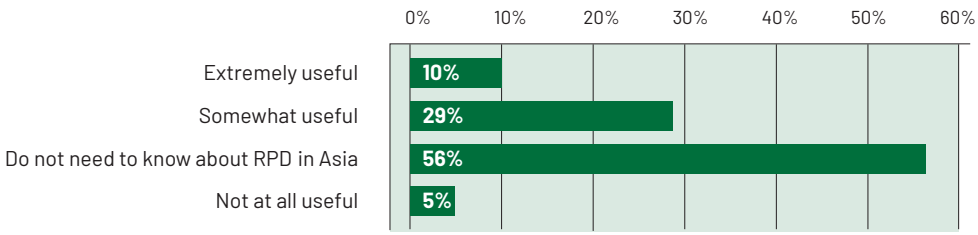

Figure 5. Usefulness of regulatory public disclosure updates from Asia

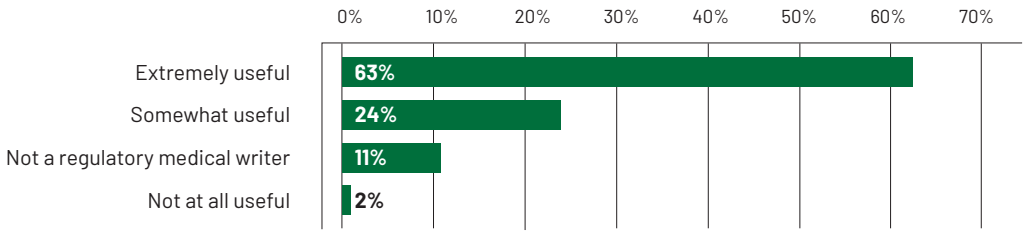

Figure 6. Overall usefulness of the CORE Reference Project to regulatory medical writers

medical writers, 7 were "other" – namely teacher, QA and GCP auditor, vice president of global clinical operations, PV writing managerial role, clinical trials project manager, clinical documents medical writer, and clinical QA senior manager.

Discussion

Uniqueness of CORE Reference among available resources

Integrated CSRs and their appendices are not necessarily destined for a CTD-compliant regulatory drug submission dossier, which will be reviewed by a regulatory authority before a decision on granting the product license is made. This is because many drugs involved in clinical studies eventually fail during clinical development. The development of these products may be terminated, and these clinical studies never progress to a product submission. A CSR written for each clinical study must stand alone for review by regulators, sponsors, investigators, investors, and other interested parties. A standalone CSR contains full description of the study and includes source tables, figures, listings, and all appendices necessary to understand the study context with minimal cross-references to other external documents. In the EU, certain clinical study documents, including the CSRs, are now required to be publicly disclosed. When the CSR stands alone and is not part of a drug submission dossier (and any EU participants are included), public disclosure takes place through the Clinical Trial Information System portal of the EU Clinical Trial Regulation; if the CSR eventually forms part of a European drug submission dossier, its public disclosure will take place through the EU Policy 0070 portal. Canada has a similar system to publicly disclose standalone and dossier submission CSRs through their equivalent portal. CORE Reference provides clarifications on how to interpret verbiage within ICH and regional guidance that is difficult to understand or is ambiguous, guiding writers in making informed choices to produce a CSR fit for reporting their study. The overwhelming majority of respondents in the 2023 survey found the CORE Reference resources extremely or somewhat useful in preparing disclosure-ready CSRs.

> There were positive responses about the usefulness of the CORE Reference Project amongst regulatory medical writers – 63% of the respondents found the CORE Reference Project extremely useful.

CORE Reference pre-dates the TransCelerate CSR template by 2.5 years, and is cited as a source for its development.[4] As well as supporting the standalone and publicly disclosable CSR need, CORE Reference is the only resource that incorporates clarifications on particular regulatory guidance or legislation applied to granular CSR content requirements. Key to understanding the value of CORE Reference to the community is that large pharmaceutical companies, which house their CSRs within complex, closed document management systems, are not the only clinical study sponsors – and they do not own all products from inception right through to licensing. Sponsors also include biotech developers, investigators, and charities, whose less elegant and agile systems may inadequately support content reuse and document linkage within the closed system and externally, for example, if the product changes hands. In the preparation of full submission dossiers, TransCelerate templates for protocols and CSRs, their content reuse solutions, and cross-talk among different documents within the submission are undoubtedly useful to the sponsor and regulator. When CSRs need to stand alone – which at some point in the product's development, they all must – extensive content reuse and hyperlinking cannot always adequately serve the needs of the mixed audience. In particular, the TransCelerate CSR template may not serve the needs of sponsors outside of large pharmaceutical companies well, including even the larger CROs who need flexibility in their reporting template to service a wide range of client types.

Value of CORE Reference in the age of artificial intelligence

The value of CORE Reference as a training tool is confirmed from the survey with more than a third of users using it to train others. With the increasing rise of artificial intelligence (AI) tools and platforms to generate CSR data and texts, AI tool developers rely on the expertise of knowledgeable medical writers who understand the content requirements of disclosure-ready CSRs and must use that knowledge to prompt the AI tools to output the correct content. Concerns around safe and effective T&D will only increase as AI tools are fed more clinical data. The role of the medical writer will evolve from de novo content creator to preparing expert-led prompts and critical review in the process of developing AI-generated CSR texts. Medical writers owning these parts of the process will reduce the potential for AI hallucination and ensure continued trust in regulatory documentation. CORE Reference stands apart from other open-access resources – including guidance and templates – with its unique clarifications that aid interpretation and understanding of reporting and public disclosure requirements, which help medical writers to confidently evolve their skillset to support innovation, which includes an onslaught of AI tools used to create texts.

CORE Reference as self-directed learning resource

Awareness of new clinical study reporting requirements since May 2016 is necessary to ensure current reporting keeps pace with regulatory developments. CORE Reference was designated an EMWA Special Project in 2022 to support expansion of CPD for medical writers through ongoing surveillance of the rapidly evolving regulatory reporting and public disclosure landscapes. To this end, CORE Reference regularly distributes a distillation of recently released new information to regulatory medical writers and other interested parties. This open-access, bi-monthly news content dissemination within the community is also unique to the CORE Reference Project, and this level of CPD for regulatory medical writers engaged in clinical study reporting, to our knowledge, is not provided, globally, by any other project. In the feedback, more than three quarters of respondents found the bi-monthly news summary either extremely, or somewhat, useful. Interestingly, although 45% of the respondents declared they were unaware that the CORE Reference Project provides regulatory reporting and public disclosure updates as CPD, 73% of the respondents were already subcribers to the bi-monthly news summary. We recognise that information overload is a common problem in today's workplace. Therefore, the discrepancy in the number of subscribers who are aware of their subscriptions could be indicative of the current high-speed and demanding work environment. However, the CORE Reference Project Team would like to emphasise that regulatory medical writing professionals who review, appraise, and evaluate the information provided in the bi-monthly news summary will keep up to date with the latest industry-specific developments and in doing so will be undertaking self-directed CPD learning, which is part of a medical writer's holistic training to enhance skills and knowledge of new developments.

With fewer than 10% of the respondents identifying as working in the T&D space, there is scope to better target and reach this group of professionals for whom both the user manual and the CPD have direct relevance. As the T&D sector grows, professional networking with T&D experts should increase to allow for the exchange of insights regarding what this group finds beneficial, while concurrently spreading knowledge about the CORE Reference Project. Sponsors outside of "big pharma" have wide-ranging regulatory knowledge in preparing disclosure-ready documents. T&D consultants will find value in the CORE Reference manual and CPD materials in providing the full spectrum of public disclosure-related insights to such clients. As multi-regional clinical trials increase, clinical data are shared among regions with differing regulations, increasing the need for an expanded knowledge base for T&D specialists. The CORE Reference CPD T&D offering supports the needs of T&D experts in this respect.

> CORE Reference stands apart from other open-access resources … with its unique clarifications that help medical writers to evolve their skillset, especially in the face of AI.

Limitation of the 2023 survey

Limitations of the survey include the absence of question(s) about the usefulness of the medical devices information included in the bi-monthly news summary. At the time of the 2023 survey development, the CORE Reference Project Team concentrated their efforts on interrogating the usefulness of the established CORE Reference resources including the user manual, mapping tool, and the CPD resources. From the survey responses, we found only 3 respondents who identified as writing medical devices documentation or worked for a medical device manufacturer. Prior to March 2024, the accelerating developments in the regulation of medical devices were captured more broadly. This extensive archive of regulatory information for medical devices writing professionals is available to that point in time. Since March 2024, more nuanced medical devices content is presented in the news summary to better align with the CORE Reference Project's aim to provide CPD in the T&D space. This ensures that developments in medical devices regulations that impact reporting in drug-device studies, including those with in vitro devices, are not missed by professionals in the medicines and devices fields. To achieve this, the "Medical Devices" subsection of the news summary has been honed to focus on transparency concerning medical devices and the emerging intersection of the medical devices and drugs spaces.

Conclusion

The results of the CORE Reference 2023 Utility Survey show the CORE Reference open-access manual continues to be perceived by the regulatory medical writing community as a useful tool when preparing disclosure-ready CSRs. It is encouraging to see that since the 2017 survey more medical writers are using the CORE Reference manual as an unofficial reference tool and to author CSRs, and that there is a slight increase in its usage to prepare CSRs submitted to Asian health authorities. The majority of respondents are subscribers of the CORE Reference bi-monthly news summary who find this useful.

The CORE Reference Team hopes the 2023 Utility Survey results allow readers to find out about how the CORE Reference manual and CPD resources have been used and perceived so far, and to increase the awareness for the regulatory medical writing and transparency and disclosure communities about the availability of the CORE Reference resources as valuable tools for their work and professional development.

Acknowledgements

The authors would like to thank all the participants who took time to participate in the utility survey; EMWA for distributing and publicising the utility survey as well as providing the survey data; and Dr Art Gertel for kindly reviewing a mature draft of this article.

Disclosures and conflicts of interest

The authors declare no conflicts of interest.

Data availability statement

The 2023 Utility Survey questionnaire is appended at the end of the article. Raw data are available to download from the CORE Reference website (https://core-reference.org/core-reference-2023-utility-survey-all-responses/). Researchers who plan to reuse these data should email contact@core-reference.org and provide a concept for data reuse and make reference to this article in any publication in which these data are used. Re-use of these data is by a priori written permission from CORE Reference.

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Appendix. CORE Reference 2023 Utility Survey – Questionnaire

1. What type of organisation do you work for?
- ☐ Large Pharma
- ☐ Mid-size Pharma
- ☐ Small Pharma/Biotech
- ☐ Contract research organisation – Large
- ☐ Contract research organisation – Mid-sized
- ☐ Contract research organisation – Small CRO
- ☐ Freelance
- ☐ Government/Regulatory Authority or Agency
- ☐ Academia
- ☐ Charity organisation
- ☐ Other (please specify)

2. What is your role?
- ☐ Regulatory Medical Writer
- ☐ Medical Writer – medical communications
- ☐ Regulatory Affairs Specialist
- ☐ Transparency and Disclosure Specialist
- ☐ Medical Writing Managerial Role (for example Manager, Associate Director, Director, Senior Director or above)
- ☐ Other (please specify)

3. What region do you prepare documents for? Select all that apply.
- ☐ USA
- ☐ Canada
- ☐ Europe
- ☐ Asia-Pacific
- ☐ Other (please specify)

4. How have you used the CORE Reference open access manual? Select all that apply.
- ☐ Downloaded only
- ☐ Incorporated into SOPs/policies/templates
- ☐ Used as an unofficial reference tool
- ☐ Used to author CSRs
- ☐ Used to identify privacy-related risks associated with CSRs
- ☐ Used to train others
- ☐ Other (please specify)

5. How have you used the CORE Reference mapping tool? Select all that apply.
- ☐ Downloaded only
- ☐ Incorporated into SOPs/policies/templates
- ☐ Used as an unofficial reference tool
- ☐ Used to author CSRs
- ☐ Used to train others
- ☐ Other (please specify)

6. How useful do you consider the CORE Reference resources when preparing disclosure-ready CSRs?
- ☐ Extremely useful
- ☐ Somewhat useful
- ☐ Do not prepare disclosure-ready CSRs
- ☐ Not at all useful - please specify and explain why

7. Are you aware that the CORE Reference Project also provides Continuous Professional Development (CPD) for medical writers by surveillance of regulatory reporting and public disclosure landscapes?
- ☐ Yes
- ☐ No

8. Have you subscribed (https://www.core-reference.org/subscribe) to receive the free CORE Reference CPD news summary email updates in real time on www.core-reference.org?
- ☐ Yes
- ☐ No

9. How useful are the real time CORE Reference bimonthly free email news summary updates for your CPD?
- ☐ Extremely useful
- ☐ Somewhat useful
- ☐ Do not subscribe to the free bimonthly news summary email updates
- ☐ Not at all useful - please specify and explain why

10. Have you accessed the archive of CORE Reference news summaries and news items on https://www.core-reference.org/news-summaries/ that support the CPD needs of regulatory medical writers?
- ☐ Yes
- ☐ No

11. In your role do you need to know about the regulatory reporting and public disclosure landscapes in Asia?
- ☐ Yes
- ☐ No

12. Overall how useful are the regulatory public disclosure (RPD) updates from Asia to you in your role?
- ☐ Extremely useful
- ☐ Somewhat useful
- ☐ Do not need to know about RPD in Asia
- ☐ Not at all useful - please specify and explain why

13. Overall how useful is the CORE Reference Project to you as a regulatory medical writer?
- ☐ Extremely useful
- ☐ Somewhat useful
- ☐ Not a regulatory medical writer
- ☐ Not at all useful - please specify and explain why

Creating educational materials about clinical research data for patients and the public: A multifaceted journey in the current digital age

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doi: 10.56012/gyeg6536

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Abstract

With scientific advances during the COVID-19 pandemic and expansion of artificial intelligence (AI) in research, there has been a simultaneous increase in misinformation about data collection, privacy, and sharing in clinical trials. This increase has been compounded by general mistrust in the clinical research industry partly because of problematic practices, such as data manipulation, withholding of safety information, and inaccurate or even non-existent results reporting. All these issues contribute to the public, patients, caregivers, and even healthcare professionals being inadequately informed about clinical research and related data usage. Through transparency, clarity, and honesty, trust can be rebuilt. Recognising the clinical research landscape has changed over the last decade and that currently available information is not developed or formatted in ways that can be easily understood, we describe creating widely accessible videos and infographics to support data literacy, utilising the most recent tools and technology for content development and dissemination.

The use of, and reliance on, artificial intelligence (AI) in technologies has grown, increasing the focus on data privacy and the individual's right to their data.[1] In 2023, 81% of U.S. adults reported concern about how companies use their data, while 67% reported having little-to-no understanding about what companies do with their data.[2] Given that clinical research necessitates the collection of personal data, it is important to address this tension by promoting education and trust through data literacy initiatives.

Data literacy is a term that describes an individual's ability to read, understand, and utilise data to inform their decision-making.[3] While health and research-related information have greater data protections than other data that are collected from and about people, there justifiably exists a heightened sensitivity about data privacy and data sharing in the health and medicine context.

Beyond the challenges presented by the introduction of new technologies related to data collection and use, there is a general mistrust of clinical research. The COVID-19 pandemic escalated misconceptions and misunderstandings about clinical trials[4–6] and highlighted the importance of access to clear, understandable, and trustworthy information. Confusion and misunderstanding can introduce fear and mistrust and create barriers to participation in clinical research. Conversely, education and clear communication about data use and protections can support participation.

The use of, and reliance on, artificial intelligence in technologies has grown, increasing the focus on data privacy and the individual's right to their data.

Patients and participants need timely, clear information to decide whether to join, and stay in, a clinical trial; they need reassurance that their data will be used only as described in the informed consent document. Therefore, print and electronic materials that use language and imagery that is understandable and familiar, and are linguistically and culturally appropriate, are needed.

The data literacy collaboration between PHUSE and the Multi-Regional Clinical Trials (MRCT) Center of Brigham and Women's Hospital and Harvard, offers a series of informational videos and complementary infographics that explain, in plain language, the clinical research process, and focuses specifically on what happens to data that is collected during a research study. The collaboration shared the goal of making accessible data materials available to patients and the public, especially those being introduced to research for the first time.

PHUSE is an independent, nonprofit organisation run by a worldwide team of volunteers providing the healthcare industry with a platform for open-access knowledge sharing of ideas, tools, and standards around data, statistics, and reporting technologies. Responding to societal misinformation and misconceptions

about clinical trials during the COVID-19 pandemic,[4–6] PHUSE initiated a collaborative pilot project[7] in 2021 to produce engaging educational content, organised into logical sections, as short, animated videos of approximately 3 to 5 minutes each.

The MRCT Center is a research and policy centre dedicated to the ethics, regulatory environment, and conduct of multi-site, multinational clinical trials. One focus has been health literacy,[8,9] including a Clinical Research Glossary[10,11] that provides plain language definitions of complex clinical research terminology. The MRCT Center developed an informational brochure series, designed in plain language, to complement the PHUSE video series.

In this article we describe the process of creating an informational video series and complementary infographics designed to explain clinical trials and data collection, explicate the critical importance of data, and clarify how clinical research data are used, shared, and protected.

A patient's perspective

"Multi-modal materials are extremely important for the patient community as they cater to different ways of processing information, different literacy levels, and different target audiences. Accessibility of information is crucial for ensuring equitable opportunity to improve health literacy, as well as increasing awareness and understanding about different aspects of clinical research, such as data science. Most importantly though, these projects are co-created with patient advocates and patient groups. Creating any resource that is linked to clinical research is not only about the content, but also about using the right tone, plain language, and appropriate format, especially when addressing topics that are complex to understand. Additionally, involving patients in the development of the resources helps to widen dissemination, as they share the resources with their own communities and through their own networks."

Trishna Bharadia, Patient Author, Buckinghamshire, UK and Centre for Pharmaceutical Medicine Research, King's College London, London, UK

The MRCT Center is a research and policy centre dedicated to the ethics, regulatory environment, and conduct of multi-site, multinational clinical trials.

PHUSE informational data literacy video series

Since its inception, the PHUSE pilot project[7] has united multiple stakeholders, including international representatives of the pharmaceutical industry, patient advocacy, and academia to develop videos that describe the foundational

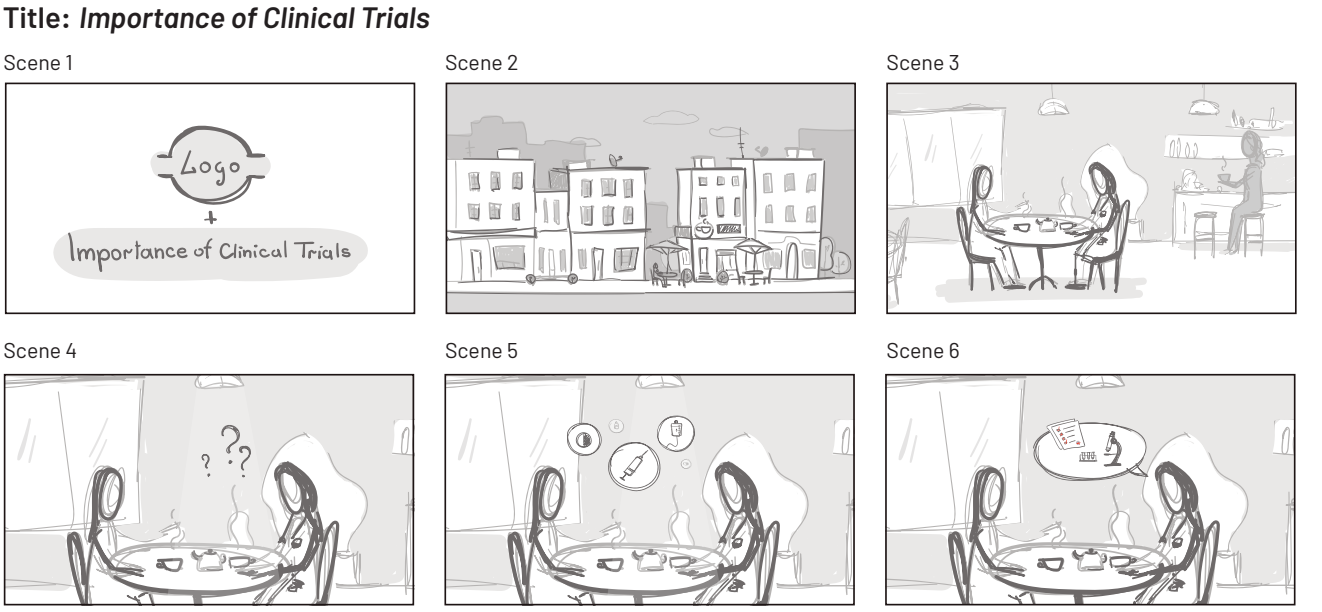

Figure 1. Example of black and white sketch drawings based on the script

concepts of clinical trials and more complex topics, such as what happens to research data.

Approaches to creating the video series

Content delivery and organisation

A video format was chosen as an engaging and accessible method for delivering content in plain language. The videos build in complexity and are intended to be watched in sequence, though each video (listed below) can also be viewed independently of the others.

- Video 0: *Introduction*
- Video 1: *Importance of Clinical Trials*
- Video 2: *What Will I Receive and When Will I Receive It?*
- Video 3: *What is Clinical Data?*
- Video 4: *Journey of a Data Point*
- Video 5: *What is Data Sharing?*
- Video 6: *What is Data Privacy?*

As of June 2024, three videos have been released (Videos 0, 1, and 2).[12]

Content and video development

The process to develop and share the content consisted of 5 steps (described below).

1. Scriptwriting
2. Audio considerations
3. Illustration and storyboard creation
4. Video animation and audio-visual integration
5. Dissemination

1. Scriptwriting

The project team started by brainstorming ideas alongside patient advocates' feedback. The script uses first-person dialogue and contractions to create a conversational tone and personable, open, and approachable setting for answering questions.

Precise word choice and concise sentences convey complex concepts clearly and technical terminology is explained within the conversation. For the videos, the project team decided to use the words "trial" and not "study" consistently and to repeat the terms "safe" and "effective" as these underpin the main objectives of clinical trials.

A draft script was reviewed by the project team, shared with PHUSE leadership, and amended based on feedback. Before sending the proofread script to the videographer, the project team highlighted part of the script for keywords to appear as bold on-screen to emphasise important words and phrases.

2. Audio considerations

The project team used a survey to reach consensus for selecting a human voiceover actor. The videographer obtained the voiceover recording from the selected actor and the project team reviewed and approved.

The project team tested AI voiceovers to reduce the financial cost of using human voice actors. AI was tested both because the videos were long and complex, making them more expensive to produce, and because of the potential benefits for choosing a character, voice, and translation in additional languages beyond English.

Through numerous rounds of review and changes to tone and empathy, using AI was proving to be more challenging than expected. Concerns included the voice sounding impersonal and robotic, and the presence of delivery issues (e.g., lack of pauses, too fast, and strange intonations and inflections).

Following discussions with patient advocacy groups and understanding the patient perspective in relation to AI, the project team

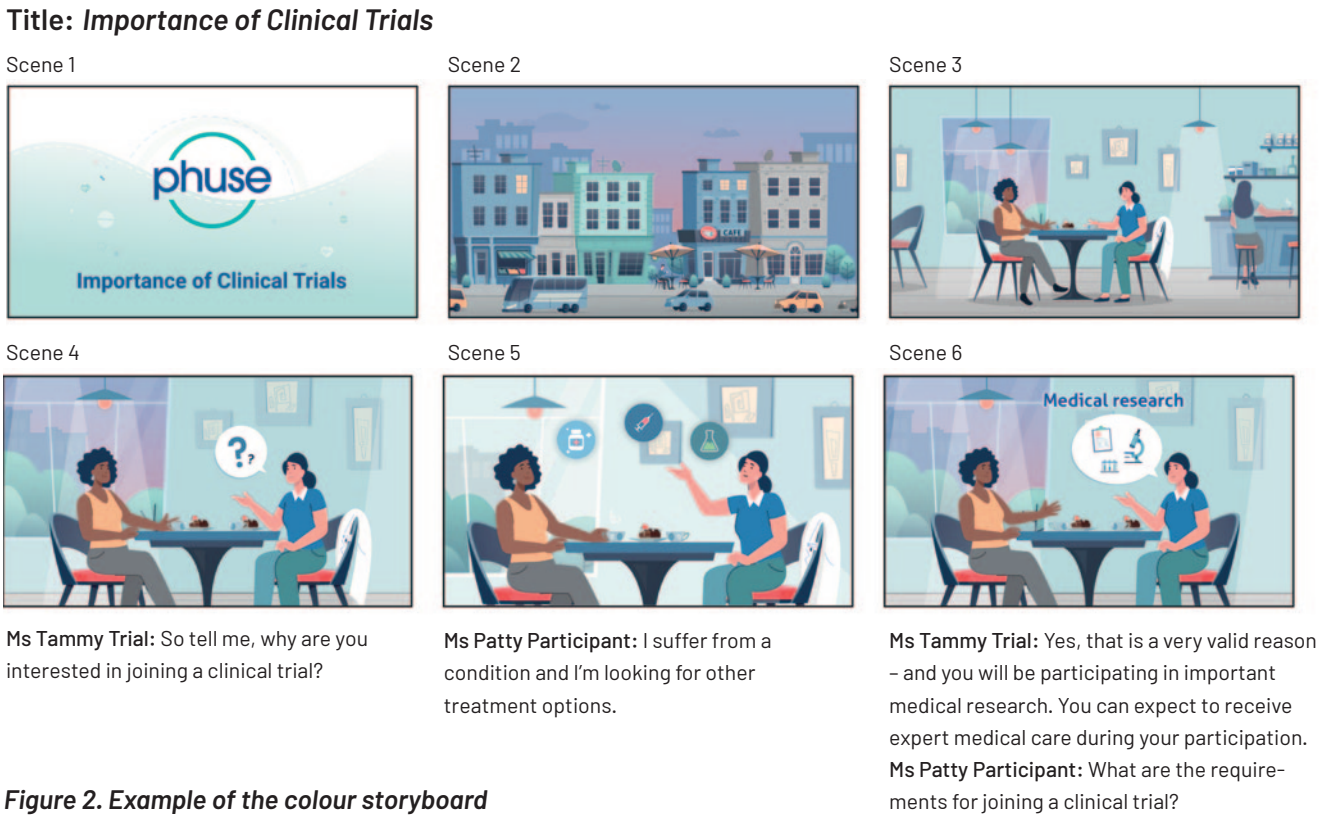

Figure 2. Example of the colour storyboard

decided to return to human voiceovers. Currently, the AI outputs do not sufficiently model the natural empathy, tone, and contextual understanding that is reflected in organic human voice speech.

3. Illustration and storyboard creation

This process started with the videographer developing black and white sketch drawings based on the script to support understanding (see Figure 1).

After project team review, the storyboard was provided as colour images, showing how the characters and images should look in the video when paired with the approved script (see Figure 2). The industry-standard animations were suitable for use in public-facing healthcare materials to cover a wide range of audiences and age groups.

Project team amendments were implemented by the videographer. For example, facial expressions were added for each character to reflect a range of emotions, as a common concern for patients is that many digital materials do not reflect the complex emotions and concerns people have about clinical trials. For Video 2 onwards, the "Ms" titles were removed from all character name labels following project team feedback around less prescriptive gender identity.

4. Video animation and audio-visual integration

For the animation, character movements and background images were prepared first, together with the integration of voiceover. The project team assessed if additional pauses needed to be included in the speech given the complexity of the information being presented and to provide the videographer with specific timepoints for where these should be included. Facial movements were added to the animation before finalisation of video together with patient advocate feedback. A running transcript was provided alongside the video while both characters were talking, and key words appear as prompt boxes.

5. Dissemination

PHUSE uploaded the approved video to YouTube, created social media posts, and e-mailed communications to the wider PHUSE Community.

Additional considerations

As of the writing of this article, the first three videos are complete, feature two primary characters that present as female, one black and the other white. As the project has evolved, there has been increased focus on ensuring the videos are representative of different populations, especially those who have been historically minoritised. Future videos will introduce new characters with other diverse backgrounds and ethnicities.

MRCT Center data literacy infographics

The MRCT Center joined the PHUSE project team in 2023 to collaborate on creating simple one-page printable infographics about research data collection, management, and use. These are complementary to the PHUSE video series and can be downloaded, saved, and printed for easy in-person access and dissemination, where technology may be limited. An infographic can deliver memorable and concentrated information on one specific topic in a digestible way using simple text, graphics, and a diversity of characters to promote engagement, comprehension, and retention.

The creation of the data literacy infographics was informed by the MRCT Center's experience developing a related resource, the Clinical Research Glossary[11], which provides measured

amounts of focused and accessible information. The infographics explain what data are, why a participant's data are important in clinical research, and how data are protected. Like the PHUSE videos, the series is intended as an educational tool to inform the public of the significance of research, while also empowering and destigmatising participation in clinical research.

Approaches to creating the data literacy infographics

Content delivery and organisation

Since PHUSE was creating videos, the MRCT Center led the production of educational materials that could be used in settings where video use may not be possible or appropriate, and a printable infographic could be helpful.

Five infographics cover key questions about research and data:

- *Infographic 1: Your Data, Your Information:* defines data and provides an elementary overview of the significance of data to research.
- *Infographic 2: What happens to data during a research study?* reviews the life cycle of data during a clinical trial, from data collection to data analysis.
- *Infographic 3: What happens to data after a research study?* explains the importance of saving data and how that is accomplished.
- *Infographic 4: What is a data repository*? defines data repositories and their role in advancing science through aggregate data collection.
- *Infographic 5: What happens to your data when you leave a study early?* provides an overview of what can happen to data after withdrawal of consent, discontinuation of interventions, or termination of a study.

Content and infographic development

The process to develop and share the infographic content consists of 4 steps (below), each of which will be further described.

1. Scriptwriting
2. Graphic design
3. Translation
4. Dissemination

1. Scriptwriting

An infographic was developed whenever a concept mentioned in the PHUSE video series was not only complex but critical for participants to understand. The infographic content was developed to be clear, simple, and in plain language, and reviewed extensively by the project team, including subject matter experts, patients, and participants. The first goal was to immediately engage the reader, making use of the human tendency to process most efficiently the first half of the page when viewing information and help encourage reading further down the page.[13,14]

Each infographic addresses its topic through informative subheadings and bullet points. Sentences are constructed to be clear and concise, using an active voice to decrease ambiguity, and using a second person to directly address the reader. As is customary in infographics, sections are short so the reader can absorb the information without trawling through dense text.

2. Graphic design

Graphic designers were utilised in the graphics development phase and were asked to follow the same general style as the PHUSE videos. Characters were created to represent a diverse range of audiences to reiterate that clinical research is for all people and not just one group. The text was distributed evenly across the layout from left to right and top to bottom to reflect the reading direction of English speakers. Bold font and italics were used to highlight key terms and concepts and blank space was introduced to ease the reading experience.

Text was divided into 3–4 digestible sections, and imagery was designed to complement the infographics' objectives to aid understanding and support viewing either online or as a printout.

The MRCT Center's graphic designers objectively developed the materials for varying visual ability levels by testing for colour contrast, using legible fonts, and ensuring suitable font sizes. Imagery was developed with the intention of depicting research as a positive social good, with the purposeful focus on using diverse characters and avoiding any potentially fear-inducing or dehumanising icons (e.g., drills, needles, test tubes, etc).

3. Translation

The infographics were initially developed in English. Prior to translation, a multi-variable assessment was conducted that focused on the target audience and intended reach. Latin American Spanish was chosen, and additional languages will be considered in the future. The English-to-Spanish infographic text translation process begins when the text is first exported and translated using an online instant translation platform (Google Translate). The English text and its Spanish translation are then sent to an MRCT Center bilingual translation partner who back-translates the text, edits, and confirms the accuracy of the translations. The edited and confirmed translated text is then used to produce the translated infographic.

4. Dissemination

The infographics will be available on the MRCT Center and PHUSE websites. A QR code will be included to facilitate access to all materials in one location. Disseminated file formats will include PDF to allow for text search function, PNG to optimise image quality for electronic sharing, and JPG to optimise image quality for printed infographics.

Video and infographic feedback collection and user testing

A process involving feedback collection, response documentation, and comment resolution has been implemented for both the data literacy videos and infographics (see Figure 3).

An important consideration was to ensure the audience remained engaged. The audience can pause and repeat sections of a video to support learning, particularly when complex and sensitive topics are discussed. As a result, the project team included a variety of images, highlighted key words, and added short pauses between concepts to allow the audience to digest and assimilate words, audio, and visuals. After the release of the two pilot videos, strategic user testing[7] was conducted through the PHUSE Community Forum as a live comment and feedback discussion, to ensure future video content aligns with audience needs and to determine the direction of subsequent videos.

It was important to engage with key partners who represent a range of knowledge of clinical trials and data literacy when the MRCT Center team determined which topics should become infographics, what information to share on the topics, and how that information should be described and depicted graphically. Brainstorming the infographic content was collaborative and involved significant participant review. Formal feedback was collected three times throughout development:

1. After initial text content generation
2. After the initial graphic layout was produced

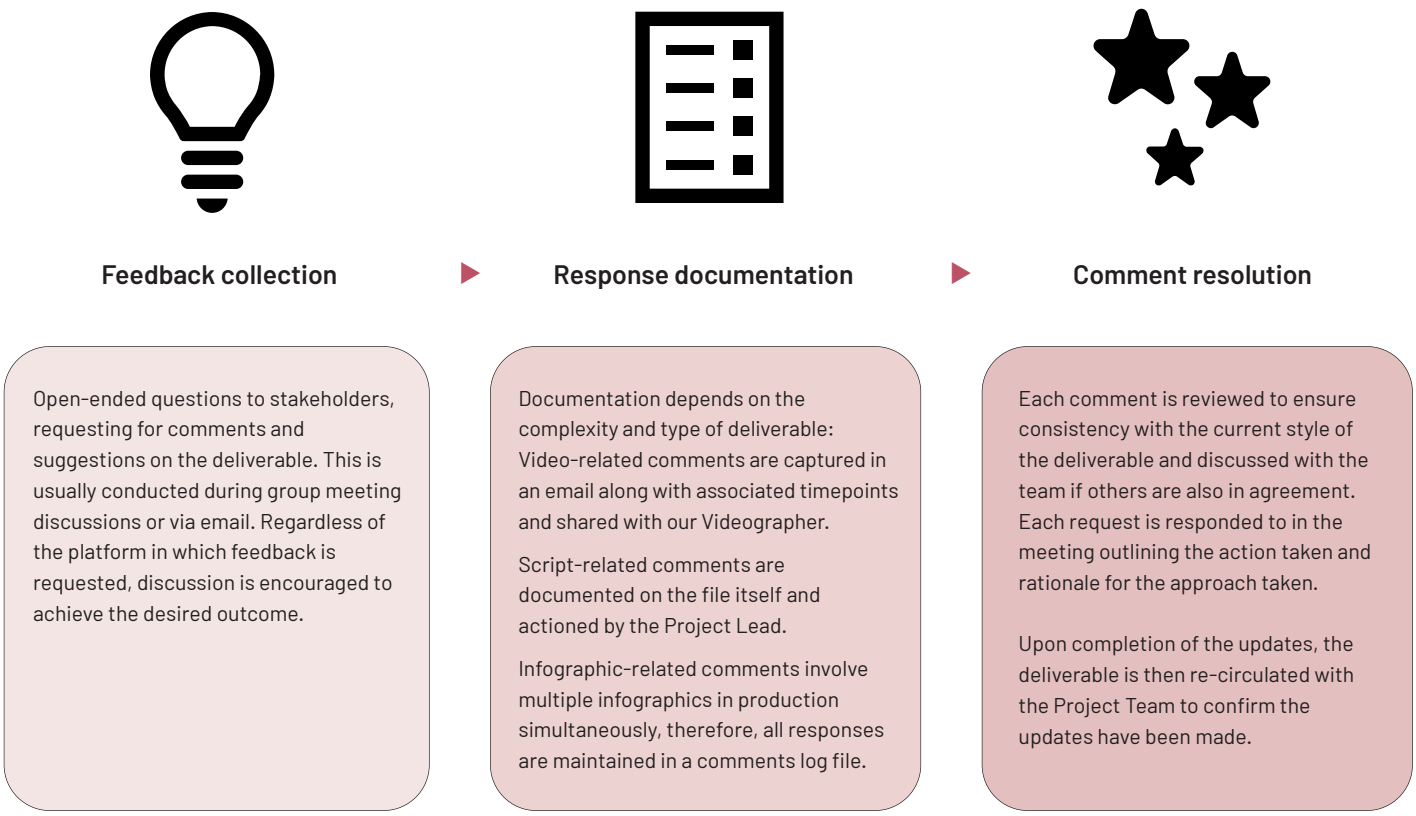

Figure 3. Feedback process for videos and infographics

3. After all the feedback has been reconciled and the infographic is considered complete

Our recommendations

Our efforts to create data literacy videos and infographics have reiterated the importance of engaging key stakeholders and performing user testing early in development, to gain feedback and understand what the audience already knows, the questions they may have, and how to convey these points in effective, patient-centric ways. Although integrating essential changes have at times lengthened the development timeline, the investment is worthwhile, as the content cannot be easily altered once released into the public domain. It is also necessary to balance the tendency to continuously edit, which has time and cost implications. Current plans are to include periodic updates into future deliverables as an evolutionary process of this project.

Finally, it is valuable to obtain feedback from different audiences across different contexts and different geographies. Having a wide range of perspectives allowed the project team to consider how to incorporate linguistic and cultural differences. For example, various options to depict travel to a research site that would resonate with the intended audience were discussed.

The limitations of this project include no language translation, a lack of low-and-middle-income country representation on the project team, and a focus that is predominantly northern/western hemisphere and high-income-centric. These factors are being continuously considered as the project evolves.

Conclusion

PHUSE and MRCT Center's journey to create easily accessible information through videos and infographics highlights the importance of clear communication, plain language, tone, and empathy, while honouring the fact that participants' data comes from individuals who care about participating, understanding what happens to their data, and protecting their privacy. In rejecting AI voiceovers, the human elements of patient-friendly materials were emphasised. Transparency, flexibility, and openness to collaboration with different stakeholders, particularly patients and their caregivers, help to ensure that content development is suitable, appropriate, and relevant for its intended audience. The videos and infographics are two examples of trustworthy resources designed with and for patients and trial participants. Both PHUSE and the MRCT Center welcome readers to share the content and contribute to this project going forward.

Our efforts to create data literacy videos and infographics have reiterated the importance of engaging key stakeholders and performing user testing early in development, to gain feedback and understand what the audience already knows, the questions they may have, and how to convey these points in effective, patient-centric ways.

Acknowledgements

The authors would like to thank the PHUSE Data Transparency Working Group's "Educate the General Population on Data Privacy and Data Sharing" workstream for assistance and input for the development of project deliverables. We also thank the wider network who participated in providing feedback during useability testing, Deborah Collyar for continued support and providing opportunities for us to showcase our work to the patient community and obtain vital feedback from the PAIR Network, and Dmytro Korolkov for his amazing expertise and talent to bring ideas to life in creating this video series. Together, collaborations with representatives from a range of disciplines and backgrounds have continued to strengthen knowledge-sharing, promote diverse discussions, and tackle misinformation.

Disclaimers

The opinions expressed in this article are the authors' own and not necessarily shared by their employer or EMWA.

Disclosures and conflicts of interest

Trishna Bharadia is the owner of The Spark Global, a patient engagement and advocacy consultancy that undertakes paid work with multiple stakeholders in the life sciences industry, including pharmaceutical companies and CROs. She also holds a voluntary position on the Advisory Board for the Patient Information Forum. The author declares no conflict of interest.

The remaining authors declare no conflicts of interest.

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Publisher perspectives on plain language summaries of scientific publications: An Open Pharma survey

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doi: 10.56012/pzwh6593

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Abstract

Plain language summaries (PLS) of scientific publications can help to make scientific literature more understandable. In healthcare, PLS can contribute to informed decision-making by healthcare professionals, patients, and their caregivers. In late 2022 and early 2023, the multi-sponsor collaboration Open Pharma developed a 16-question survey to collect the perspectives of journal editors and publishers on PLS and whether they align with the Open Pharma PLS recommendations. A total of 29 surveys were completed, representing 26 individual journals and seven publisher portfolios. Of these, 19 journals and two portfolios did not offer PLS as an option to authors, and one portfolio respondent was unsure. The survey showed variability in format, location, and peer review practices for PLS, and inconsistent tagging of PLS for PubMed indexing. The results highlight the need for more journals to accept PLS and follow best practice recommendations to ensure PLS are peer reviewed and discoverable.

Supplemental materials are available for this article at: https://doi.org/10.6084/m9.figshare.25886779.v1

Within the context of scientific and medical research publications, plain language summaries (PLS) are concise summaries written in jargon-free and non-technical language for a broad, non–specialist audience. Although the term *PLS* may be used to describe other accessible language documents,[1] here we exclusively refer to PLS that are hosted with the associated scientific publication.

PLS can help to bridge information gaps and enable individuals with diverse backgrounds, levels of health literacy, and accessibility needs to read and understand research.[2-7] PLS may be of particular value in healthcare, where patients, patient advocates, caregivers, and healthcare professionals (both specialist and non-specialist) need to work and make decisions together to improve patient outcomes.[8,9] In recent years, one pharma company has publicly committed to publishing PLS with all research publications that meet certain criteria,[10] and industry-wide publication guidance[11] has been updated to recommend adoption of PLS.

In an effort to support the standardisation of PLS, Open Pharma – a multi-sponsor collaboration working to improve the communication of pharma-sponsored research – published a set of minimum recommendations for PLS of peer-reviewed medical journal publications.[12-14] Published in 2021, these recommendations state that PLS should be "in the style of an abstract, understandable and readable, free of technical jargon, unbiased, non-promotional, peer reviewed, and easily accessed".[13]

Several of the Open Pharma PLS recommendations[12,13] fall under the responsibility of journals, such as ensuring that PLS are explicitly linked to the source article, fully peer reviewed alongside the accompanying manuscript, and tagged with appropriate metadata and keywords to improve their discoverability.[12,13]

In late 2022 and early 2023, Open Pharma carried out a survey to investigate whether current publisher practices aligned with the Open Pharma PLS recommendations.[12,13] Here, we summarise the results of the survey and identify areas for improvement in PLS publication practices.

The survey

The objectives of this study were: to understand the PLS policy landscape across publishers; to engage with publishers regarding PLS; and to encourage more publishers of medical research to offer their authors the chance to include PLS. The survey (Supplementary Material) was developed through consultation with the Open Pharma PLS working group. It consisted of 16 questions, including "Does your journal/publisher offer PLS options for authors to submit?", "Where are your PLS located?", "What formats of PLS do you accept?", and "Are PLS included in the peer review package?".

Journal publishers and editors attending three international conferences focused on scientific and medical publications were invited to complete the survey: the ninth annual International Congress on Peer Review and Scientific Publications, September 2022, Chicago, Illinois, USA; the Association of Learned and Professional Society Publishers Annual Conference and Awards, September 2022, Manchester, UK; and the European Meeting of the International Society for Medical Publication Professionals, January 2023, London, UK. The survey was made available to delegates both as a Microsoft Form accessible via a QR code and as a hard copy that could be returned either in person or via email.

A second group of journal publishers and editors with a perceived interest in completing the survey were identified through web searches and previous contact with the survey authors. The survey was sent to these individuals as a Microsoft Form via email.

Publisher perspectives on PLS

In total, 29 surveys were completed representing the perspectives of 22 unique publishers or publishing imprints (according to responses to survey question 2, "What publisher do you work for?"). Of these, 18 surveys (18/29, 62%) reported on one individual journal, four surveys (4/29, 14%) reported on two journals each, and seven surveys (7/29, 24%) provided insights pertaining to a portfolio of multiple journals

Plain language summary of this article

Plain language summaries (PLS) are short, easy-to-read summaries of scientific research articles. They are sometimes published next to research articles to help non-specialist readers understand what the articles mean.

In 2022 and 2023, we surveyed publishers to ask if their journals publish PLS and how they publish them. The survey was completed by 29 people. They provided information about 26 individual journals and seven groups of journals (known as publisher portfolios).

Our survey results suggest that journals do not always allow authors to submit PLS alongside their research articles. Of the 26 individual journals, 19 did not offer PLS as an option to authors. Two of the seven publisher portfolios did not offer PLS as an option to authors. The most common reason journals gave for not offering PLS was "lack of reader demand".

The journals that allowed PLS varied in how their PLS looked and where in the research article they were found. Some journals asked independent experts to review PLS before publication (a process called peer review), but others did not. Journals do not always give PLS a tag that makes them easier to find on a website widely used to search for biology and medical publications called PubMed.

Overall, our results show an opportunity for more journals to allow authors to publish PLS of scientific research articles. We believe that journals should follow best practice recommendations to make sure that PLS are peer reviewed and readers can easily find them.

An infographic and a video summary of this article are available in online supplementary materials, which are available at: https://doi.org/10.6084/m9.figshare.25886779.v1.

(Figure 1). If each of these seven responses (7/29, 24%) apply to the full portfolio of journals issued by the corresponding publishers, the responses would reflect PLS practices at 6–418 journals (mean: 100; median: 30).

Most surveys represented "medical" or "health" journals (21/29, 72%); two surveys represented journals publishing "basic science and some medical science" (2/29, 7%). Overall, the respondents provided information regarding seven publisher portfolios and 26 individual journals.

Publisher portfolios

Of the seven publisher portfolios surveyed, four (4/7, 57%) allowed authors to submit PLS to some or all of their journals, two (2/7, 29%) did not offer PLS options, and one (1/7, 14%) respondent was unsure of their publisher's PLS offerings (Figure 1).

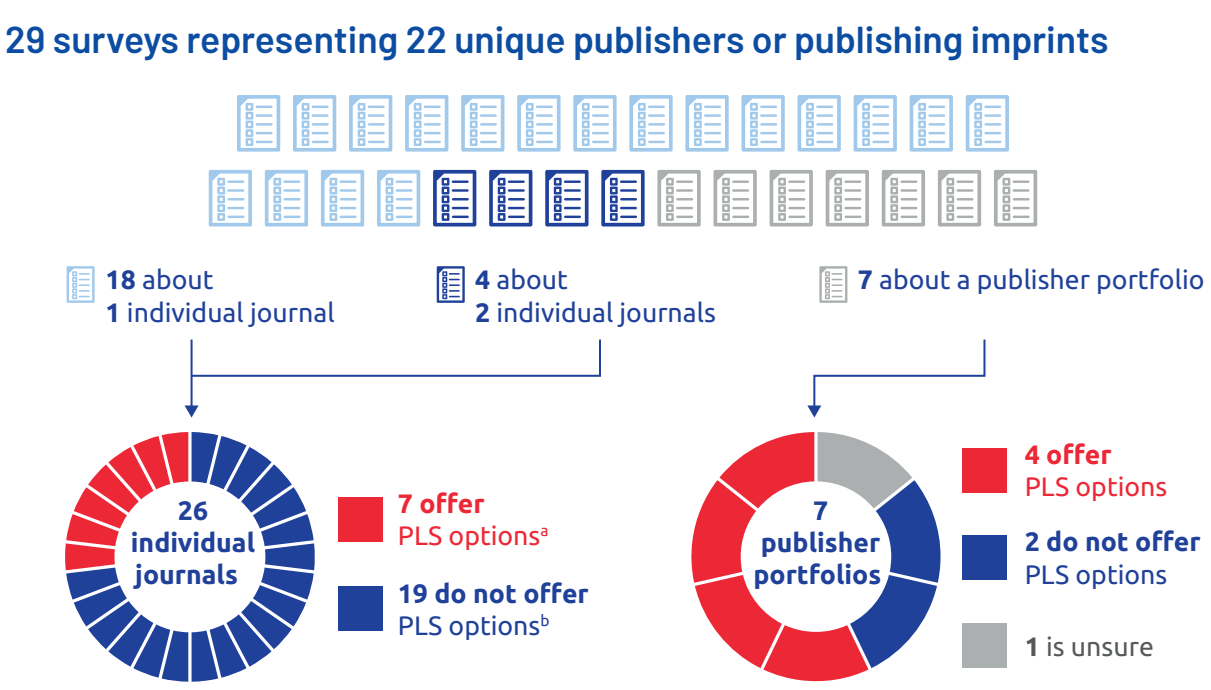


Figure 1. Surveys were completed by 29 individuals, representing the perspectives of 22 unique publishers or publishing imprints

[a] Data from seven surveys[c] submitted by seven respondents representing seven unique publishers or publishing imprints.

[b] Data from 16 surveys[c] submitted by 16 respondents representing 13 publishers or publishing imprints; two respondents reported that their journals generate their own PLS for selected articles written in-house.

[c] Data do not add to 22 because one survey reported on two individual journals that differed in their PLS offerings. This response is counted in both groups of individual journals: those that offer PLS options and those that do not offer PLS options.

PLS, plain language summary(ies).

What is the primary reason for not currently offering PLS?

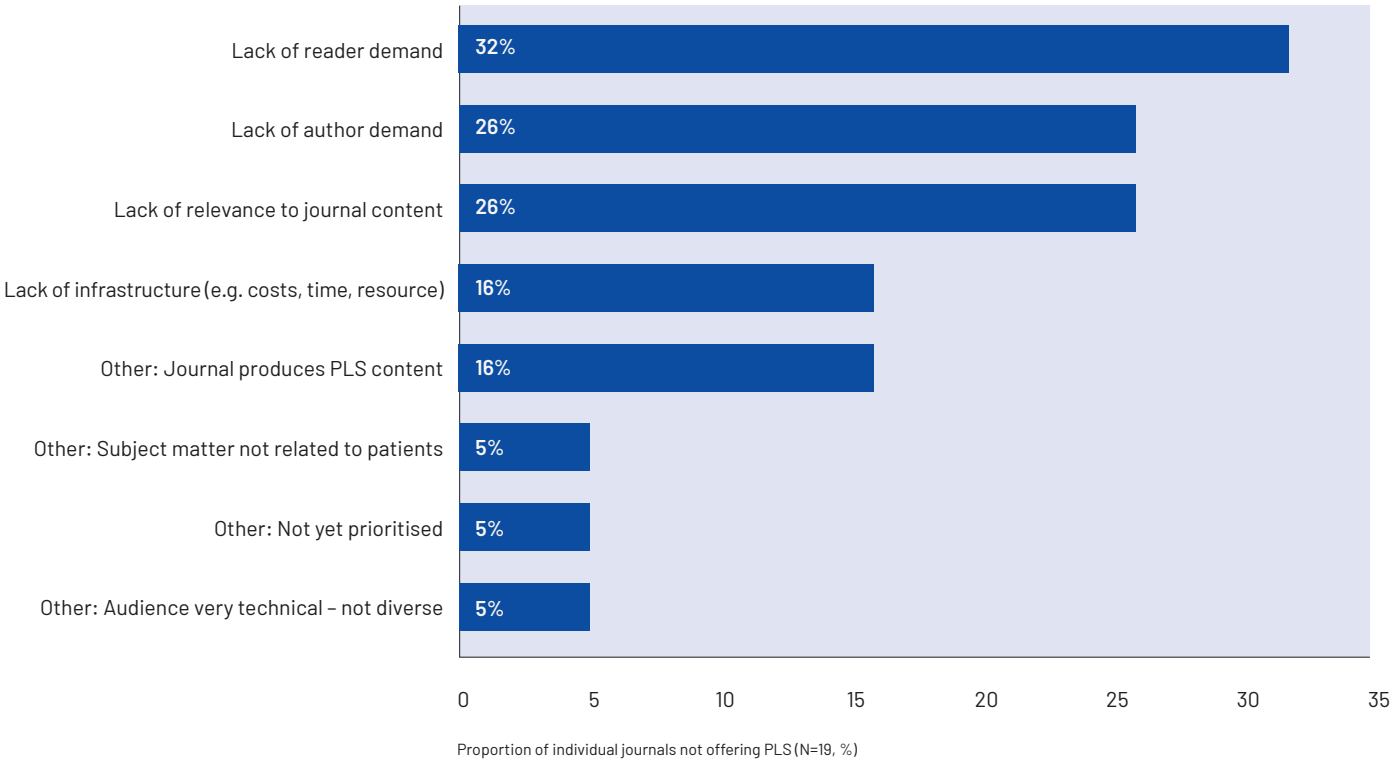


Figure 2. Of the individual journals that responded to the survey, 19 (19/26, 73%) did not allow authors to submit PLS. The most common reason these journals gave for not offering PLS was lack of reader demand (6/19, 32%)

Respondents could select more than one reason from a pre-defined list.

PLS, plain language summary(ies).

Individual journals

Prevalence of PLS

Of the individual journals surveyed, the majority did not offer PLS options to authors; seven (7/26, 27%) allowed authors to submit PLS, while 19 (19/26, 73%) did not (Figure 1). However, two of the 19 journals that did not allow authors to submit PLS do write summaries themselves in more accessible language than the scientific abstract for selected articles – these were described by the respondents as "summaries for patients" and "plain language versions".

The most common reasons for not offering PLS, as selected from a list of pre-determined multiple-choice options, were lack of reader demand (6/19, 32%), lack of author demand (5/19, 26%), lack of relevance to journal content (5/19, 26%), and lack of infrastructure (e.g. costs, time, resource) (3/19, 16%) (Figure 2).

Format and location

Each of the seven individual journals (7/7, 100%) that allowed authors to submit PLS offered text-based, abstract-style publication formats (Figure 3). Three of these journals (3/7, 43%) also offered single-page plain language infographics, and one journal (1/7, 14%) accepted multipage infographics or video content.

The location of the PLS in relation to the article varied between journals. Of the journals that allowed authors to submit PLS, six (6/7, 86%) indicated that they position PLS in a single location: either located directly after the scientific abstract (3/7, 43%), in the supplementary material (1/7, 17%), or embedded in a text box within the article (2/7, 29%). One journal (1/7, 14%) indicated that PLS could be located directly after the scientific abstract and/or in the supplementary materials (Figure 4).

Audience

The most commonly cited target PLS audiences from a pre-defined multiple-choice list were patients, their organisations and advocacy groups (5/7, 71%), healthcare and research professionals (4/7, 57%), and students (4/7, 57%). Less commonly cited audiences included policy and governance professionals (3/7, 43%), educators and trainers (2/7, 29%), and others (free-text responses included funders [1/7, 14%], people with lived experience [1/7, 14%], media and social media [1/7, 14%], and anyone [1/7, 14%]) (Figure 5).

Six of the seven journals (6/7, 86%) offering PLS agreed that publishing PLS alongside the scientific abstract and article may increase or diversify journal readership. The remaining journal (1/7, 14%) was unsure of the benefits of including plain language content.

Indexing

The survey results indicate that indexing practices are inconsistent among journals offering PLS. Only one of the seven journals (1/7, 14%) that

Most common PLS formats

Figure 3. Of the seven journals that allowed authors to submit PLS, all (7/7, 100%) offered text-based, abstract-style PLS formats

Respondents could select more than one format from a pre-defined list.

PLS, plain language summary(ies).

Most common locations of PLS in an article

Figure 4. PLS were most commonly located directly after the scientific abstract (4/7, 57%)

Respondents could select more than one location from a pre-defined list. One journal (1/7, 14%) indicated that PLS could be located directly after the scientific abstract and/or in the supplementary materials.

PLS, plain language summary(ies).

Most common target audiences for PLS

Figure 5. While patients, patient organisations, and advocacy groups were reported to be the most prominent target audience for PLS (5/7, 71%), journals also expected plain language content to be of use to healthcare and research professionals (4/7, 57%)

Respondents could select more than one target audience from a pre-defined list.

PLS, plain language summary(ies).

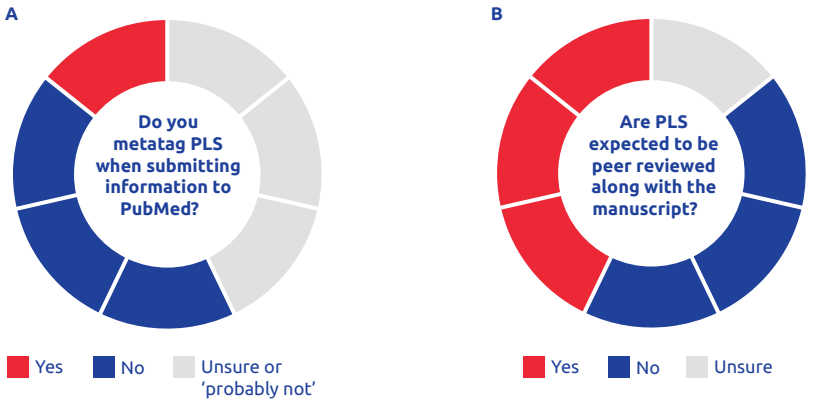


Figure 6. Just one of the seven individual journals (1/7, 14%) that publish PLS uses a PLS-specific metatag when sending information to PubMed (A), and three of the seven journals (3/7, 43%) send PLS for peer review alongside the manuscript (B)

PLS, plain language summary(ies).

accepted PLS from authors used a PLS-specific metatag when submitting information to PubMed for indexing. The remaining journals either did not use a PLS metatag (3/7, 43%) or were unsure of their metatagging processes (3/7, 43%). One respondent who was unsure stated that they "probably" did not metatag PLS (Figure 6A).

Supplementary material

Infographic
Open Pharma. Publisher perspectives on plain language summaries (PLS): A survey study. 2024 Available from: https://doi.org/10.6084/m9.figshare.25886779.v1.

Video summary
Open Pharma. Open Pharma summit 2023 | Publisher perspectives on plain language summaries: an Open Pharma survey. 2024. Available from: https://doi.org/10.6084/m9.figshare.25886836.v1.

Survey
Open Pharma. Plain language summary (PLS) publishing practices survey. 2024 Available from: https://doi.org/10.6084/m9.figshare.25867135.v1.

Peer review

The results of the survey show that PLS are not always peer reviewed alongside the manuscript (Figure 6). Three of seven journals (3/7, 43%) that allowed PLS submission included them in the peer review package alongside the manuscript, whereas three (3/7, 43%) did not peer review PLS (Figure 6). The remaining respondent (1/7, 14%) was unsure of their journal's PLS peer review policy (Figure 6B).

Two journals (2/7, 29%) provided specific guidance on PLS to their peer reviewers. However, one journal that answered "no" to "Does your journal/publisher offer PLS options for authors to submit" answered "yes" to "Do you provide specific guidance on PLS for your peer reviewers". No further details about this apparent discrepancy were provided in the free-text section of the survey.

Of the seven journals that allowed authors to submit PLS, three (3/7, 43%) involved "lay or non-expert" reviewers in the peer review process; three journals (3/7, 43%) that allowed authors to submit PLS did not include non-expert reviewers, and one journal (1/7, 14%) was unsure of whether they involved non-expert peer reviewers. Interestingly, two journals (2/7, 29%) that answered "no" to this question explained in free-text responses that they did use non-expert reviewers in other journal processes, but that they were "not involved in PLS review" or that the reviewers were "not specific to PLS".

Discussion

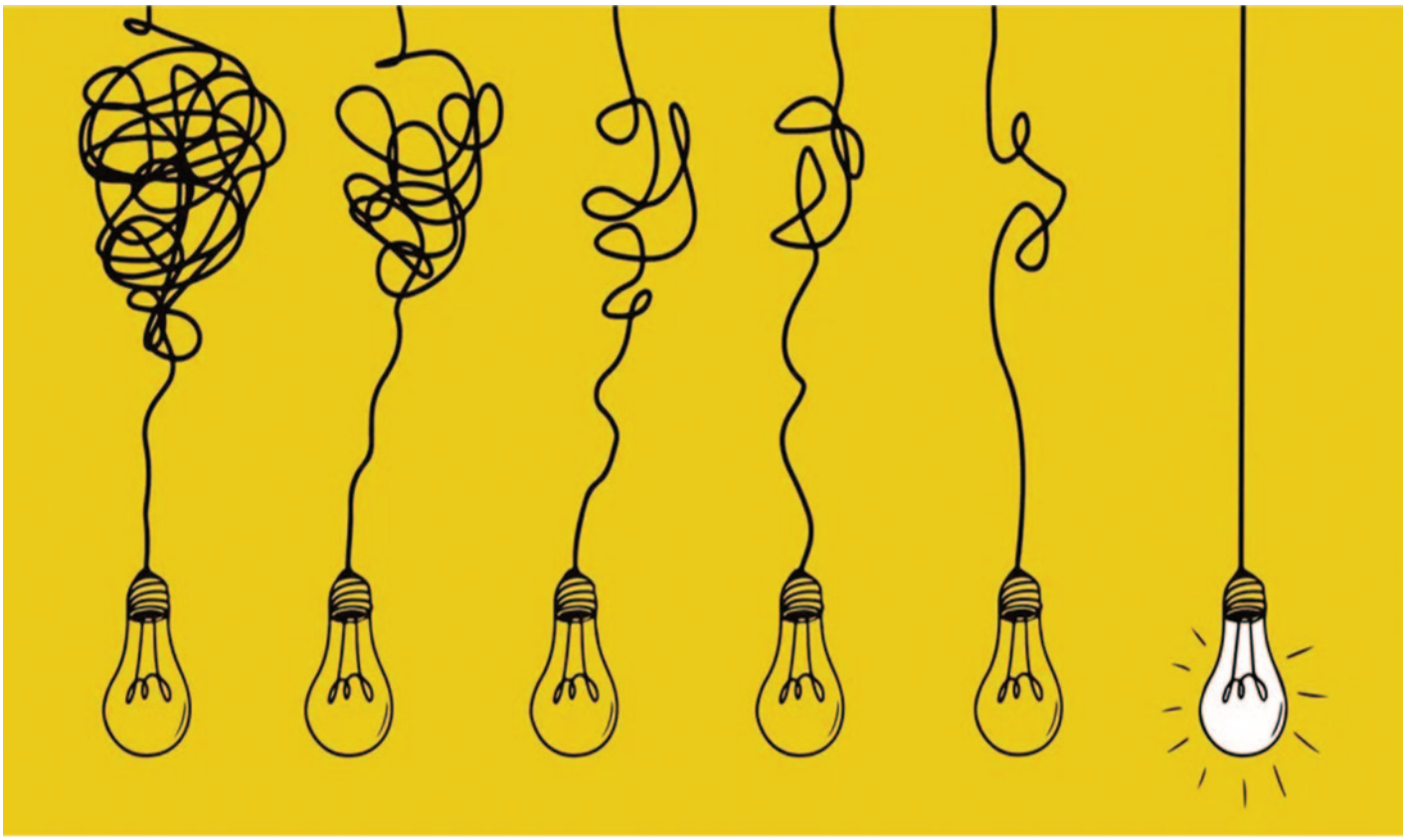
Despite the role of PLS in improving the understanding of scientific research, our survey suggests that many journals are yet to adopt PLS. Among the journals that do support PLS submission (7/26 individual journals surveyed), publishing practices often differ from the Open Pharma best practice recommendations for PLS.[12,13] For example, some journals do not send PLS for peer review or do not use the PLS-specific metatag that enables correct PubMed indexing. Encouragingly, however, our results suggest that when journals publish PLS, they offer the recommended minimum-standard, text-based, abstract-style format.

Our results are consistent with previous research showing that although the publication of PLS alongside scientific articles is increasing, it is yet to be a widespread practice across scientific journals. For example, a 2022 analysis found that just 10 journals were responsible for 73.5% of text-based PLS indexed in PubMed.[15] Previous research has also identified great variability in the content, format, and visibility of published PLS,[16,17] and has highlighted a need for journals that publish PLS to provide consistent, standardised instructions to guide authors in how to develop these summaries.[18]

> Most of the PLS-publishing journals captured in our survey believe that PLS enable them to reach various non-specialist audiences.

Most of the PLS-publishing journals captured in our survey believe that PLS enable them to reach various non-specialist audiences. As the majority of survey respondents represented medical and health journals, a focus on patients and caregivers as target audiences is not unexpected. However, it is noteworthy that healthcare and research professionals, as well as students, were also common target audiences for this small sample of PLS-publishing journals. To be a trusted educational resource to specialist and non-specialist audiences alike, it is imperative that PLS are peer reviewed alongside the associated manuscript. Peer review ensures that the content is scientifically accurate, a true reflection of the source article, and free from bias.[19]

Our results suggest that few journals (1/7, 14%) are using PLS-specific metatags when sending information to PubMed, which may lead



to incorrect indexing. In a 2022 Open Pharma analysis, 14.6% of PubMed records using the <plain-language-summary> tag were using it incorrectly: in these cases, the tag was found to be erroneously associated with a non-English language abstract, other non-PLS content, or a duplicate of the scientific abstract.[17] While standardisation of metatagging processes would improve the indexing of PLS in PubMed, it is as yet unclear if such improvements would truly enhance the visibility and discoverability of PLS for non-scholarly, general audiences, including patients and caregivers. For PLS to be truly accessible and discoverable, general readers must know where to find them and be able to access them free of charge – potentially via other medical information sources with links to published results in PubMed.

Strikingly, the survey results also indicate that publishers and editors are not always aware of their own PLS policies and practices, highlighting the need for improved internal information sharing and training.

Strikingly, the survey results also indicate that publishers and editors are not always aware of their own PLS policies and practices, highlighting the need for improved internal information sharing and training.

This survey is limited by its small sample size, and it is unlikely that our results are representative of PLS practices across the whole publishing industry. However, when taken together with other explorations into the current state of PLS publication standards,[15,16,18,20,21] and an increased reader and study sponsor demand[10] for this content, the survey highlights a need for change in journal practices related to PLS. We believe that this should start with all journals allowing authors to submit text-based PLS of 250 words or fewer with any manuscript submission. Further action to implement peer review of PLS alongside the manuscript and to tag PLS with metadata for intuitive PubMed indexing would improve the accuracy and discoverability of this type of content for specialist and non-specialist audiences alike.[12]

Acknowledgements

The authors would like to thank Francesca Ounsworth of Oxford PharmaGenesis, Janet Davies and Linda Feighery of UCB, Klaus Boberg of Novo Nordisk, Louise Roch of Boehringer Ingelheim, Radha Narayan of AstraZeneca, Rikke Egelund Olsen of F. Hoffmann-La Roche, Sally-Anne Dews of Pfizer, Santosh Mysore of GSK, Taija Koskenkorva of Novartis, and William Gattrell formerly of Ipsen, now of Bristol Meyers Squibb, for their contributions to the development of a previous iteration of the survey; Fran Young of Takeda for her contribution to the collection of survey responses; the members of the Open Pharma PLS and discoverability working group for their contributions to and guidance during the development of this survey; the respondents for completing the survey; and Sophie Nobes, BSc, (https://orcid.org/0009-0000-7816-0862) and Velissaria Vanna, PhD, of Oxford

PharmaGenesis, Oxford, UK, for providing medical writing and editorial support, respectively, which has been co-funded by Oxford PharmaGenesis, Oxford, UK and the Open Pharma Members and Supporters, in accordance with Good Publication Practice 2022 (GPP 2022) guidelines (https://www.ismpp.org/gpp-2022).

Disclaimers

This work was supported by Open Pharma. Open Pharma is a multi-sponsor collaboration at and facilitated by Oxford PharmaGenesis. At the time of this work (2022–2023), Open Pharma received sponsorship funding from AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim International GmbH, Bristol Myers Squibb, F. Hoffmann-La Roche AG, Galapagos NV, Gilead Sciences, Inc., GlaxoSmithKline Biologicals SA, Ipsen Biopharm Ltd, Janssen Scientific Affairs, LLC, a Johnson & Johnson Company, John Wiley & Sons, Inc., Novartis Pharma AG, Novo Nordisk A/S, Pfizer Inc., Takeda Development Center Americas, Inc., Taylor & Francis an Informa Plc company, and UCB Biopharma SRL.

Disclosures and conflicts of interest

SB was an employee and shareholder of Galápagos NV, Mechelen, Belgium at the time of data collection and first draft development, and is now an employee of Alfasigma S.p.A., Bologna, Italy. AR, CW, JG, and JO are employees of Oxford PharmaGenesis Ltd, Oxford, UK, of which CW is also a shareholder and Director. AR receives departmental funding from the Centre for Pharmaceutical Medicine Research, King's College London, London, UK for doctoral research on patient involvement in publications, which is unrelated to this work. VP is an employee and shareholder of UCB Biopharma SRL.

Data availability statement

Anonymised data are available on request from OxfordProject@pharmagenesis.com.

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Medical writing in Italy in 2024: Results of the first Italian business and compensation survey

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doi: 10.56012/zgzn6726

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Abstract

In Italy, little is known about the roles, activities, and compensation of medical writers and scientific communicators. A survey, tailored to local aspects and regulations, was conducted to capture a contemporary snapshot of the medical writing profession in Italy. Most of the 68 respondents were female (84%), with the most common age category being 40–49 years (38%). Both Italian (78%) and English (78%) were commonly used for work. Despite gross annual salaries (mean €45,860) being lower than those of European colleagues, overall professional satisfaction was high (72% reported being satisfied or very satisfied with their work). Medical writing certification was uncommon (16%), but 37% of respondents were affiliated with the European Medical Writers Association (EMWA). The results highlight the need for local efforts to address professional recognition and training needs, with the crucial support of EMWA.

Introduction

Medical writing and scientific communications have been growing globally for years and it is estimated they will grow by 10% annually until 2030.[1] This growth is driven by several key factors, including European requirements to report results for authorised clinical trials registered in the European Union Drug Regulating Authorities Clinical Trials Database (EudraCT), the advent of medical device regulations, increased public awareness of health information needs post-COVID pandemic, and the growing demand for training and information about personalised therapies and new biotechnological molecules.[2] Italy is no exception.

Most professionals working in medical writing in Italy operate in isolation, so the first meeting of Italian medical writers and scientific communicators in March 2023, under the aegis of the European Medical Writers Association (EMWA), was a welcome development. Participants discussed the results of the most recent EMWA salary survey,[1] which highlighted many peculiarities of the medical writing environment in Italy. Participants agreed to create a local network. Both a LinkedIn group[3] and an Italian Local EMWA Group (LEG) were established. LEG members developed a document to define the activities of Italian medical writers.[3] Later, during the virtual EMWA congress in November 2023, the Italian LEG decided that an evaluation of the Italian environment and compensation trends was also necessary.

Several surveys have been performed by the American Medical Writers Association (AMWA) in America[4] and in Italy by employment companies.[5,6] While the surveys conducted by AMWA have a systematic and well-defined methodology, surveys conducted in Italy by employment companies did not define their methodology and only included results about employed professionals.

EMWA has performed periodic surveys to understand the activities of medical writers and their compensation since 2003,[1,7–10] using an increasing level of accuracy to understand the evolving scenario of both employed and freelance professionals, and assessing which factors influence satisfaction and compensation in individual European countries. The participation of Italian medical writers has always been poor, hindering any meaningful elaboration of country-specific data.

Therefore, an *ad hoc* questionnaire, based on the most recent EMWA surveys,[1,8] was developed by the core group of the Italian LEG to investigate the environment and compensation of both freelance and employee Italian medical writers.

Methods

Study design

In January 2023, the core group of the Italian LEG (including the authors of this article) met to define the clusters of interest and related questions to be submitted to Italian medical writers. The survey was disseminated through EMWA's information channels and by the Italian LEG through direct e-mails to Italian EMWA members, social media posts, and word of mouth. A link to the online survey was included in all correspondence.

All medical writers living in Italy or Italian medical writers living overseas were invited to participate in the survey, regardless of professional level. Three types of participants were identified: employees or professionals working according to a hybrid model (offering both partial contractual and occasional services; with individual taxation [VAT] registration), freelancers (with VAT registration or single-person companies), and agencies (>1 employee or working partner). The survey was available online from February 1, 2024, to February 29, 2024, and data were collected anonymously, under the General Data Protection Regulation.[11,12] Voluntary participation was considered consent for research inclusion.

Survey

The online survey was conducted in Italian and was distributed via a platform created by the technology partner Officine Telematiche,[11] which ensured secure and anonymous data collection. Clusters of questions included demographic data

(gender, age group, geographic area, mother tongue), education, medical writing experience, types of employment, work performed, compensation, and associated satisfaction levels. The survey was divided into four sections with specific questions for each employment type:

1. Demographics, education, and basic professional characteristics
2. Employee/hybrid responsibilities and salary
3. Freelance taxation, clients, outsourcing, income, payment, and services
4. Agency taxation, employee/freelance/client and income, payment, and services

Most questions were fixed (with single or multiple-answer solutions). When necessary, free text was enabled (i.e., salary-related questions). Fixed responses were common categories (sex, age, region of residency, mother tongue, work location, academic title and specialty, experience, hours worked, main work activity, main difficulties, employer, responsibilities, ways of finding new clients, clients, time to payment, and useful services), Likert scales (satisfaction), and free-text (taxation code, annual salary/income, and number of employees/freelancers used).

Data analysis

The answers were automatically collected through the platform technology solution, and a software procedure exported the data into a Microsoft Excel spreadsheet. In the free-text fields, some automatic corrections to the values were performed, including the systematic presentation of values; where values were null (e.g , 0000) or inappropriate (e.g., xxxxx), data were rated as null and were not considered for analysis. Analyses were performed using Microsoft Power BI to calculate medians (min, max), averages, and percentages and to prepare graphics. No inferential analyses were carried out.

Results

Demographic and educational characteristics

Most of the 68 medical writers who responded to the survey were female (84%). About three-quarters (74%) of respondents were between 30 years and 49 years of age, and 22% were older than 50 years (Table 1). There was an equal distribution among respondents in terms of employment type: 32 employees (47%) and 34 freelancers (50%); 2 respondents (3%) were owners of medical writing agencies. As this last subset was too small, it was reported in the Total, but not analysed in subgroups. Most respondents declared Italian as their first language (*n*=64, 94%), but more than three-quarters reported that their prevalent languages at work were English (*n*=53, 78%) and Italian (*n*=53, 78%). Only 11 respondents (16%) had obtained professional medical writing certification, though more than half had advanced academic titles (*n*=41, 60%; Table 1).

Table 1. Demographic and educational characteristics, by occupational status

Respondent characteristics	Total (*N*=68)		Occupational status* Employee (*n*=32)		Freelance (*n*=34)	
Gender						
Female	57	84%	25	78%	30	88%
Male	11	16%	7	22%	4	12%
Age groups, *years*						
<29	3	4%	2	6%	1	3%
30–39	24	35%	9	28%	14	41%
40–49	26	38%	11	34%	14	41%
50–59	9	13%	3	9%	6	18%
≥60	6	9%	2	6%	4	12%
First language						
Italian	64	94%	31	97%	31	91%
Other°	4	6%	1	3%	3	9%
Italian region of residency						
North	36	53%	20	63%	15	44%
Central	15	22%	4	13%	11	32%
South and Islands	13	19%	6	19%	6	18%
Non-Italian state	4	6%	2	6%	2	6%
Prevalent languages used at work						
English	53	78%	23	72%	28	82%
Italian	53	78%	22	69%	29	85%
EMWA affiliation						
Yes	25	37%	13	41%	10	29%
No	43	63%	19	59%	24	71%
Medical writing certification						
Yes	11	16%	4	13%	7	21%
No	57	84%	28	88%	27	79%
Academic title						
Advanced^	41	60%	17	53%	22	65%
Master's degree	20	29%	10	31%	10	29%
Bachelor's degree	3	4%	3	9%	0	0%
Other§	4	6%	2	6%	2	6%

Percentages were calculated by occupational status per column.

* 2 respondents are small business owners; their responses are included in the Total columns.

° English (*n*=2), Spanish (*n*=1), French (*n*=1) ^ MD, PhD, MBA, or equivalent § Master's or equivalent

The distribution of gender, age groups, and academic titles was similar among both employees and freelancers. Employees were primarily located in Northern Italy (*n*=20, 63%), whereas freelancers were more commonly found in either the Northern (*n*=15, 44%) or Central regions (*n*=11, 32%). A higher percentage of

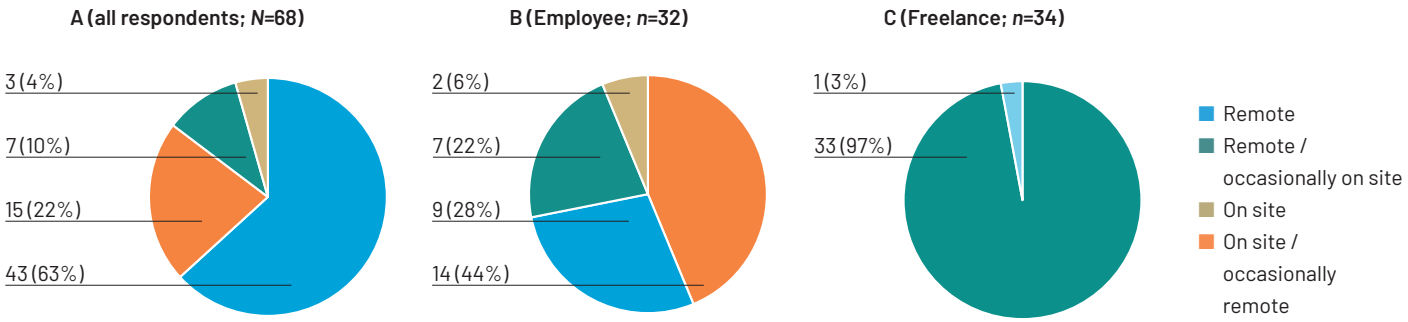

Figure 1. Work location

employees were members of EMWA (*n*=13, 41%) compared to freelancers (*n*=10, 29%), though employees were less likely to hold medical writing certification (4 employees [13%] vs. 7 freelancers [21%]; Table 1).

Professional characteristics

More than half of the respondents reported <10 years of medical writing experience (*n*=40, 59%); Table 2. The primary activity most frequently reported was medical communications (*n*=20, 29%). Freelancers were more likely to translate (0 employees [0%]; 4 freelancers [12%]) and moderate advisory boards (1 employee [3%]; 4 freelancers [12%]) as their principal activity, while employees were more likely to write regulatory documents (8 employees [25%]; 1 freelancer [3%]) and promotional material (9 employees [28%]; 7 freelancers [21%]).

Most respondents worked 31-40 hours per week (*n*=30, 44%); only 4 (6%) reported working more than 50 hours per week. Half of the employees (*n*=16, 50%) worked 31–40 hours per week while more than half of the freelancers (*n*=19, 56%) worked 30 hours per week or less (Table 2).

Most respondents (*n*=43, 63%) worked exclusively from remote locations (Figure 1A). Fourteen employees (44%) worked predominantly on site and remotely on occasion, and nine employees (28%) only worked remotely (Figure 1B). Almost all freelancers (*n*=33 97%) only worked remotely (Figure 1C).

Work and salary satisfaction, location, and workload

Nearly three quarters of respondents (*n*=49, 72%) reported being satisfied or very satisfied with their work, with no difference between

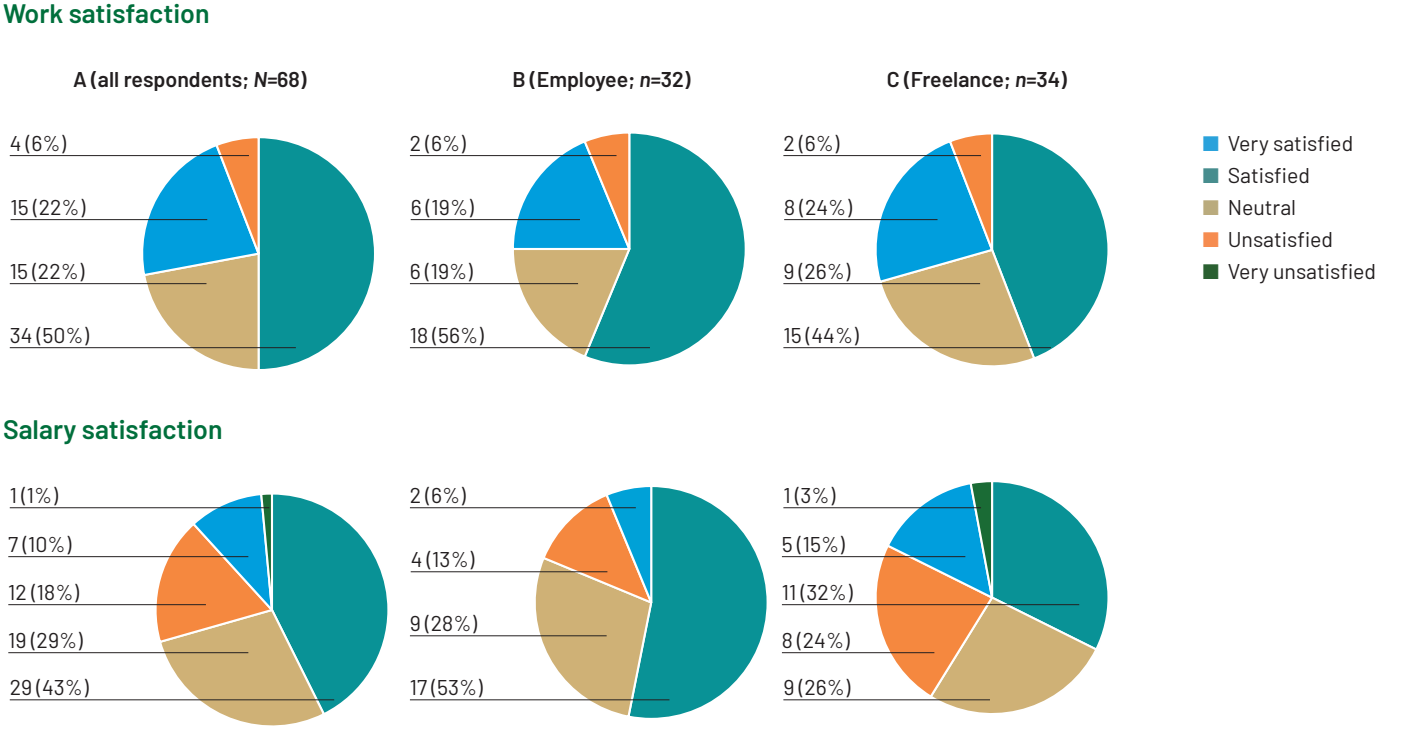

Figure 2. Satisfaction with work and compensation

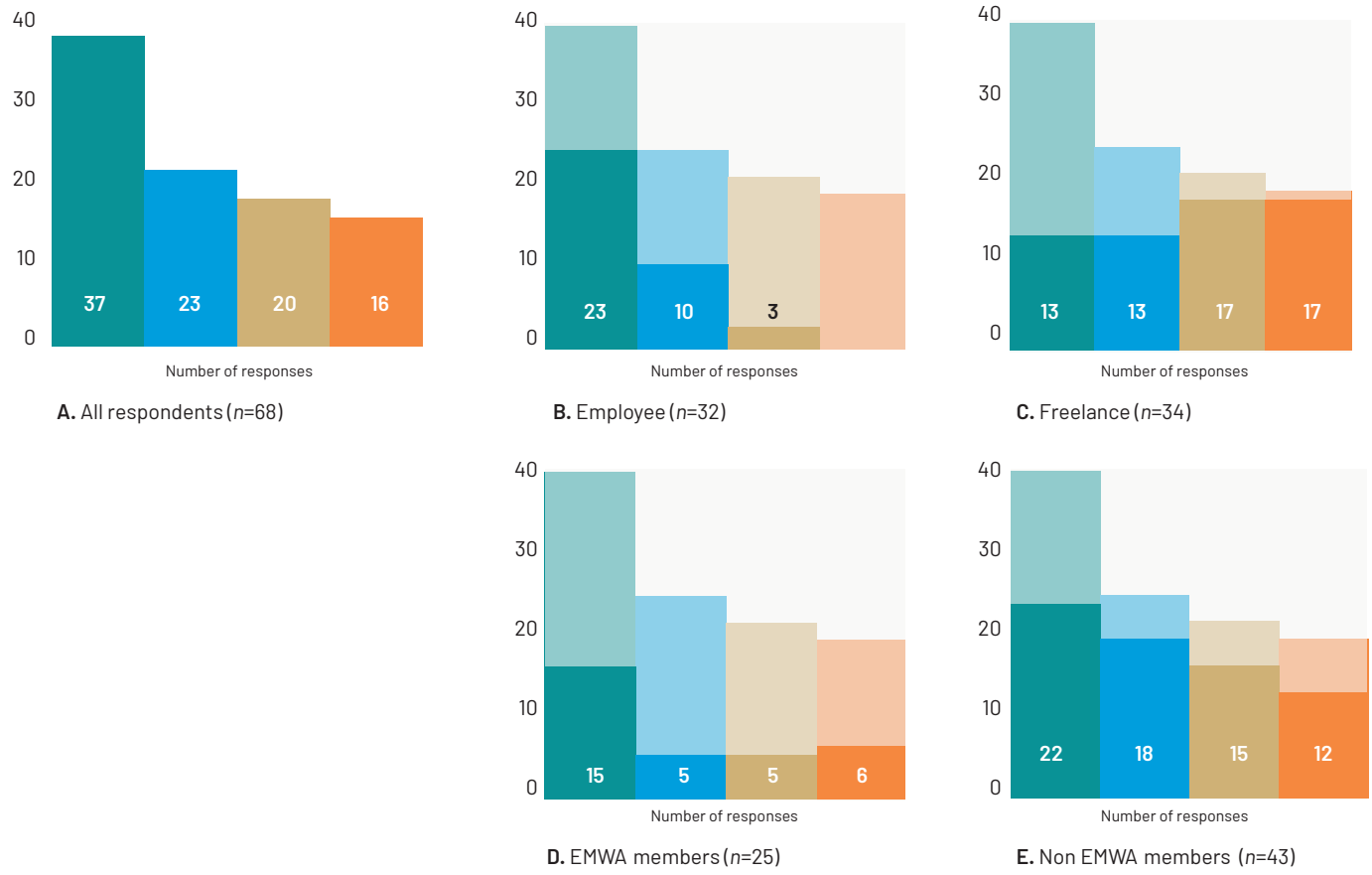

Figure 3. Major difficulties encountered at work

All respondents: (A) and subanalysis according to different status: employee (B), freelance (C), EMWA member (D), and non-EMWA member (E).

The colours, from left to right, refer to: Deadlines | Professional education and courses | Finding new customers | Delayed payments

employees and freelancers. More than half of respondents (*n*=36, 53%) reported being satisfied or very satisfied with their salary, more often for employees (*n*=21, 59%) than freelancers (*n*=16, 47%). Freelancers were more likely to be unsatisfied or very unsatisfied with their compensation (*n*=9, 27%) than employees (*n*=4, 13%; Figure 2).

Difficulties encountered at work

The main reported source of difficulties at work included deadlines (*n*=37, 54%), followed by professional education and courses (*n*=23, 34%; Figure 3A).

While strict deadlines were the main issue for most employees (*n*=23, 72%; Figure 3B), finding new clients (*n*=17, 50%) and delayed payments (*n*=17, 50%) were the most frequently reported issues by freelancers (Figure 3C).

Professional education was of concern for both employees and freelance medical writers, but less for EMWA members (*n*=5, 20%; Figure 3D) than for non-EMWA members (*n*=18, 42%; Figure 3E). Finding new clients was also reported to be an issue for a higher proportion of non-EMWA members (*n*=15, 35%) than for EMWA members (*n*=5, 20%).

For most freelancers (19 of 34 respondents), the mean time from invoice to payment is 60 days. For five freelancers, the mean time to payment was 90 days or more (Figure 4).

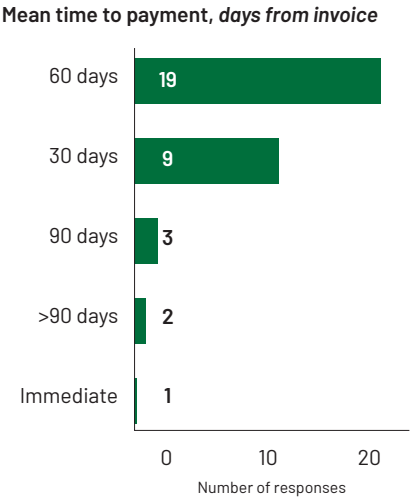

Figure 4. Time from invoice to payment for freelancers (n=34)

Gross annual salary of employees

Almost half of employees worked for a communication/promotional agency (*n*=15, 47%; Figure 5A) The median annual full-time gross income of Italian employees was €40,000 (€14,000-€110,000; mean €45,860; Figure 5B).

Relationship between employee salary and responsibilities

Median annual salaries were highest (€45,000 [mean €50,210]; Figure 5C) among employees with mentoring responsibilities (*n*=27, 84%), followed by those with team management responsibilities (€41,000 [mean €48,530]; *n*=26, 81%; Figure 5D) and those with project management responsibilities (€40,000 [mean €45,730]; *n*=31, 97%; Figure 5E).

Freelance clients

About two-thirds (*n*=22, 65%) of Italian freelance medical writers have communication/promotional agencies as their main clients (Figure 6A). Freelancers mainly find new customers via their professional or social networks and clients or colleagues (*n*=23, 67%; Figure 6B). Many freelancers (*n*=14, 41%) outsourced their activities to colleagues (Figure 6C).

Freelance annual income and hourly rates

The median annual income for Italian freelance medical writers was €32,000 and the mean annual income was €41,900 (Figure 7). The overall median hourly rate was €50 per hour and the overall mean hourly rate was €62 per hour.

Relationship between salary and experience

Median annual salary was similar (about €40,000/year) for the 24 (77%) employees with up to 15 years of experience. The median annual salary of the seven (23%) employees with more than 15 years' experience was €70,000 (mean €68,000; Table 3). Both annual income and hourly rates for freelancers increased with medical writing experience, especially for those who had worked as a medical writer for more than 15 years (Table 3). For the same level of experience, median annual compensation for Italian freelancers was less than that for Italian employees with up to 10 years' experience. Once freelancers had more than 10 years' experience, their median annual compensation exceeded the median annual salaries of employees with the same level of experience (Table 3).

Table 2. Professional characteristics, by occupational status

Respondent characteristics	Total (*N*=68)		Occupational status* Employee (*n*=32)		Freelance (*n*=34)	
Medical writing experience range, *years*						
≤2	7	10%	2	6%	5	15%
2–5	19	28%	11	34%	8	24%
5–10	14	21%	6	19%	8	24%
10–15	15	22%	6	19%	7	21%
>15	13	19%	7	22%	6	18%
Main medical writing activity performed						
Medical communication^	20	29%	10	31%	10	29%
Promotional materials°	18	26%	9	28%	7	21%
Regulatory documents§	9	13%	8	25%	1	3%
Advisory board moderation	5	7%	1	3%	4	12%
Web communication	4	6%	1	3%	3	9%
Translation	4	6%	0	0%	4	12%
Lay communication	3	4%	1	3%	2	6%
Editing/copywriting/proofreading	2	3%	1	3%	1	3%
Medical education	2	3%	1	3%	1	3%
Other (bioethics communication)	1	1%	0	0%	1	3%
Working week, *hours*						
1–10	1	1%	0	0%	1	3%
11–20	8	12%	2	6%	6	18%
21–30	13	19%	1	3%	12	35%
31–40	30	44%	16	50%	13	38%
41–50	12	18%	11	34%	0	0%
>50	4	6%	2	6%	2	6%

Percentages were calculated by occupational status per column.

* 2 respondents are small business owners; their responses are included in the Total columns.

^ Journal papers, abstracts, congress materials, etc. ° Leaflets, visual, carrier, newsletter, etc.

§ Study protocol, clinical study reports, dossiers, etc.

Table 3. Salary and compensation according to medical writing experience and occupational status

Experience° *N*=66	Employee Median annual salary (mean, min-max, *n*)	Freelance Median annual compensation (mean, min-max, *n*)	Median hourly rate (mean, min-max)
<2 years (*n*=7)	€40 K (*n*=1)*	€22 K (25.0, 15-40, *n*=5)	€40/h (41.0, 30-55)
2-5 years (*n*=19)	€37 K (37.5, 14-70, *n*=11)	€23 K (22.1, 8-37, *n*=8)	€50/h (43.1, 10-75)
5-10 years (*n*=14)	€39 K (42.2, 30-62, *n*=6)	€30K (33.9, 12-87, *n*=7)*	€50/h (53.6, 30-85)
10-15 years (*n*=13)	€38 K (40.1, 30-55, *n*=6)	€48 K (54.0, 20-100, *n*=5)**	€50/h (56.0, 35-90)
>15 years (*n*=13)	€70 K (68.0, 47-110, *n*=7)	€82 K (81.7, 36-150, *n*=6)	€90/h (121.7, 60-300)

Percentages were calculated by occupational status per column. * 1 missing value ** 2 missing values

° The median annual salary according to seniority was evaluated only for employees and freelancers. The two agency owners reported a seniority of 10–15 years but were not included in the salary survey results

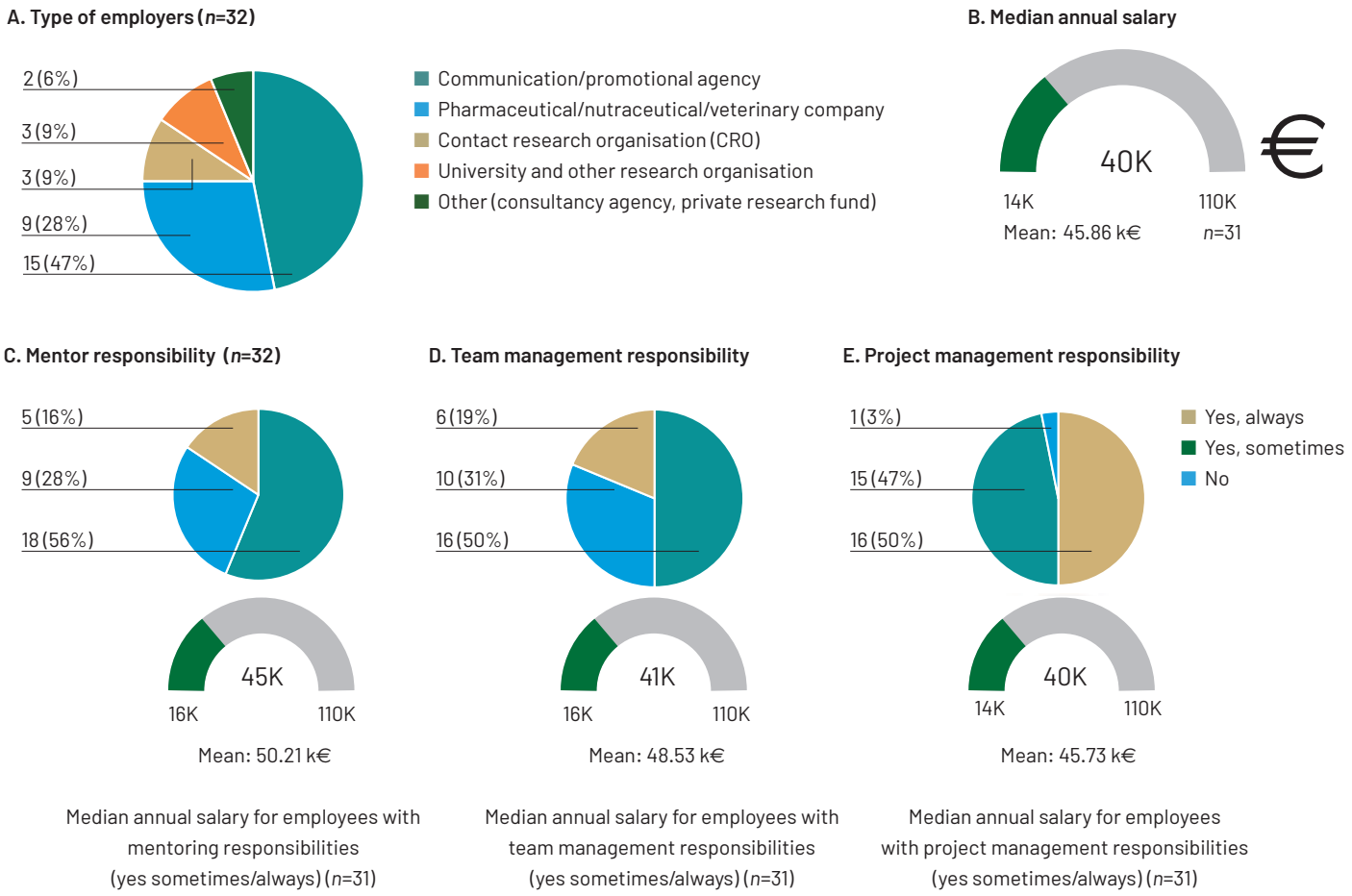

Figure 5. Employers, annual salaries, and responsibilities of employee medical writers

Employment type (A) and gross annual income (B) of employees, and income by mentoring (C), team management (D), and project management (E) responsibility

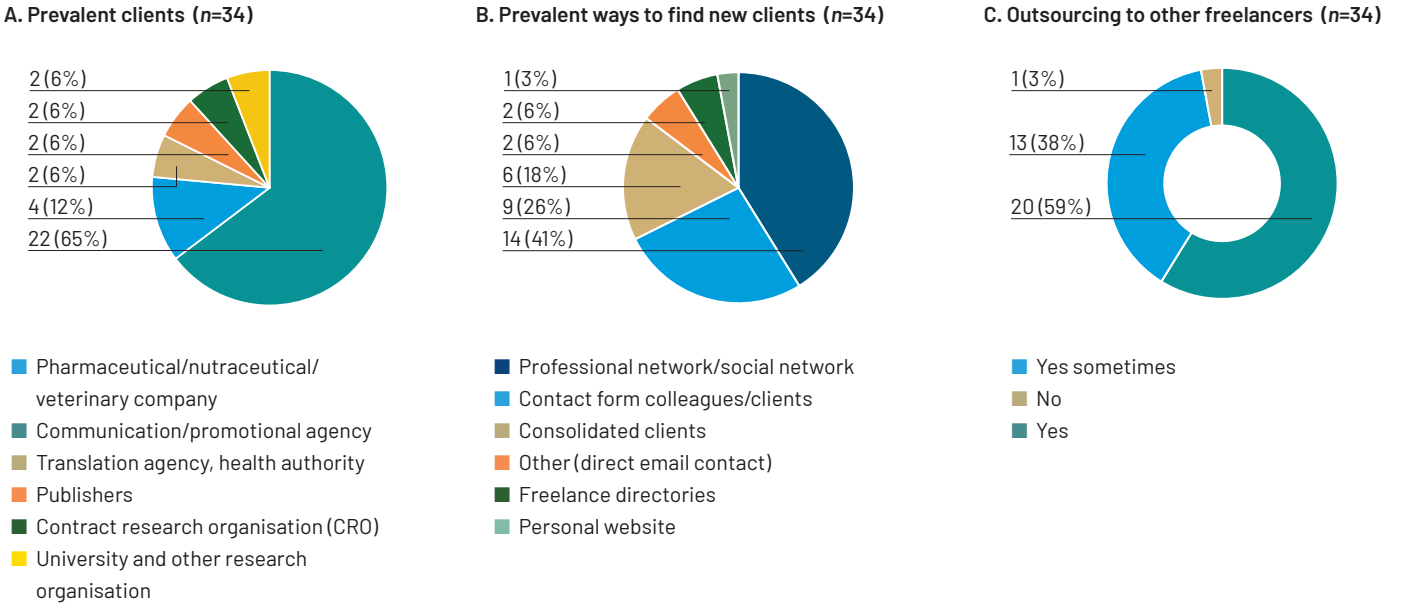

Figure 6. Freelance customer and business characteristics

Services used by freelancers

The survey asked freelancers for their "economic activity classification" (classificazione delle attività economiche - ATECO) code, a code used in Italy to identify economic activities for tax and statistical purposes. Italian freelance medical writers are currently registered with at least 10 different ATECO codes (Table 4). Freelancers were asked which services they most needed. Accountancy was the most requested service (*n*=27, 79%). Education (*n*=18, 53%) and IT support (*n*=14, 41%) were also widely required (Figure 8).

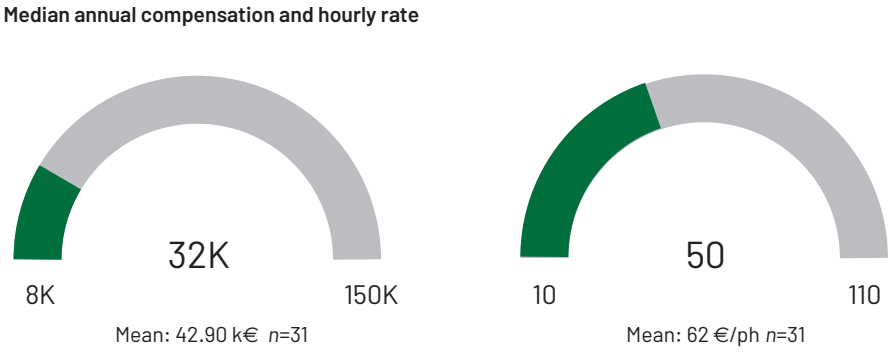

Figure 7. Freelance annual income and hourly rates

Discussion

Medical writing is a female-dominated profession, and the results of this survey confirm that this is also the case in Italy, with a similar percentage of female respondents as those reported in the most recently published EMWA surveys.[1,8] The observed population is mostly aged between 30–50 years old, with 83% of respondents working remotely or remotely with some days in the office. According to the 2023 data from the official Italian Institute of Statistics (ISTAT), 73.9% of Italian women aged between 25 and 49 years without children are employed. This percentage drops to 53.9% for women with at least one child under the age of 6 years.[13] Caring for young children or dependent relatives at the same time as working entails devoting time to family. Women with family responsibilities are unable to participate in the labour market to the same degree as women without these responsibilities.[14] This makes the flexibility of medical writing, especially part-time freelance work, particularly attractive to professional women.

The mean salary for employed medical writers in Europe grew from €54,924 in 2006 to €67,205 in 2021.[1] The 2023 results from the Italian survey highlight that Italian colleagues have a lower mean salary of €45,860 (the median Italian annual wage in 2022 was €30,284).[15] Despite difficulties in drawing direct comparisons to data from previous EMWA surveys, the average annual income declared in Italy in 2023 is lower than that recorded in Europe almost 20 years ago; this value is confirmed to be lower than in other countries also considering that the mean annual salaries in Italy in 2021 were close to the European mean.[16] Furthermore, most Italian medical writers and scientific communicators reported having mentoring, team management, and project management responsibilities, which seems to be unrelated to a higher salary in Italy, unlike in Europe.[1]

Similarly, the overall mean hourly rate of Italian freelancers was €62 per hour, far lower than the mean rates of €82.20 per hour in the EMWA 2023 freelance survey,[8] €78 per hour in the 2021 EMWA salary survey,[1] and €81 per hour in 2017.[1] In line with previous EMWA surveys, the median hourly rate did not increase steadily with increasing medical writer or communicator experience, though rates were similar among European professionals with more than 15 years of experience (€82 vs €80).[1] This value is difficult to justify in the local market considering that mean hourly rates in Italy are practically identical to the European mean.[17]

Our survey also explored, for the first time, the average annual income of freelancers. Considering that the Italian cohort included a high proportion of freelancers working less than 30 hours per week, the mean annual income identified in this survey (€41,900) is comparable with that of European employee medical writers working up to 20 hours per week (€39,500).[1] However, the average annual income for freelancers is far below European levels.[1,8]

The majority of Italian medical writers and scientific communicators report being satisfied or very satisfied with their job, which is consistent with satisfaction outcomes from previous EMWA surveys.[1] The percentage of Italian freelancers unsatisfied or very unsatisfied with their compensation was higher than that reported by European freelancers (19% vs 6%).[1] Considering the lack of relationship between compensation and medical writing experience or responsibility and the high workload declared by most of the participants, this sentiment is not surprising. Moreover, medical writers face many different challenges. Time constraints often stem from clients' lack of awareness about the time required for content production or the difficulties in scheduling various production phases. While resolving time constraints can be challenging, the need for training could be more easily addressed. This is not only because of the widespread availability of private training organisations, but also EMWA's expanding training programme. The reduced need for education observed among

Table 4. Economic activity classification ("classificazione delle attività economiche – ATECO") codes used by freelancers

ATECO taxation code	*N*	%
74.90.99	10	29%
74.30.00	4	12%
72.11.00	3	9%
90.03.09	3	9%
70.22.09	2	6%
56.45.45	1	3%
58.11.00	1	3%
70.21.00	1	3%
72.19	1	3%
Unspecified	8	24%

Figure 8. Services used by freelancers

EMWA members who responded to this survey confirms this trend. Similarly, EMWA members demonstrated less need for networking opportunities with colleagues and simpler access to potential customers.

In Italy, medical writers have access to a broad ecosystem of specialised services, such as accountancy, IT, and statistical support (Figure 8). These services provide significant support to medical writers, highlighting the economic spin-off that medical writing generates. Trade associations can play a critical role in not only offering contracted services, but also fostering a network of professionals who can support the medical writer with customised solutions, such as technology partners.

Surprisingly, to date, there is no uniformity in the identification of the medical writing profession in Italy. The authors suggest that the creation of a specific ATECO code for medical writing and scientific communication activities should be the starting point for proper professional recognition in Italy.

The sample of Italian responders to this survey (n=68) was far higher than those in previous EMWA surveys, where no more than eight Italians responded.[1,10] This high response rate was achieved thanks to continuous engagement by the Italian LEG, the personal involvement of the members of the Italian Medical Communicators LinkedIn Group, and the support of the EMWA Executive Committee. The variability of responses is high, and results are certainly influenced by the heterogeneity of types of services, levels of experience, and geographical origins of the respondents. However, the sample was too small for reliable and meaningful sub-analyses.

This questionnaire was created by IT professionals *ad hoc* to ensure standardised data collection; some questions were designed specifically according to occupational status, and the platform streamlined their presentation accordingly. Previous EMWA surveys have used commercially available surveys without this functionality.[1,7,8]

The results of this survey should be interpreted with caution. Despite achieving a higher participation rate among Italian medical writers and scientific communicators compared to other surveys promoted by EMWA, the number of participants was still relatively small. Additionally, since the survey was completed voluntarily and respondents remained anonymous, the data cannot be validated. Consequently, these findings cannot be generalised to the broader global or even the local Italian medical writing community.

Conclusion

This first Italian survey provides a panoramic overview of the Italian medical writing profession. The survey reveals the heterogeneity of services offered and the various opportunities available, paving the way for future in-depth studies. Key aspects of the Italian medical writing landscape include the lack of standardisation in professional recognition at both sector and taxation levels and comparatively low compensation rates. Italian medical writers are underpaid compared to European colleagues. This survey also underlines the need to raise awareness about the training and networking opportunities offered by EMWA, with targeted strategic development at local levels.

Acknowledgments

The authors thank all the survey respondents and the local EMWA group for their generosity in participating. Special thanks go to Erika Nerini of PopMED for strategic support with the survey creation, Alessandro Sillato of Officine Telematiche (www.officinetelematiche.com) for technical assistance and hosting the survey, and to Simona Purrello of Osmosia for her fundamental support in revising the survey and this manuscript.

Disclaimers

The opinions expressed in this article are the authors' own and not necessarily shared by employers or EMWA.

Disclosures and conflicts of interest

The authors declare no conflicts of interest.

Data availability statement

For enquiries about data and other supplemental information, please contact the corresponding author.

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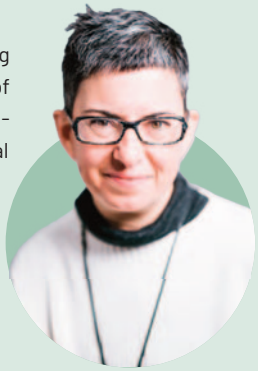

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News from the EMA

The articles included in this section are a selection from the European Medicines Agency (EMA)'s News and Press Releases archive.
More information can be found on the Agency's website: www.ema.europa.eu.

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One Health: a joint framework for action published by five EU agencies

May 7, 2024

Today, the European Centre for Disease Prevention and Control (ECDC), the European Chemicals Agency (ECHA), the European Environment Agency (EEA), the European Food Safety Authority (EFSA), and the EMA published a joint framework for action to strengthen cooperation to support the implementation of the One Health agenda in the European Union (EU).

One Health recognises the complex interplay between human, animal, and plant health, food safety, the climate crisis, and environmental sustainability. Implementing this approach across different sectors will be key to making the EU and its Member States better equipped to prevent, predict, detect, and respond to health threats. It will mitigate the impact and societal cost of such threats, or even prevent their emergence, while also helping to reduce human pressures on the environment and safeguarding key societal needs such as food security and access to clean air and water.

A cross-agency task force will work on implementing the joint framework for action over the next three years (2024-2026), focusing on five strategic objectives: strategic coordination, research coordination, capacity building, stakeholder engagement and joint inter-agency activities. This will ensure that the scientific advice provided by the agencies is increasingly integrated, that the evidence base for One Health is strengthened and that the agencies are able to contribute with a common voice to the One Health agenda in the EU.

In November 2023, the five EU agencies that provide scientific advice on the environment, public health and food safety topics issued a joint statement expressing their shared commitment to supporting the One Health agenda in Europe. On the occasion of the launch of the joint framework for action, the Executive Directors of the five EU agencies reinforced their commitment to the One Health approach in a joint video statement.

European medicines network designated as WHO Listed Authority

May 20, 2024

The European Medicines Regulatory Network (EMRN) has been designated as WHO Listed Authority (WLA) by the World Health Organisation (WHO). This means that the network, composed of the European Commission, EMA and the 30 national authorities of the European Economic Area Member States, are recognised as meeting international regulatory standards, guidelines and practices. The assessment process was facilitated by the Steering Group for Benchmarking of European Medicines Agencies (BEMA SG).

The EMRN is the cornerstone of EMA's work and success. The Agency operates at the heart of the network, coordinating and supporting interactions of national competent authorities for human and veterinary medicines in Europe. The designation as WLA follows a comprehensive assessment by WHO. It covers each individual regulatory authority of the EMRN, as well as the EMRN overall, which is recognised as a single entity and has also been designated as a "regional regulatory system".

Collaboration with WHO is specifically highlighted in the legislation establishing EMA. The WLA designation complements the cooperation between these organisations in the context of global public health networks and initiatives.

A WLA is a regulatory authority or a regional regulatory system which has been judged to comply with all the indicators and requirements specified by WHO. The WLA initiative is being implemented by WHO to promote access to and supply of safe, effective, and high-quality medical products. It ensures optimal use of limited global regulatory resources by facilitating reliance on the work and decisions of trusted regulatory authorities. The reliable and highly performing WLAs listed by WHO can be used as a reference point by regulatory authorities that lack the resources to perform all necessary regulatory functions, or which have not yet reached higher maturity levels for medical product oversight. Overall, the WHO Listed Authority framework is expected to promote confidence and reliance, whilst fostering regulatory convergence, harmonisation of approaches and international cooperation.

Medical devices: New guidance for industry and notified bodies

May 21, 2024

A new revision of the guidance has been published and is available to applicants, marketing authorisation holders, and notified bodies of medical devices. This question-and-answer document[1] provides practical considerations on the implementation of the medical devices and in vitro diagnostic regulations for combinations of medicinal products and medical devices.

Products that combine a medicinal product (or substance) and a medical device are regulated either under the pharmaceutical framework or the medical device framework, depending on their main mode of action. The revision is based on the experience gained since the implementation of the new regulations and actual cases encountered. The document covers regulatory and procedural guidance for:

- integral drug-device combinations (medical devices that form an integral product with a medicine, such as pre-filled syringes) and their lifecycle management
- medicinal products that include a medical device in their packaging (referred to as co-packaged) and how these should be labelled
- the consultation procedure for medical devices with an ancillary medicinal substance (a substance that supports the proper functioning of the device)
- the consultation procedure for companion diagnostics, diagnostic tests that are essential for the correct use of a specific medicine.

The guidance is provided to support the application of the regulations on medical devices (Regulation (EU) 2017/745) and on in vitro diagnostic devices (Regulation (EU) 2017/746). These two regulations changed the European legal structure for medical devices, introducing new responsibilities and requirements for EMA and national competent authorities in the assessment of certain categories of medical devices used in combination with medicines.

Reference

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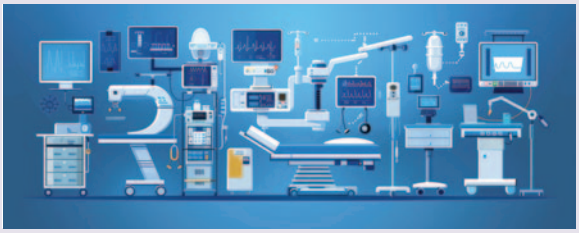

First vaccine to protect adults from Chikungunya

May 31, 2024

EMA has recommended granting a marketing authorisation in the European Union (EU) for Ixchiq, the first vaccine in the EU to protect adults 18 years and older against Chikungunya. It is given as a single dose.

Chikungunya (also called CHIK fever) is a viral disease caused by Chikungunya virus (CHIKV), a virus transmitted to humans by infected mosquitoes (primarily Aedes aegypti and Aedes albopictus). Most people infected with CHIKV develop symptoms within 3–7 days. The most common symptoms of acute disease are fever and joint pain. Other symptoms can include headache, muscle pain, joint swelling, or rash. Most patients recover within a week, but some develop joint pain for several months or longer, which can be disabling. A small proportion of patients may develop severe acute disease, which can lead to multiorgan failure and is most often observed in newborns exposed to the virus during childbirth and adults over 65 years old. There is currently no licensed treatment for Chikungunya.

CHIKV infections affect people mostly in the tropics and subtropics, and the majority of countries reporting high disease burden are located in Central and South America. Chikungunya is not endemic in Europe. The majority of cases in the EU concern travellers who were infected outside of mainland Europe. However, there have been sporadic incidents of onward transmission by infected travellers after their return, mainly in Southern Europe where the Aedes. albopictus mosquito is established. Spread of the mosquito due to climate change could lead to cases of Chikungunya in regions so far spared.

Considering the significant global public health implications of this vaccine, Ixchiq was assessed under EMA's OPEN initiative that fosters international collaboration and sharing of scientific expertise to promote global public health. The OPEN framework allowed the World Health Organisation and ANVISA, the Brazilian medicines regulator authority, to participate in the discussions of EMA's Human Medicines Committee (CHMP) and its advisory bodies. Brazil is currently experiencing outbreaks of Chikungunya in a number of regions, reporting over 160,000 cases in the first quarter of 2024.

The CHMP's opinion is largely based on data from a placebo-controlled study that assessed the immunogenicity and safety of the vaccine in adults from 18 years. The immune response was evaluated in 362 participants (266 treated with Ixchiq and 96 with placebo). The clinical efficacy of Ixchiq was inferred from a post-vaccination CHIKV-specific neutralising antibody titre threshold. At 28 days after vaccination, 98.9% of individuals administered Ixchiq had antibody titres against CHIKV above the threshold. At 12 months and 24 months after vaccination, antibody titres above the threshold persisted in 99.5% and 97.1% of individuals administered the vaccine, respectively. Antibody titres will be monitored for up to five years. The CHMP has requested a post-authorisation efficacy study to confirm the effectiveness of Ixchiq in preventing Chikungunya in adults.

The safety profile of Ixchiq is based on pooled data from three completed clinical studies with 3,610 participants with a 6-month follow-up. The most common side effects reported were headache, tiredness, muscle pain, joint pain, fever, nausea, tenderness, and injection site pain. Chikungunya-like adverse reactions are an important identified risk and will be further characterised with post-authorisation safety studies.

Climate change can drive many of the health threats we are facing today. The rise in cases of vector-borne diseases transmitted through mosquitoes such as Chikungunya is a clear example of the impact of climate change on health and reinforces the need for a One Health approach. EMA, together with other EU agencies, has recently published a joint One Health framework for action to support the implementation of One Health in Europe and help build a region better able to prevent, predict, prepare, and respond to emerging public health threats.

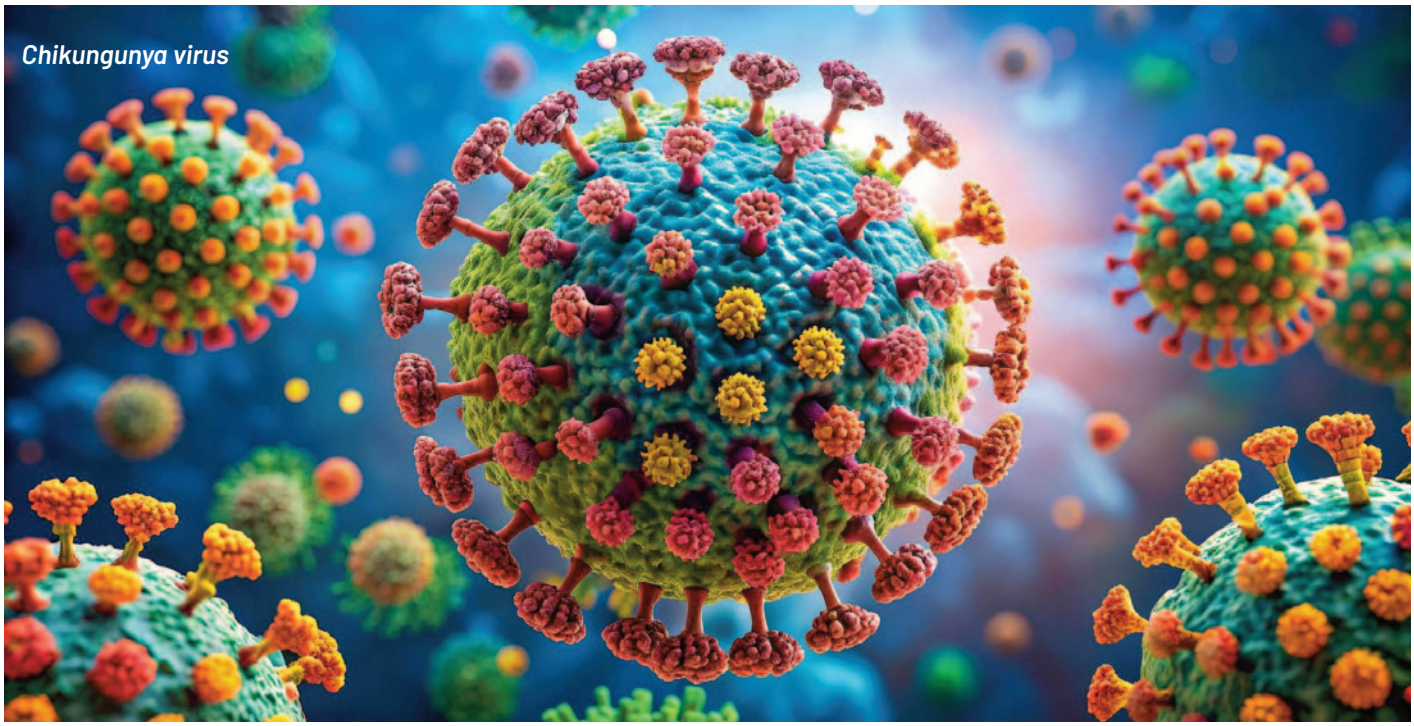

Photo: Freepik

Faster access to clinical trial information in Europe

June 18, 2024

The launch of a new version of the Clinical Trials Information System (CTIS) will allow earlier and more efficient access to information about clinical trials in the European Union (EU) for patients, healthcare professionals, and other stakeholders. This is due to the revised transparency rules that become applicable today in Europe. Several resources have been created to help sponsors understand the revised transparency rules, including a user guide[1] and an overview[2] of which data and documents with key information will be published in CTIS.

CTIS is the single-entry point for the submission and assessment of applications for clinical trials in the EU for sponsors and regulators. The system includes a public searchable database for healthcare professionals, patients, and the general public to deliver the high level of transparency foreseen by the regulation. The authorisation and oversight of clinical trials is the responsibility of EU/EEA Member States while EMA is responsible for maintaining the CTIS. The European Commission oversees the implementation of the Clinical Trials Regulation.

One of the key changes in the new version of CTIS is earlier availability of information on authorised clinical trials. Importantly, the new rules eliminate the previously available deferral mechanism, which allowed clinical trial sponsors to delay publishing certain data and documents for up to seven years after a trial's completion to protect commercially confidential information. Under the new rules, approximately 4,000 clinical trials with issued decisions are now publicly accessible through the CTIS search. The CTIS portal will add approximately 500 newly authorised clinical trials per month. This includes ongoing trials that have been transitioned to CTIS from the Clinical Trials Directive. Over the next few months, additional features will be added to the CTIS public portal to further enhance overall usability.

The updated rules strike a balance between transparency of information and protection of commercially confidential information. They benefit patients, because key clinical trial information, that patients flagged as being most relevant for them, is published early. They also benefit clinical trial sponsors because they introduce process simplifications. Finally, they benefit healthcare professionals because the resulting system is more user-friendly, facilitating access to information on clinical trials and enrolment in clinical trials, and also increasing awareness of possible treatment options.

The revised transparency rules were adopted by EMA's Management Board in October 2023 following a public consultation held between May and June 2023.

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Photo: Freepik

Positive CHMP opinion on first-in-class medicine to treat pulmonary arterial hypertension

June 28, 2024

EMA has recommended granting a marketing authorisation in the European Union (EU) for Winrevair (sotatercept) to treat adult patients with pulmonary arterial hypertension (PAH), in combination with other specific PAH therapies, to improve exercise capacity.

Pulmonary arterial hypertension is a rare, long-term, debilitating and life-threatening condition in which patients have abnormally high blood pressure in the arteries in the lungs. Many patients experience breathing difficulty that limits their physical activity. Despite approved therapies, long-term prognosis remains poor: it is estimated that around 50% of patients will die within five to seven years after diagnosis.

Winrevair (sotatercept) is the first activin signalling inhibitor therapy approved to treat PAH. In the body, proteins called activins attach to a receptor called ActRIIA to stimulate the growth of cells that make up the blood vessels. These receptors are over-active in patients with PAH. Sotatercept is a copy of ActRIIA, and because it also attaches to activins, it prevents them from activating the receptor. In this way, sotatercept regulates the growth of new blood vessel cells in the lungs. This leads to reduced narrowing and thickening of the blood vessels, thus improving the symptoms of the disease.

The medicine is administered once every 3 weeks as a single injection under the skin and may be administered by patients or caregivers with guidance, training and follow-up from a healthcare provider.

The recommendation is based on the results of a randomised, double-blind, placebo-controlled, multicentre clinical trial that evaluated the efficacy and safety of sotatercept in 323 adults with PAH on stable treatment for more than 90 days with background PAH therapy (monotherapy or combination therapy).

Results of the trial show that patients on sotatercept had significantly improved exercise capacity measured by how far they were able to walk within six minutes at the start of treatment and after 24 weeks. This increase is considered clinically relevant as it compares to the results of the pivotal study of already-authorised products for PAH.

The most common side effects associated with this medicine are headache, nose bleeds, rash, tiny blood vessels that look like pink or red lines on the skin (telangiectasia), diarrhoea, dizziness and redness. Although Winrevair is generally well tolerated, there have been rare reports of serious side effects affecting the blood, such as increased blood pressure, low platelet count (thrombocytopenia) which can increase the risk of bleeding, and increased haemoglobin concentrations which can lead to thromboembolic events such as a stroke. The last two conditions listed are considered manageable by modifying the dose of Winrevair.

Winrevair was supported through EMA's PRIority MEdicines (PRIME) scheme, which provides early and enhanced scientific and regulatory support to medicines that have a particular potential to address patients' unmet medical needs.

The opinion adopted by the CHMP is an intermediary step on Winrevair's path to patient access. The opinion will now be sent to the European Commission for the adoption of a decision on an EU-wide marketing authorisation. Once a marketing authorisation has been granted, decisions about price and reimbursement will take place at the level of each Member State, taking into account the potential role or use of this medicine in the context of the national health system of that country.

First nasal adrenaline spray for emergency treatment against allergic reactions

June 28, 2024

EMA's Human Medicines Committee (CHMP) has recommended granting a marketing authorisation in the European Union for Eurneffy (epinephrine), the first medicine to be taken through the nose for the emergency treatment of allergic reactions (anaphylaxis).

According to the European Academy of Allergy and Clinical Immunology (EAACI), allergy is the most widespread chronic disorder in Europe, with 150 million Europeans affected in 2015. Around 20% of people suffering from severe allergic conditions live in fear every day of an anaphylactic shock or of dying from an allergic reaction.

Anaphylaxis is the most severe form of allergic reaction that can occur within minutes of exposure to an allergen, most often from food, medication, or insect stings. It is almost always unexpected and can be life-threatening. Delay in clinical diagnosis and treatment can result in airway obstruction or cardiovascular collapse, which can turn fatal.

Treatment with epinephrine, also known as adrenaline, decreases the anaphylactic reaction. Adrenaline binds to a specific type of receptors, known as adrenergic receptors, and lessens the widening of blood vessels and blood vessel permeability induced by histamine (a substance in the body that causes allergic symptoms) during anaphylaxis. Adrenaline also relaxes the smooth muscles in the lungs. Administration of adrenaline during an anaphylactic reaction leads to better blood flow and improved breathing.

While epinephrine autoinjectors have been shown to be highly effective when properly used, some patients and caregivers delay or do not administer treatment in an emergency situation due to fear of the needle, lack of portability, or fear of people without medical training to give an injection, among others. The adrenaline nasal spray is absorbed rapidly by the nasal mucosa and distributed through the body.

For ethical and practical reasons, it was not feasible to conduct controlled clinical trials on Eurneffy's effectiveness in people experiencing a severe allergic reaction, but there is extensive information available about the use of adrenaline to treat severe allergy and it is currently the standard treatment for anaphylaxis. The efficacy and safety of Eurneffy were evaluated in 537 healthy people aged 19 to 55 years old enrolled in fourteen clinical studies. These trials compared Eurneffy with medicinal products where the adrenaline was injected intramuscularly and looked at the blood pressure and heart rate (pharmacodynamics), as well as at how the medicine is absorbed, modified and removed from the body (pharmacokinetics). The results demonstrate that the effects in the body of nasally-administered adrenaline are comparable to products given by an intramuscular injection.

No significant adverse events have been reported in clinical studies with Eurneffy. The most common adverse events were similar to those experienced with injections such as nausea, headache, throat irritation and dizziness, but also included nasal discomfort and a runny nose.

The CHMP recommended additional risk minimisation measures to reduce and prevent the potential risk of an inappropriate use of the device. These include training videos and other digital educational materials for patients, carers, and healthcare professionals. A training demonstration device of Eurneffy will also be available for these groups of people to simulate correct handling of the device.

The opinion adopted by the CHMP is an intermediary step on Eurneffy's path to patient access. The opinion will now be sent to the European Commission for the adoption of a decision on an EU-wide marketing authorisation. Once the marketing authorisation has been granted, decisions about price and reimbursement will take place at the level of each Member State, taking into account the potential role/use of this medicine in the context of the national health system of that country.

EMA supports pilot for joint African continental assessment procedures

July 30, 2024

EMA has awarded a grant to the African Medicines Regulatory Harmonisation (AMRH) initiative of the African Union Development Agency (AUDA-NEPAD) to support a pilot to test procedures for the joint continental evaluation of medicines in Africa.

AUDA-NEPAD has been working on harmonisation activities for a decade, paving the way for the creation of the African Medicines Agency (AMA). The launch of the continental pilot is one of these activities that aim to validate procedures and processes ahead of the establishment of the AMA. The pilot, which is co-funded with the Bill & Melinda Gates Foundation, will run for a year.

During the pilot, the AMRH Evaluation of Medicinal Products Technical Committee (EMP-TC) will evaluate the quality, safety, and efficacy of priority medicinal products with the support of the continental Good Manufacturing Practices Technical Committee (GMP-TC). The learnings from the evaluations will help to develop continental processes and procedures, facilitate national authorisations of recommended medicines and strengthen information sharing and reliance.

The two AMRH technical committees visited EMA in June 2024 to share knowledge and get insights into EMA's regulatory procedures and processes, which could serve as possible model for the African continental regulatory system. EMA and the European medicines regulatory network (EMRN) will continue making available their unique experience and expertise in continental medicines regulation to support the establishment of the AMA by providing technical expertise and training both online and in person.

EMA's involvement in the AMA project officially started in December 2023 when the Agency received a contribution from the European Commission to support the setting up of the AMA. The project forms part of the European Union (EU) Global Gateway strategy and Team Europe Initiative on Manufacturing and Access to Vaccines, Medicines, and Health Technologies.

The two most important keys on your keyboard

This is called the hash, pound, or number character. A hashtag is a keyword or set of keywords that is preceded by the # character. It is used in social media to create a thread of conversations around a specific theme or topic conveyed in short texts or microblogs. It is commonly used in Twitter, Instagram, YouTube, Pinterest, etc.

A dictionary of most common hashtags can be found at https://www.hashtags.org/definition/~h/.

For your info, EMWA is compiling a list of standarised hashtags for our social media use.

@ This is called the "at" sign or symbol. The @ sign is part of email addresses and social media user names ("handles"). Our EMWA handles are as follows: @Official_EMWA (Twitter), @EMWA (LinkedIn), and @europeanmedicalwritersassociation (Facebook)

Digital Communication

Editorial

In an era of abundant information and fleeting attention spans, the ability to communicate complex scientific concepts quickly and effectively has never been more important. Given our innate attraction to visuals, they are undoubtedly a powerful tool in science communication. Visuals don't just simplify concepts; they leave lasting impressions that text alone cannot achieve, as evident during the COVID-19 pandemic. As digital tools evolve, the capacity to create impactful visual content is increasingly within reach. Yet, many medical writers may feel daunted by the specialised skills required to produce high-quality visuals. This is where artificial intelligence (AI), specifically Microsoft's Copilot, steps in.

Freelance medical writer Jacqueline Bersano explores how AI is revolutionising the creation of scientific visuals, with key insights from experts on the topic. Whether you're a seasoned professional or new to the field, this article offers valuable perspectives on leveraging AI to enhance your science communication toolkit, making it easier than ever to engage and inform diverse audiences with eye-catching, precise visual content. Happy reading!

Nicole

SECTION EDITOR

Nicole Bezuidenhout
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Exploring the role of Microsoft's Copilot in visual communication: Current use and considerations through science communicators' lens

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doi: 10.56012/pacl5831

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Ninety percent of the information our brains receive is visual.[1,2] This natural attraction to visual elements allows us to process images at a speed 60,000 times faster than text. In science communication, we often leverage this natural affinity to visuals to render complex scientific content more accessible – engaging the reader with informative yet appealing images, illustrations, diagrams, infographics, and other visual content.[3,4] By doing so, important scientific information can reach larger audiences, avoid misinterpretation, and have a powerful impact on how we absorb and remember complex concepts. For instance, if we never saw the double-helix structure of DNA illustrated in detail, would we have been able to understand and study it as we do today?[5]

In today's fast-paced world, where information is abundant, it becomes essential to create attention-grabbing images capable of conveying messages quickly while leaving a lasting impression. A prime example could be seen in the COVID-19 pandemic. As the world grappled with a novel virus, clear and effective communication was crucial, and visuals played an important role.[6,7] From infographics to animations, visuals were used to explain, for example, how vaccines work, the importance of epidemiology and clinical trials, how the virus spreads, or why social distancing measures were necessary. Additionally, through visuals, the benefits of wearing a mask could be communicated effectively, reinforcing the message that masks are a simple yet powerful tool in reducing the spread of the virus.[6–11]

It's clear that pursuing accurate, clear, and engaging scientific visual content is essential in creating effective medical or science communications.

It's clear that pursuing accurate, clear, and engaging scientific visual content is essential in creating effective medical or science communications.[3,5] Digital tools for this purpose have become indispensable in a medical writer's repertoire, providing a wide range of features and functionalities that make it easier and faster to create visualisations.[12,13] However, not every medical writer may feel comfortable or capable of taking on this task. Creating visual assets requires specialised knowledge and skills, not to mention the time to acquire them. Or does it? This article explores how artificial intelligence (AI) can support novices and even experts in developing eye-catching visuals that hit their mark.

AI for visual communication in science

The use of AI to create different visuals is an attractive solution, adding to the plethora of possibilities that AI tools provide to science communication.[14–17] With the use of AI, machine learning, and neural networks, textual descriptions (or prompts) are converted into digital images, thus improving the accessibility and speed with which visual elements are created.[18]

AI models for text generation use sophisticated natural language processing models, i.e., large language models (LLMs), that analyse large datasets of text to determine patterns in words and phrases. By identifying these patterns, LLMs can produce a new text similar in style and content to the training data. They learn the structure of the sentences and how often certain words follow each other, but also complex aspects like context.[19] On the other hand, AI models for visual generation are trained on an extensive amount of text that is translated into numerical formats with the use of a natural language processing (NLP) model. These numerical representations are guidelines for the

AI image generators that help them interpret the text and eventually visually represent text prompts.[18] In both cases, AI models do not "understand" the content of the text. Instead, they predict content based on patterns observed in the training data.[18,20,21]

Today, AI is largely used to generate attractive images in an increasing number of fields, not excluding science communication. Newspapers like *The New York Times* and *The Washington Post* have used AI-generated content to create visuals that tracked the COVID-19 virus spread or informative maps and charts, respectively. Similarly, NASA's Mars rover utilises AI algorithms to analyse data from the rover to create sophisticated images (3D models and topographical maps) of the surface of Mars.[22] In advertising and marketing, several campaigns have been created using AI with great success, such as those of big brands across various sectors like Nutella, BMW, and Nike.[23–25]

While in other sectors like finance and education, AI applications (apps) have been created for data visualisation or creating educational material, private companies and tech giants like IBM and Google have naturally also leveraged AI, developing tools to produce interactive visualisations of complex data sets.[26] IBM's Watson Analytics is a data analysis tool that utilises AI algorithms to create charts, maps, and graphs to analyse trends and insights, while Google's TensorFlow Data is a group of tools that can be used to produce histograms, scatter plots, and heat maps that enable more in detail data analysis.[22]

In science communication or medical writing, AI tools are beneficial in a variety of ways, including accelerating our creation of, for example, slide decks, infographics, conference posters, illustrations for articles or educational purposes, graphical abstracts, diagrams, or images to illustrate methods and concepts in scientific articles. Several online services already provide AI-powered tools to create different types of visuals for academic institutions and biotech companies.[27,28] However, rising concerns about how these constantly-evolving tools are being used to create scientific content have sparked necessary discussions regarding the accuracy of AI in representing scientific notions. Another topic of debate is the intellectual property ownership that must be attributed to the original artists and illustrators.[29] Microsoft 365 Copilot is an evolving AI tool that not only promises to significantly advance AI-driven workplace tools, but could also help overcome some of these concerns.

(Co)piloting visual content creation with Microsoft 365

When Microsoft first launched Copilot in March 2023, it was only available to specific enterprises for testing.[30,31] Since January 2024, Copilot has been available to businesses of all sizes, as well as personal and family subscribers (called Copilot Pro).[32] It has been adopted by over 75 million devices worldwide, with the number of paying Office 365 users surpassing 400 million.[33] Favourably, reports indicate that 70% of Copilot's early adopters increased their efficiency by 29% across a range of tasks, including searching, writing, and summarising.[33] ChatGPT was listed as one of the top AI tools in 2023 and 2024, and given that Copilot is powered by ChatGPT, these statistics suggest that Copilot is among the most used AI tools today.[34,35] Indeed, since its launch, Copilot has rapidly advanced in the functions and features it offers, becoming one of the best AI-image generator tools available online.[36–38]

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Copilot is straightforward to use and can create very detailed, highly resolute images with a variety of styles.[36,38] "Designer" is Copilot's AI tool capable of creating images from prompts with the use of DALL-E, the text-to-image generator developed by Open AI, which converts text descriptions generated by Copilot into visual elements.[39] DALL-E 3 is the last version released in October 2023, which increased the number of image generation boosts from 15 to 100 per day and aims at providing more accurate results.[38,40]

Advantages and disadvantages of using Microsoft 365 Copilot

Advantages

Copilot's most attractive quality is its integration with apps we already use every day, like Microsoft Word, Excel, PowerPoint, Outlook, OneNote, and Teams, providing real-time support and a level of ease of use and accessibility that perhaps other AI tools do not.[41] This integration allows users to utilise Copilot's features within their preferred Microsoft 365 app without the need to switch between different tools.[37,42,43] For instance, Copilot can create a PowerPoint presentation with a collection of slides starting from the content of a Word document and can also enhance the overall appearance of the presentation by suggesting layouts and designs.[44,45] Copilot was also added to Whiteboard, Microsoft 365's collaborative digital canvas app for brainstorming, where its content can be used to create images, while in Excel, it can make illustrations from tables of data.[43]

Additionally, Copilot addresses one of the top concerns with AI use in the medical communications/scientific field, privacy, by adhering to Microsoft 365's privacy and security policies.[41] Copilot's business licence ensures safety and confidentiality to organisations: clients' data are protected, prompts created by a user are not shared with other users within the same business environment, and Copilot can't use information in SharePoint and OneDrive unless permitted by the end user.[46,47] With the assurance of privacy, Copilot can, without a doubt, dive into your Microsoft 365 environment with ease to enhance productivity and work across your existing apps, assisting in multiple daily activities.

Another positive aspect of Copilot is its ability to improve its tailoring of content to each user over time. Its integration into Microsoft 365 allows Copilot to have access to an individual user's emails, documents, chats, calendars, meetings, and contacts, learn from all this information, and provide contextualised, accurate results related to a specific user or organisation.[41,46,48] As with other AI tools, LLMs for Copilot are trained on large publicly available datasets. Based on these data, LLMs summarise, predict, and generate content. In the free version of Copilot, results are created based on this publicly available information. What differentiates Copilot is "Microsoft Graph", which is similar to a huge database of all user content, able to create answers more tailored to the user.[41]

Disadvantages

Copilot's top limitations are the time to be invested in trial and error before achieving the desired results and the word character limit (Copilot can process 18,000 to 20,000 words for a single query or prompt).[48,49] Moreover, the user must be aware of the risk of creating "deep-fake" images and the data that are shared while using AI tools. It must also be taken into account that advanced features are not accessible for free but only with the premium account.[36]

Comparison with other AI tools for graphics

Table 1 highlights the key features of some of the most used AI image-generator tools: DALL-E (Copilot's graphic generator), Midjourney, Stable

Diffusion, and Canva. The intent of this summary is not to determine which is the best AI image-generator tool since they are all rapidly evolving and have distinctive strengths that could meet users' needs differently. The key features of each tool are insights taken from popular AI-focused websites.[36,50–53]

User insights on Copilot in science communication

Interviews with professionals who work in science communication provided valuable insights into user experiences with Copilot for visual communication (Table 2 and Table 3), enabling a better understanding of the advantages and challenges Copilot can bring to visual communication in science.

Recent updates and future directions

In April 2024, future updates for Copilot Microsoft 365 were announced.[40] These updates will be available for users with Copilot Pro and Copilot for Microsoft 365 licences. Firstly, the number of chats per day and the length of conversations won't be limited anymore. Regarding privacy and safety, Microsoft specified that commercial data protection will also cover the web context, thus ensuring that a user's data won't be used to train their models. Of note, the number of images we can generate will increase from 15 to 100 daily.[40]

As Copilot and other AI tools are evolving so quickly, it's easy to imagine that innovative developments and improvements are yet to come and will potentially revolutionise how visual content is created.

However, we have to remain cautious of when they are applicable to use. The rapid advancement of AI-generator tools, particularly in terms of quality and data protection, raises questions about when we will see similar progress in ensuring appropriate copyright regulations, privacy, and a reduced risk of inaccurate scientific fake images with AI tools used for developing visual communication. Tracing the sources of data and images used by AI tools is not yet possible, and generating falsified, manipulated, or scientifically incorrect data is considered a major threat to scientific integrity, especially among those in the scientific community.[18,54–56] In fact, the *Nature* journal recently announced that it will not publish visual content generated with the assistance of AI, except for articles published in their AI section.[57] Nevertheless, it is crucial for the scientific community to take proactive measures to uphold scientific accuracy and integrity. Copilot and AI technology, in general, offer a wide range of applications across many different fields, including medical communication. As they continue to evolve swiftly, medical communicators must face the current challenges these innovative tools bring to exploit their potential and apply the correct regulations simultaneously.

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Table 1. Key features of some of the most popular AI image-generators

AI image-generator	Model	Features	Free trial?
DALL-E (Copilot)	Integrated with ChatGPT	• Easy to use, ideal for beginners • Advanced ability to convert text to images • High variety of image styles • High-resolution, realistic, and detailed images • Fast image production	Yes
Midjourney	Proprietary machine learning model	• Abstract and artistic style • Extensive customisation • High range of resolutions and editing tools • Abstract and artistic imagery • Intuitive user experience, user-friendly interface • Connected to an active community of users	Yes
Stable Diffusion	Open source	• Extensive customisation • Fast and efficient in creating high-quality images • Consistent and reliable results • User-friendly interface • Most suitable for users with technical knowledge • Less creative	Yes
Canva	Web-based design service	• Simple and intuitive • Rich set of features • Limitations in replicating complex designs • Limit of 100 AI-generated images per day • Flexibility in editing images	Yes

Table 2. Q&A with Noelle Ochotny (medical writer) and Mario Morel (Principal, Copilot, and Microsoft 365 Services), both of Foremost Medical Communications

Questions by: Jacqueline Bersano	Answers from: Noelle Ochotny and Mario Morel
Q: What do you use Copilot for?	**A:** We have used Copilot graphic generation and graphic recognition capabilities for four use cases: 1. **Graphic/diagram legends**: We asked Copilot to write a legend for diagrams or graphical illustrations. Truly, we have been blown away! Copilot was so good at identifying what's going on in an illustration and providing a relevant description that we can use as a legend. 2. **Promotional material**: As freelancers, we need to conduct frequent promotional campaigns. Since we have Copilot, it has created all of our promotional illustrations. 3. **Creating project logos for the engagements with our clients**: It is certainly important to maintain a professional and dynamic "look" with our clients. For each engagement, we create a dedicated and secure team in Microsoft Teams where we run our project and develop deliverables. We create a special logo for each project. This is important for our branding. Now, virtually all of our logos are generated by Copilot. Figure 1 is a logo we created for a research paper in regenerative medicine in the first quarter of 2024. The logo shows DNA and lab equipment. The colours, light blue above and darker blue below, suggest the innovative "before/after" flow of the research. 4 **Graphical abstracts:** For this use case, I think Copilot is still a work in progress. We tried hard to create different prompts to make Copilot understand what we needed, but the results have been mixed at best. We will keep trying as Copilot gets better over time. Maybe one day, Copilot will get it.
Q: Why do you think Copilot has more difficulties creating graphical abstracts than other material?	**A:** I think that DALL-E is stubborn. When providing an abstract and prompting for a graphical illustration, DALL-E will come up with a surprisingly sophisticated image. However, no matter how we adjust our prompt thereafter, DALL-E would just stick to its initial concept. In one of our attempts, DALL-E produced an image that looked like an infographic, but we wanted the format of a graphical abstract. DALL-E just would not budge. Based on our trials, I am thinking of two possible reasons why creating graphical abstracts with Copilot is still challenging: the first is that we cannot use "grounding"[1] with DALL-E through Copilot. For example, we wanted to use a graphical abstract template as a reference file for grounding, but DALL-E just wouldn't accept it. The second reason has to do with what Copilot was trained for. Among the millions of pictures available on the internet used for training DALL-E, there are far more infographics than graphical abstracts. For example, try googling images for both. Chances are you won't find many good graphical abstracts. Therefore, I think that DALL-E hasn't been trained to specifically generate graphical abstracts.
Q: Do you have any experience creating presentations by integrating Copilot into PowerPoint?	**A:** Yes, we have created many presentations with Copilot within PowerPoint. We are quite impressed with the results. For example, we created an ad for presenting a poster at a conference, and Copilot did it all by itself in PowerPoint. Another example was a manuscript summary in PowerPoint where Copilot produced the structure, the slides, and the pictures.
Q: What other kinds of scientific material for visual communication do you think we'll be able to create with Copilot in the future?	**A:** I am sure Copilot will get to create graphical abstracts eventually. It can already produce infographics and I am sure they will get better and better over time. I think that Copilot will be able to create molecules, cells, proteins, "test" X-rays (that can be used for education), body organs with a focus on a mechanism of action and illustrated guides for how to administer a treatment. I think there is no limit.
Q: In your opinion, what advantages does Copilot have compared to other AI tools?	**A:** I think the most dominant advantage is that Copilot Microsoft 365 understands a user's business context. Copilot can access users' emails, files on OneDrive, pages in SharePoint, etc. It uses this data as part of preparing its responses. This makes Copilot able to produce images that are far more relevant to the user than any other AI tool that doesn't have such comprehensive access to the user's data.
Q: What did you use before Copilot was launched, and how does it compare in terms of resources needed?	**A:** Before Copilot, we were doing the work mostly manually with limited automation, such as with PerfectIt™. The reason we were limiting our use of automation tools was due to confidentiality and privacy. We did not want to submit any sensitive material to a third-party tool outside of our environment. Now, thanks to Copilot being integrated into our environment, no sensitive data leaves our environment (i.e., our Microsoft 365 tenant), so we can use the full power of AI and automation confidentially.

1. "Grounding is the process of using large language models (LLMs) with information that is use-case specific, relevant, and not available as part of the LLM's trained knowledge. It is crucial for ensuring the quality, accuracy, and relevance of the generated output".[60]

Figure 1. Logo created with Copilot using the prompt: "Create a logo emphasising the [core innovation]".

Table 3. Q&A with Tania Sultana (medical writer) and Serena Diana Ghezzi (freelance scientific graphic consultant)

Questions by: Jacqueline Bersano (JB)	Answers by: Tania Sultana (TS) and Serena Diana Ghezzi (SDG):
JB: What do you use Copilot for in the context of visual communication?	**TS:** I use Copilot to get inspiration for images and illustrations I need for my YouTube channel and books. Copilot can create basic PowerPoint presentations and infographics, but I don't create scientific illustrations with any AI tool. They are not advanced enough for this yet. **SDG:** So far, I have been using Copilot to create images for my LinkedIn posts, infographics, and PowerPoint presentations. It helps me generate introductory and general images (Figure 2), for example, when I need to introduce a scientific topic to students, but it can't create specific scientific visualisations as I show in Figures 3 and 4.
JB: What AI tool do you prefer or use the most for graphics?	**TS:** Midjourney is the AI tool I use the most to create my content. It's fast, and at the moment, I prefer it compared to Copilot. **SDG:** From a technical point of view, Midjourney is my favourite AI tool to generate images. With a properly detailed prompt and the right settings, I can get the desired image. Midjourney is a great tool for generating very detailed images, but unlike Copilot, it does not prevent the creation of controversial images.
JB: What are your personal opinions on the use of Copilot and other AI tools for visual science communication?	**TS:** Copilot can help to brainstorm ideas for images as a starting point, but for more sophisticated images, the time I spend tweaking the prompt is not worth it. Indeed, we need to invest time in prompts before we get what we want; that's why, for now, I rather use other AI tools dedicated to image generation to create the content I need. I use Midjourney if I have to create something from scratch, but first, I try to find good images in Canva and Freepik. **SDG:** Copilot, like the other AI image generator tools, can´t be used for creating precise and accurate scientific content for peer-reviewed journals or in other contexts where scientific accuracy is fundamental. It can provide context or a reference point, but the time when we can use it for data visualisation is not here yet. However, I´m impressed by the rapidity with which Copilot and other AI tools are evolving. As a scientific graphic designer who has been exploring their features and uses, I think they have great potential. DALL-E allows you to customise settings and get highly tailored images. We can enter instructions that will be automatically added to our prompts without having to repeat them. We can generate a series of images with a certain objective style without repeating the same basic commands every time. Besides, a key difference of DALL-E from the other AI tools is the possibility to dialogue directly with ChatGPT to create our images, without the need to enter the image generator program. This means that ChatGPT creates the prompt for us and submits it to DALL-E. How ChatGPT translates our request into a prompt for DALL-E is very interesting because it can be much richer and more detailed than ours. Nonetheless, DALL-E needs very detailed, clear commands to create the desired image. Maybe, over the next few years, we will create more accurate scientific content with the use of AI. This would raise debates regarding ethical issues related to the use of artificially generated images in specialised scientific communication. Furthermore, addressing the longstanding issues with the peer review system will become more urgent, especially in light of the growing prominence of open-access publishing.

Figure 2. A, B, and C are images that were used for web pages of human health fundraising. a, b, and c, are respective images made with Copilot's DALL-E

Images **a** and **c** were created with the prompt: "Create an image of two hands holding a clod of earth from which two kidney-shaped seedlings are growing. Sky background. Backlit. Balanced **(a)** or precise **(c)** style." Image **b** was created with the prompt: "Create an image to be attached to a fundraising project for the study of a new drug to cure kidney disease. Balanced style."

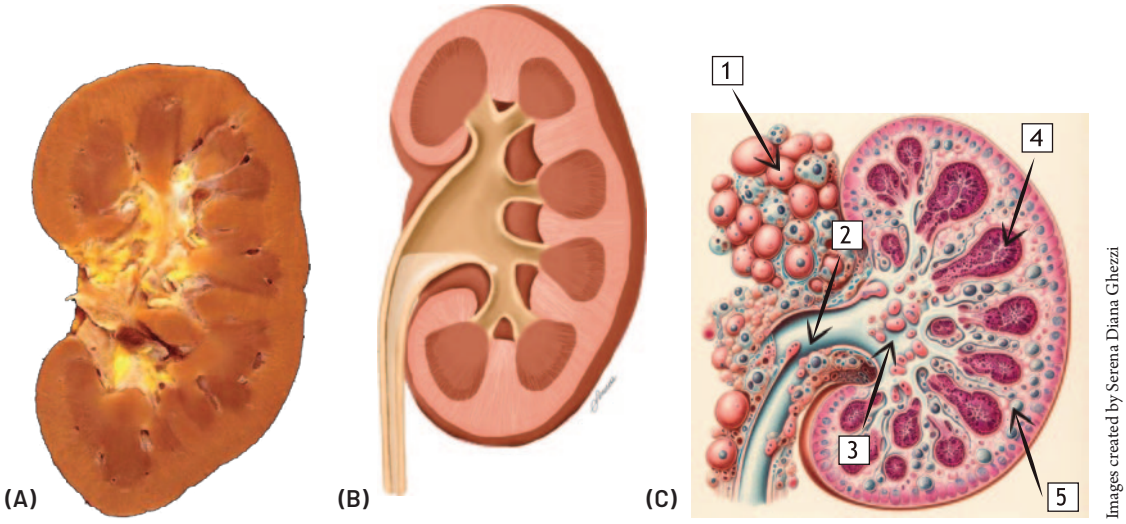

Figure 3. Comparison between a cross-section of a human kidney drawn by a scientific illustrator with the use of Clip Studio (B) and an illustration made by Copilot's DALL-E (C).

(A) is a real microscopic image from Renal pathology showing the section of a human kidney.[58] AI illustration **(C)** presents multiple mistakes: The external tissue around the kidney is adipose: in the picture it should be more regular, smaller, and homogenous (1). The ureter is not interrupted (2). The renal pelvis should be empty (3). The medullary (4) and cortical (5) stroma are characterised by rays structures (nephron ducts and tubules). Prompt used: "human kidney section".

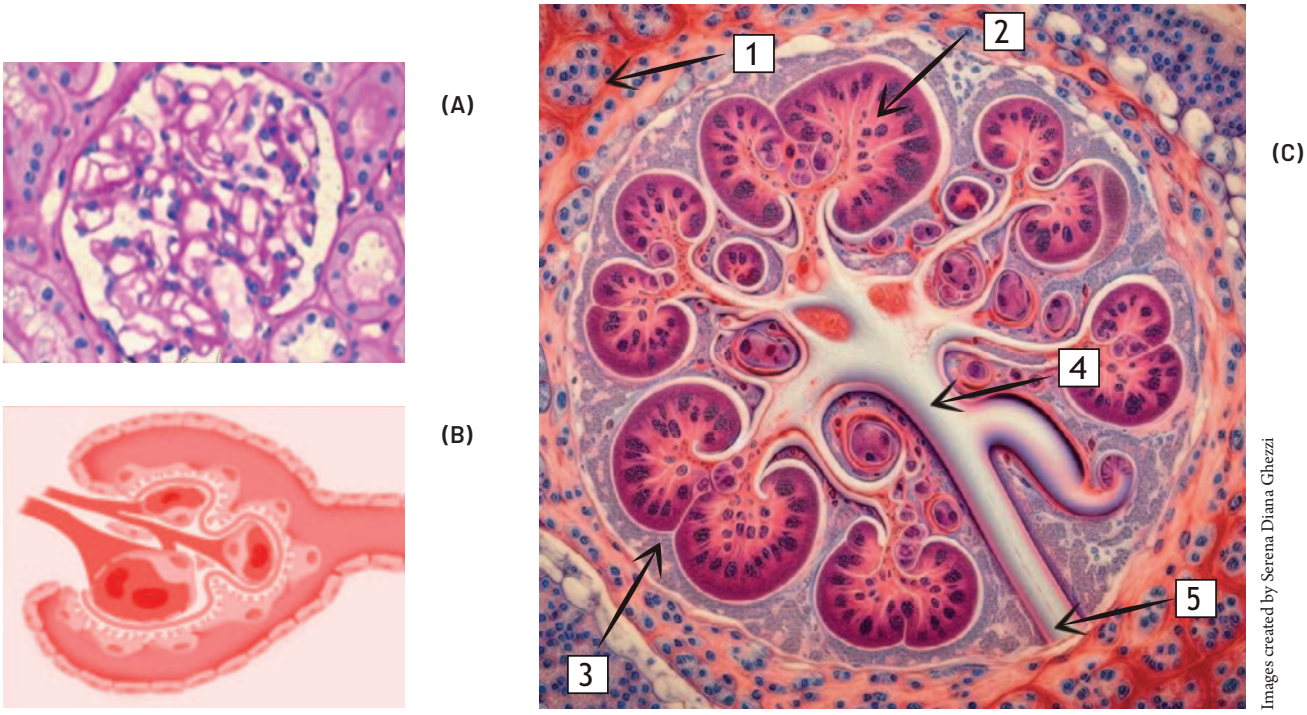

Figure 4. Comparison between a cross-section of a renal glomerulus drawn by a scientific illustrator with the use of Clip Studio (B) and an illustration made by Copilot's DALL-E (C).

(A) is a real macroscopic image from Miller-Hodges et al., 2017, showing the section of a renal glomerulus.[59]

AI illustration **(C)** presents multiple mistakes:

1. External Bowman's capsule tissue is actually characterised by epithelial tubules.
2. The structure inside the glomerulus is one singular capillary boll, not several epithelial bean shapes.
3. Bowman's capsule must be empty.
4. The glomerulus has two exit points: the hilum for the blood system and the proximal tubule for urine collection.
5. The proximal tubule does not stop but continues to the collecting duct. Prompt used: "histological renal section with glomerulus rounded by podocytes."

Acknowledgements

I would like to thank Serena Diana Ghezzi for creating Figures 2, 3, and 4, and for proofreading this article as an expert on AI tools. I would also like to thank Noelle Ochotny, Mario Morel, Serena Diana Ghezzi, and Tania Sultana for providing their experience and insights.

Disclosures and conflicts of interest

The author declares no conflicts of interest.

Disclaimers

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

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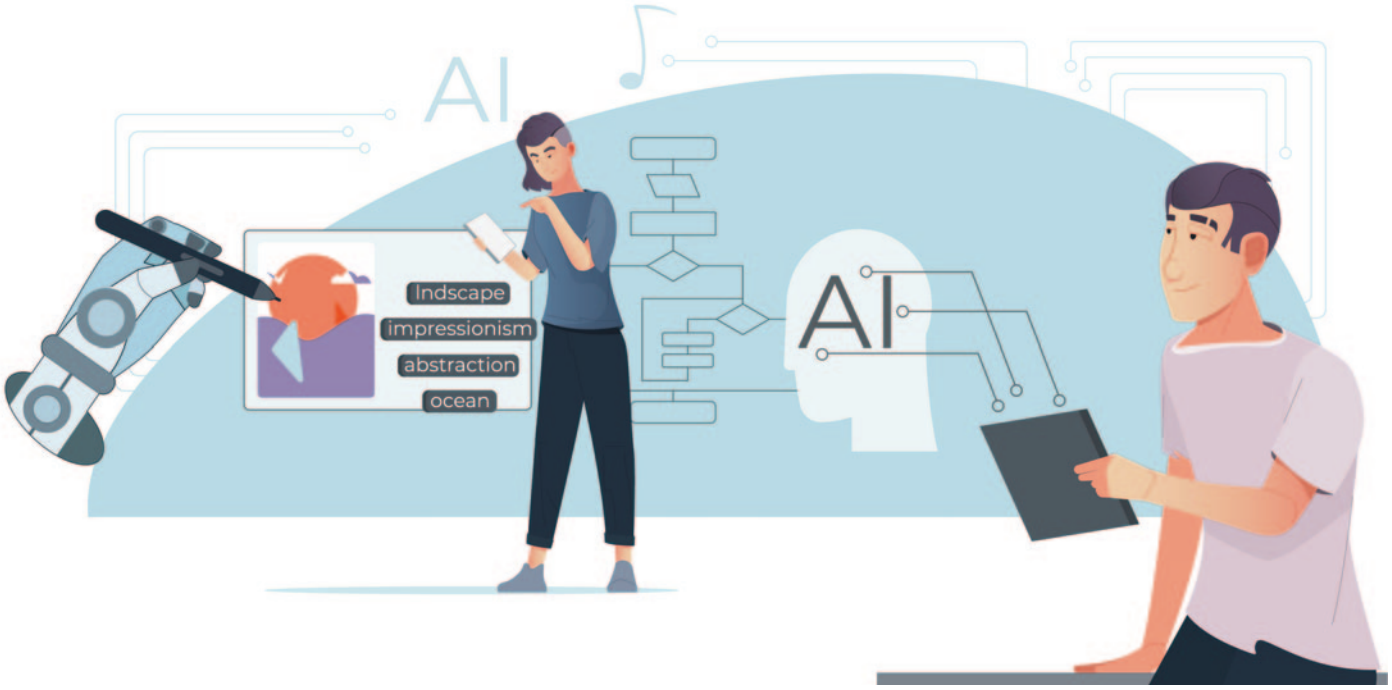

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Medical Communications and Writing for Patients

Editorial

This edition of *Medical Writing* offers a fascinating insight into the work being done by a group at Eli Lilly Japan, who describe their work with a patient advocacy group – from the start of the research right through to the publication of the results. We read a lot about all the positive aspects of working with patients (and clearly there are many!), but new ways of working do come with their challenges. This article is refreshingly honest and beautifully describes the concept, how the collaboration was set up, and the challenges that the authors faced in bringing patients into the process.

I'm incredibly grateful to Aki Yoshikawa and colleagues for sharing their experience and knowledge so thoughtfully. There is no doubt that the positives of involving patients in our work far outweigh any challenges along the way, but it's wonderful to be able to learn from others so that we can pre-empt and overcome any difficulties more easily. And not least – it's very inspiring to read how the Eli Lilly group dealt with their challenges and overcame them.

SECTION EDITOR

Lisa Chamberlain James
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I hope that you enjoy Aki's article as much as I did, and in the meantime, stay safe and sane – enjoy the sunshine (if you have any!), and see you in the December issue!

Bestest,
Lisa

Involving patients in company-sponsored medical publications: Learning from collaboration with a patient advocacy group to engage patient authors

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doi: 10.56012/rowv7554

Abstract

Patient authors can clarify the disconnect between patients and healthcare providers. This can make publications more relevant to the real world and support better shared treatment decision-making between patients and physicians. Eli Lilly Japan K.K. collaborated with a patient advocacy group (PAG) in Japan from the study planning to publications from 2021 to 2022. Our intention was to co-author publications with patient authors, but patients declined to be authors for the publications. It is vital to share the value and expectations of author participation with potential patient authors. This article outlines the challenges in involving patient authors and how to overcome these challenges based on our experiences in collaboration with the PAG for company-sponsored medical publications.

Plain language summary of the article

More people are realising the importance of involving patients in the process of developing new drugs. One way to do this is to have patients contribute as authors in publications. Having patients as authors in medical publications can help bridge the gap between patients and doctors. It can make publications more applicable to the real world and help patients and doctors to make better decisions about treatments together.

Eli Lilly Japan K.K., a pharmaceutical company, worked with a patient advocacy group (PAG) in Japan from the start of our research until we published our findings. We aimed to include patients' views in the publications, making it easier for doctors to help patients decide on treatments together. Although we wanted three patients as authors in our publications, they didn't agree to be authors.

Working with the PAG, we found some challenges in getting patients to be authors. We learnt that it is very important to be clear about our expectations and find patients who can meet those expectations. It is also important to explain why being an author matters and to make sure patients agree. Needless to say, good communication is key. We need to talk with patients about what we would like to achieve with them, give them enough time to think about it, and work together based on mutual understanding. By doing these things, we believe companies can successfully collaborate with patients as authors.

Introduction

The value of engaging patients throughout the drug development process is gaining greater attention.[1] An example of patient engagement is patient authorship in publications, and its presence and implementation are expected to increase.[2] It has been reported that patients and healthcare providers (HCPs) can have different opinions on diseases and treatment options.[3] Patient authors can clarify the disconnect that exists between patients and HCPs, and make publications more relevant to the real world.[2] Therefore, it is increasingly valuable to involve patient authors and reflect patient perspectives in publications. In fact, in recent history, pharma-

ceutical companies have published manuscripts co-authored with patients in peer-reviewed journals that incorporate and reflect patient perspectives.[4-5] Furthermore, many patients and caregivers want to know about new treatments, be better informed about treatment options, and have a voice in making treatment decisions.[6] Evidence shows that patient involvement in their own care leads to better treatment outcomes.[7-8]

Eli Lilly Japan K.K. (ELJ) has taken the initiative to actively involve patients in publications as part of the Patient-involved Publications (PivoP) project. The vision of the PivoP project is that publications are made more relevant to the real world and contribute to better patient-physician shared treatment decision-making by including patient perspectives. This aligns with the pharmaceutical industry's direction of empowering the voices of patients in the development of medical treatments.[9] In this article, we will discuss ELJ's patient-involved publication initiatives, especially patient authors, and share what we have learnt from our experiences in collaborating with a patient advocacy group (PAG) for company-sponsored medical publications.

> It is vital to share the value and expectations of author participation with potential patient authors.

Co-creating publications with a patient advocacy group (PAG)

ELJ's first collaboration with a PAG from study planning to publications

ELJ conducted an observational study by means of a web survey on early-stage breast cancer (EBC) patient adherence to treatment, and the data were published in 2022.[10] The purpose of this study was to investigate adherence to adjuvant endocrine therapy (ET) as well as the factors affecting demotivation and motivation to continue adjuvant ET.[10] Although the efficacy of ET for hormone receptor-positive breast cancer has been established, it is not easy to complete treatment because the recommended duration of treatment lasts 5 to 10 years.[11]

To make the study results and publications more relevant to the real world, we wanted to reflect patient perspectives in the study protocol and survey questionnaire (hereinafter referred to as "study materials"), data interpretation, and publications (i.e., a manuscript and congress abstract/presentation). Furthermore, we created a plain language summary (PLS) as part of the manuscript to provide a summary of our article written in easy-to-understand language.[12-13] We believed that a PLS could help physicians and other HCPs acquire a better understanding of the data more quickly.

We collaborated with a PAG in Japan (NPO Breast Cancer Friendship Association Kirara) to reflect patient perspectives in the study materials, data interpretation, and publications including a manuscript PLS. This was ELJ's first collaboration with a PAG from the study planning stage to publications. Figure 1 shows what we planned to do, what actually happened, and the gap between them regarding patient involvement in this project (Figure 1).

What we planned

We planned to involve patients from the PAG in study planning and data interpretation, then co-author the publications with these same patients to reflect patient perspectives in the study materials and publications.

What actually happened

Three members from the PAG were involved in the study planning of the observational study using a web survey, and their perspectives were reflected in the study materials and data interpretation. ELJ asked the three patients to consider co-authoring the publications (i.e., congress abstract/presentation and manuscript including PLS). While they had never previously authored a publication, one of them agreed to review the manuscript PLS and congress abstract/presentation. The patient reviewer pointed out medical jargon that was too difficult for the audience to understand, and in addition, suggested better visual aids.

The PAG appreciated the opportunity to become involved in these activities (i.e., study planning, data interpretation, and publication review) and being acknowledged in the publications. It was recognised by the PAG that the publications raised awareness of the importance of shared decision making between patients and physicians.

Gap analysis

None of the three patients who were involved in study planning and data interpretation agreed to be an author. The reasons for their reluctance were varied and included the following:

1. Not wanting to disclose their name
2. Not having sufficient time to contribute
3. Believing that others are more qualified to be an author.

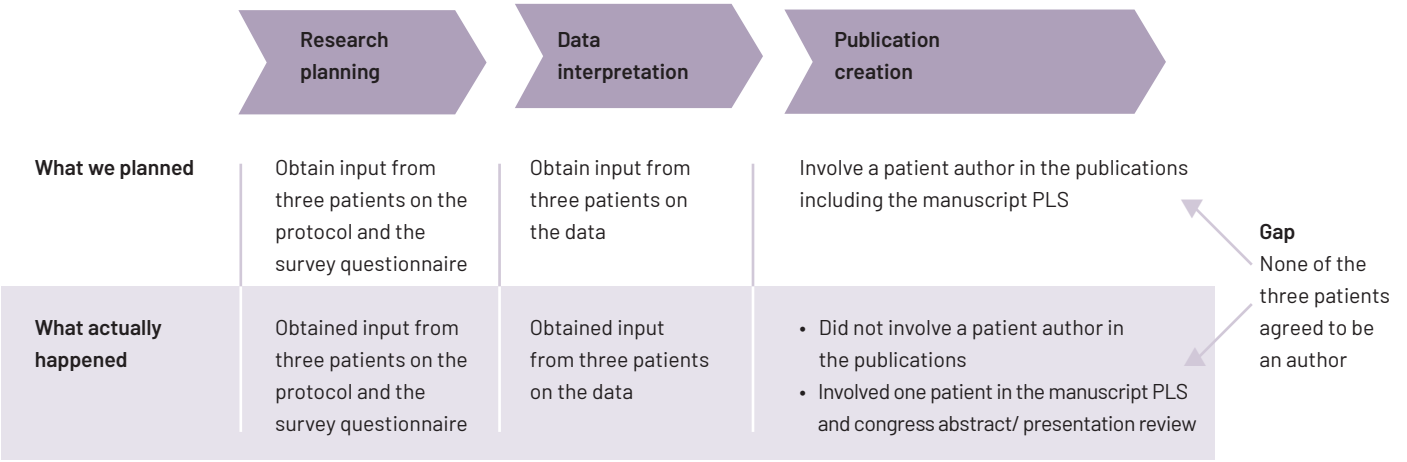

Figure 1. What we planned to do, what actually happened, and the gap between them in ELJ's first attempt to involve patients from the research planning stage to publication

Challenges in involving patient authors

Based on our experiences with the study on EBC patient adherence, we have identified the following challenges in involving patient authors.

Obtaining consent from patient author candidates

It is important for patients to fully agree on the value of their author participation before deciding to become authors. When we approached the patients who had never co-authored a publication, we needed to help them understand the essential significance of their author participation, then the authorship criteria[14] and relevant rules.[15]

Since the three patients had been involved in study planning, we believed that they would prioritise the importance of incorporating patient perspectives in publications and be motivated to co-author publications. In addition, drawing from our practice with authors in general, we presumed that it was our responsibility to assist patients in comprehending the authorship criteria and relevant rules. This is why we focused more on explaining the authorship criteria and relevant rules rather than sharing and discussing the importance of reflecting their perspectives in publications, why we wanted to co-create publications with the patients, and what we hoped to achieve by involving patient authors.

Moreover, we did not fully consider the priorities from their perspective and what would deter them from being involved in publications as authors. Our approach could have considered how patients who had never been involved in publications would feel when they were approached to become authors and the impact on their daily lives. For example, we did not thoroughly take into account the fact that becoming an author would be a public announcement of their illness and how they would feel about it, as their name would be published, or that their physical and mental conditions might not allow them to participate as an author.

We should have spent more time and effort on reaching a mutual agreement and how to address patients' concerns about authorship and relevant rules. In fact, the PAG president commented that when we proposed the patients to participate as authors, she observed a similar lack of communication that sometimes happens between patients and physicians in daily clinical practice.

Clarifying our expectations for patients when we ask them to become involved in publications

We offered authorship of the publications to patients who had been involved in study planning and data interpretation. We asked the PAG president to refer patients from different backgrounds because patients with EBC have different demographic characteristics (e.g., age, work status) and we wanted to reflect the lived experiences and perspectives of multiple patients. However, we did not properly convey what we expected patient authors to do. This unfortunate oversight was due to the fact that we did not realise that our expectations for patients could be different for the study planning compared with publications.

When the three patients declined our proposal to be authors, we realised that what we wanted to achieve with patients was different for study planning and publication authorship. For study planning, we wanted to involve patients with lived experiences, and it was not mandatory for them to have motivation to be involved in the publication-related activities. However, for publications, we needed to involve patients who had an understanding and willingness to be involved in publication-related activities and who were willing to provide input on behalf of the patient community. We should have clarified our expectations for patient authors before requesting that the PAG president introduce patients to us.

How to overcome the challenge of involving patient authors

Sharing the value of patient author participation

It is important that patients fully understand, and empathise with the value of their author participation, and are motivated to become authors when we propose authorship to them. The main value of patient authorship is that patients have insight into their disease that even clinicians and pharmaceutical companies may be unaware of.[16] Patient author participation clarifies areas of a disconnect between patients and HCPs.[2] As a result, patient perspectives help publications to become more relevant to the real world and support patient-physician shared treatment decision-making, which will hopefully improve patient outcomes.

When approaching candidate patient authors, it is vital to first fully share our view of the significance and value of patient author participation with them, aiming to gain their understanding, and to provide a clear description of the author's role in concrete terms. Only then can we carefully explain the authorship criteria and relevant rules. Moreover, it would be better to discuss with patient author candidates how their author participation can contribute to solving issues faced by their PAG community and patients in general, so that they feel aligned with, and motivated to, co-create publications.

In addition, we learnt that communicating closely and thoroughly with patients, allowing sufficient time for explanations and questions, and proceeding based on a mutual understanding are key considerations. We need to fully validate their concerns, being aware of what patient author candidates know and what they do not know about being authors on a publication.

Clarifying expectations for patient authors

We believe that it is important to clarify our expectations for patient authors before asking them to become authors. It is also necessary to convey our expectations to patient author candidates and to involve patients who can meet these expectations. Furthermore, we should take actions to help patients meet these expectations as a majority of patients have never co-authored a publication.

We have clarified ELJ's expectations for patient authors: those who have an understanding and motivation to be involved in publication-related activities and are willing to provide input

on behalf of the patient community. It is vital to communicate our expectations with patient author candidates and obtain their agreement to meet these expectations prior to starting the publication creation process. Table 1 details ELJ's expectations for patient authors and what we should do for them so that these expectations can be met.

Discussion/Conclusion

We collaborated with the PAG from the study planning stage to publications, with the aim of making our research results more relevant to the real world and supporting patient-physician shared treatment decision-making. We asked three patients to become authors of publications. They did not agree to this proposal, but one of them agreed to review the manuscript PLS and congress abstract/presentation. During the collaboration with the PAG, we identified several challenges to involving patient authors and how to overcome them.

As indicated above, it is important to clarify our expectations before asking candidate patients to become authors, then to involve patients who can meet these expectations. It is vital that we share our view of the value of author participation and that they understand that value. In addition, we learnt that taking steps to help them meet those expectations is a key factor. It may be better to approach patients who already have sufficient knowledge and experience to become a patient author (e.g., a PAG president) because they are likely to understand the importance of patient involvement in publications and to meet the expectations for patient authors (Table 1). Needless to say, it is also important to communicate closely and thoroughly with patients, allowing sufficient time for explanations and questions, and to proceed on the basis of mutual understanding.

We believe that addressing the above points will help medical writers to successfully collaborate with patient authors. That said, this article is based on a limited number of projects in ELJ. As such, there may be other challenges that have not yet been identified. We will continue involving patients in publications to make publications more relevant to the real world and valuable. We hope our insight will help readers create publications with the invaluable contributions and perspectives of patients, which will contribute to improving patient outcomes.

Authors' contributions

AY drafted the article, and all authors (AY, AI, MH, and YK) were engaged in revising it critically. All authors read and approved the final version of the article.

Acknowledgements

The authors would like to thank Ms. Kei Nakagawa, President of NPO Breast Cancer Friendship Association Kirara, a specified non-profit organisation, for providing valuable insight on patient involvement in publications. We also would like to express our gratitude to the members of ELJ who provided ongoing support for the PivoP project to involve patients in publications.

Disclosures and conflicts of interest

All authors (AY, AI, MH, and YK) are employed by ELJ and are minor stockholders of Eli Lilly and Company. This article was funded by ELJ.

Table 1. Eli Lilly Japan's expectations for patient authors

No.	Criteria	What the company should do so that patients can meet these criteria
1	Be able to understand and accept the company's publication activities and recognise the value of patient author participation in the publication for which the patient will be an author	• Fully communicate the value of patient author participation which would allow patients and the company to reach a mutual understanding • Give sufficient time to patient author candidates to consider if they would like to become patient authors • Answer questions from patients
2	Have sufficient knowledge, experience and understanding of the disease and general roles of publications to become a patient author	• Provide relevant information to help patients increase their knowledge of the disease and publications as needed • Answer questions from patients
3	Be able to understand the rules of authorship and publication guidelines[14-15]	• Explain authorship and relevant international rules in plain language • Answer questions from patients
4	Be willing to share their own opinions to improve the publications	• Explain the research plan and data • Schedule a meeting with patient authors as appropriate to explain the publication content and the key points of the review • Notify patients in advance of the review periods • Answer questions from patients when they review publication drafts
5	Be able to independently confirm that their opinions are reflected in the publications and point out any issues that are not reflected in the publications	
6	Be able to secure the time to review publication drafts and to review the publication drafts as scheduled	

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Regulatory Public Disclosure

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doi: 10.56012/vhdv1639

Editorial

EU CTR and CTIS

Since the EU Clinical Trials Regulation (CTR) 536/2014 came into force on January 31, 2023, the platform supporting it – the Clinical Trials Information System (CTIS) – and the underlying transparency rules were updated with a site relaunch on June 18, 2024. In brief, the aim of the relaunch is to strike a balance between transparency of information and protection of commercially confidential information. As well as the publication deferral mechanism being removed for all documentation, the number of documents published has been streamlined. For example, the Investigator's Brochure is no longer published (as is now specifically mentioned in Annex 1, Table VI of Version 2 of the EMA Guidance document on how to approach the protection of personal data and commercially confidential information while using the CTIS, June 18, 2024). The welcome overall outcome is a rationalisation of the published documents to reduce complexity and workload for users engaged in redactions.

Furthermore, there is alignment between the requirements for publication of clinical data under the CTR – when documents and data are submitted in a clinical trial application (CTA) in CTIS – and when documents and data are submitted in the context of a marketing authorisation application under Policy 0070. Thanks to Alison McIntosh for nicely summarising the detail in Table 1 "A bitesize guide to clinical data publication under Policy 0070 and the CTR".

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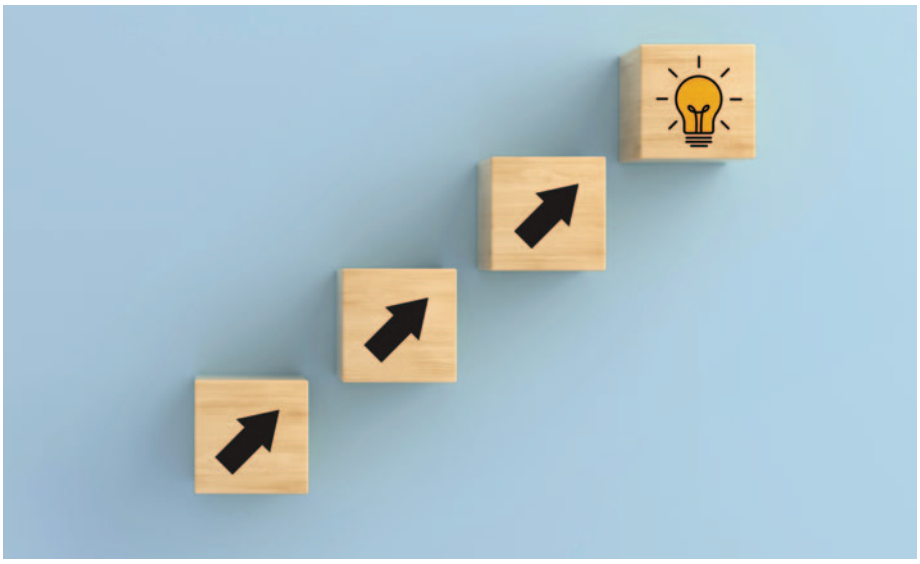
Continuing professional development for regulatory medical writers

At the May 2024 EMWA Valencia conference, the CORE Reference Team presented a live update on the project, its aims, and its recent resources. We repeated the presentation in a well-attended open webinar soon afterwards in June 2024. Topics covered were:

- Value of CORE Reference for disclosure-ready clinical study reports and Continuing Professional Development (CPD) resources
- A real-life Policy 0070 submission, including a planned versus actual timeline
- Policy 0070 relaunch: Anonymisation Report (AnR) template and insights on its completion
- Medical devices CPD, including the devices and drugs spaces intersection
- An overview of the CORE Reference 2023 Utility Survey results
- Breaking news in the public disclosure arena.



The full recording of the presentation and the slides are available here: https://www.core-reference.org/news-summaries/core-reference-seminar-emwa-valencia-may-2024-and-webinar-07-june-2024/ Do feel able to share them widely.

Although we cover the survey results in our slides and presentation, I encourage you to read the full feature article "The 2023 CORE Reference Utility Survey: Perceptions on a best practice tool for globally applicable clinical study reporting and provision of continuing professional development resources for the regulatory medical writing community" on page 38. As well as reporting on the community's perception of the usefulness of the original CORE Reference manual 7 years after its publication, we share how you perceive the value of the CPD that we disseminate monthly. As we go into an era that includes AI-generated clinical study report texts, the need for regulatory medical writers to fully understand the content requirements of CSRs and keep up to date with evolving requirements is more important than ever. CORE Reference's original resources and ongoing CPD support you to critically review those AI-generated texts that you may now be seeing more frequently. The medical writer's role is undoubtedly evolving from pure de novo content creator to encompass curious and robust content interrogator – both of which need a sharp regulatory eye.

Finally, the RPD section would be incomplete without a handy tabulation (see Table 2) of the most relevant information in the world of RPD in the last few months. Thanks to Vivien Fagan for compiling it.

Table 1. A bitesize guide to the publication of clinical data in the EU: Policy 0070 versus EU CTR[a]

	EMA Policy 0070	EU CTR
Medicinal products covered	Centrally authorised products only	Investigational medicinal products regardless of whether they have a marketing authorisation
Clinical studies covered	Clinical studies submitted to the agency in the context of a MAA, Art 58 procedure, line extension or new indication, *regardless of where the study was conducted*	Clinical trials conducted in the EU and paediatric trials conducted outside the EU that are part of paediatric investigation plans
Documents published	Includes publication of: • Clinical overview (Module 2.5) • Clinical summaries (Module 2.7) • Module 5 – Individual CSRs (Sections 1-15) with a limited number of CSR appendices: 16.1.1 Protocol/amendment(s) 16.1.2 Sample CRF 16.1.9 Documentation of statistical methods including SAP	Includes publication of clinical trial-related information generated during the life cycle of a clinical trial, e.g. protocol, synopsis, patient-facing documents, final summary of trial results, lay summary of results, CSRs Following revised CTIS transparency rules, the focus is now on publishing key documents of interest. Applicable to all trials submitted post June 18, 2024
Publication channel	EMA Clinical data website https://clinicaldata.ema.europa.eu/web/cdp/home	Clinical trials website https://euclinicaltrials.eu/
Uploads are made independently but make use of the same data protection and CCI rules [b,c,d]		

Abbreviations: EMA, European Medicines Agency; EU CTR, European Union Clinical Trial Regulation; MAA, marketing authorisation application; CSR, clinical study report; CRF, case report form; SAP, statistical analysis plan; CTIS, Clinical Trials Information System; CCI, commercially confidential information

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[a] https://www.ema.europa.eu/en/human-regulatory-overview/ marketing-authorisation/clinical-data-publication (last accessed -25 Jun 2024)

[b] https://accelerating-clinical-trials.europa.eu/system/files/2023-07/ guidance-document-how-approach-protection-personal-data-commercially-confidential-information-while–.pdf (last accessed June 25, 2024)

[c] https://www.ema.europa.eu/system/ files/documents/other/ wc500174796 –en–0.pdf (last accessed June 25, 2024)

[d] https://www.ema.europa.eu/system/ files/documents/report/ wc500174378– en.pdf (last accessed June 25, 2024)

Table 2. Selected regulatory information shared via CORE Reference (April 2024 – July 2024)

April 2024 highlights	Brief description	Link
HMA/EMA draft guidance for public consultation: "HMA/EMA guidance document on the identification of personal data and commercially confidential information within the structure of the marketing authorisation application (MAA) dossier"	An update to the guidance adopted in 2012 defining the common approach on what should be considered as PD and CCI in the MAA dossier of medicinal products for human use.	https://www.ema.europa.eu/en/documents/other/draft-revised-heads-medicines-agency-european-medicines-agency-guidance-document-identification-personal-data-commercially-confidential-information-within-structure-marketing-authorisation-application_en.pdf?trk=article-ssr-frontend-pulse_little-text-block
PHUSE's EU Clinical Trial Regulation (CTR) Implementation project within the Data Transparency Working Group	Blog gives a summary of Year 2 of implementation of the EU CTR from a sponsor perspective, with a focus on transparency aspects.	https://advance.phuse.global/display/WEL/EU+CTR+Implementation https://phuse.s3.eu-central-1.amazonaws.com/Deliverables/Data+Transparency/EU+CTR+Update+%E2%80%93+Year+2.pdf

April 2024 highlights	Brief description	Link
ICMJE Recommendations for the conduct, reporting, editing, and publication of scholarly work in medical journals	Key updates to the ICMJE recommendations include guidance on the use of AI by authors, editors, and reviewers. Other important updates include statements on fair authorship assignment, sustainability goals, funding support declarations, and protection of research participants.	https://thepublicationplan.com/2024/04/02/icmje-recommendations-update-2024-whats-new-and-whats-next/
Best practices in clinical study protocol writing	Blog provides an outline/guide on how to approach protocol development. Key points for different functions include knowing your scope, developing a study outline (synopsis) with a schedule oactivities (schedule of events) early, clearly defining objectives and endpoints, and keeping the end user (i.e., investigators, site staff, regulators, study personnel) in mind when writing and structuring content.	https://www.allucent.com/resources/blog/best-practices-clinical-study-protocol-writing
A cost-effective approach to EU Medical Device Regulations (MDR) compliance	Article focusing on being cost-effective in the face of the cost of compliance as it pertains to maintaining EU MDR activities.	https://www.meddeviceonline.com/doc/a-cost-effective-approach-to-eu-mdr-compliance-0001
May 2024 highlights		
CTIS newsflash –May 17, 2024	For all clinical trial applications submitted on or after June 18, 2024: • it will no longer be possible to defer the publication of data and documents • data and documents will be published according to the established timelines for the trial category, population age and trial phase • publication of documents will be focused on key documents of interest. Data on all clinical trial applications submitted before June 18 2024 will be made publicly available in line with the principles and timelines defined in the revised transparency rules.	https://www.ema.europa.eu/en/documents/newsletter/ctis-newsflash-17-may-2024_en.pdf
Guidance for the transition of clinical trials from the Clinical Trials Directive to the Clinical Trials Regulation, Version 4	What has changed compared to Version 3, dated March 2024: • Clarification of consequences of non-compliance with transition requirements • Addition of Annex II (Decision tree administrative transition clinical trial) • Clarification on the interface with medical devices and in vitro diagnostic • Clarification on active sites • Minor amendments to elements related to the CTIS transparency rules.	https://health.ec.europa.eu/document/download/10c83e6b-2587-420d-9204-d49c2f75f476_en?filename= transition_ct_dir-reg_guidance_en.pdf
MHRA policy paper	Considers the impact of AI on the regulation of medical products, which also considers the opportunities and risks of AI and is the MHRA's response to the letter from the UK Department of Science, Innovation & Technology and Department of Health & Social Care Secretaries of State to the MHRA.	https://assets.publishing.service.gov.uk/media/662fce1e9e82181baa98a988/MHRA_Impact-of-AI-on-the-regulation-of-medical-products.pdf https://www.gov.uk/government/publications/request-for-regulators-to-publish-an-update-on-their-strategic-approach-to-ai-secretary-of-state-letters/letter-from-dsit-and-dhsc-secretaries-of- state-to-the-medicines-and-healthcare-products-regulatory-agency-html

Disseminated Information	Brief description	Link
May 2024 highlights		
Council for International Organizations of Medical Sciences (CIOMS) consensus report	This freely available report describes the potential use of RWE for decision making; RWD and data sources; key scientific considerations in the generation of RWE; and ethical and governance issues in using RWD. It reflects the opinions of the CIOMS Working Group XIII on RWD and RWE in regulatory decision making and was finalised after considering comments received during a public consultation.	https://cioms.ch/publications/product/real-world-data-and-real-world-evidence-in-regulatory-decision-making/#description
EMA Policy 0070 relaunch	EMA has released the new anonymisation report form template together with the anonymisation report form instructions. The new template was developed jointly by EMA and the Health Canada PRCI team. The guidance document contains instructions and a set of definitions to guide applicants on how to complete the anonymisation report form for the clinical document package.	https://www.ema.europa.eu/en/human-regulatory-overview/marketing-authorisation/clinical-data-publication/support-industry-clinical-data-publication
June 2024 highlights		
EMA CTIS relaunch, June 18, 2024	Clinical Trials Information System (CTIS) – and the underlying transparency rules were updated with a site relaunch on 18 June 2024	https://www.ema.europa.eu/en/human-regulatory-overview/research-development/clinical-trials-human-medicines/clinical-trials-information-system
EMA Guidance document on how to approach the protection of personal data and commercially confidential information while using the Clinical Trials Information System (CTIS) Version 2, June 18, 2024	This document provides guidance to users on the revised Clinical Trials Information System (CTIS) transparency rules and on the protection of personal data and commercially confidential information (CCI) submitted to CTIS. Changes include alignment with revised CTIS transparency rules, including removal of chapter 5 (no longer applicable), new sections on the 'historical trials' publication principles and on transition trials. Principles of protection of personal data and CCI remained unchanged compared to the former versions. It should be read in conjunction with its Annex I A Questions and Answers (Q&A) document is also available	**EMA Guidance on how to approach protection of PD and CCI while using the CTIS, Version 2, 18 June 2024:** https://accelerating-clinical-trials.europa.eu/system/files/2023-07/guidance-document-how-approach-protection-personal-data-commercially-confidential-information-while_.pdf **Revised CTIS Transparency Rules:** https://www.ema.europa.eu/en/documents/other/revised-ctis-transparency-rules_en.pdf **Annex 1:** https://accelerating-clinical-trials.europa.eu/document/ download/824905dd-3033-41e6-a871-67b20c4f4c94_en? filename=annex-i-guidance-document-how-approach-protection-personal-data-commercially-confidential_.pdf **Questions and Answers (Q&A):** https://accelerating-clinical-trials.europa.eu/document/ download/33702a5d-13be-4c4f-936d-3627dd73085b_en? filename=ACT%20EU_Q%26A%20on%20protection%20of%20Commercially%20Confidential%20Information%20and%20Personal%20Data%20while%20using%20CTIS_v1.3.pdf
EMA CTIS Information Day, October 17, 2024	To be held the day after the closure of the window for expedited transition of clinical trials, join this information day for comprehensive guidance and practical insights, covering both the transition and the subsequent steps. Your questions will be answered live by EMA, NCA, and industry representatives during the Q&A session.	**Register here:** https://www.diaglobal.org/en/ema/conference-listing/2024/10/ema-clinical-trial-information-system-ctis-information-day?utm_source=Social+Media&utm_medium=LinkedIn&utm_campaign=24526#showcontent **Submit questions here:** emaevents@diaglobal.org

Disseminated Information	Brief description	Link
June 2024 highlights		
FDA updated the Top Questions and Answers about the Transition to the Modernised ClinicalTrials.gov and Modernised PRS document along with a series of short videos	The Q&A document has been updated to include new information about the retirement of the classic version of ClinicalTrials.gov and additional questions on PRS modernisation while the series of short videos describe how to complete basic tasks on the modernised website.	**Q&A:** https://cdn.clinicaltrials.gov/documents/Modernization_Transition_Top_Questions_RELEASE_508.pdf?utm_medium=email&utm_source=govdelivery **Videos:** https://www.nlm.nih.gov/oet/ed/ct/demo_videos.html?utm_medium=email&utm_source=govdelivery
ACT-EU has launched two advice pilots to improve the quality of applications for clinical trials in Europe	Pilot 1 offers scientific advice on clinical trials and on requirements for MAA.Pilot 2 is coordinated by the Clinical Trials Coordination Group and provides technical and regulatory support on the dossier of a CTA prior to its submission through the CTIS.	https://www.ema.europa.eu/en/news/two-new-advice-pilots-improve-clinical-trials-europe **Pilot 1 Guidance:** https://accelerating-clinicaltrials.europa. eu/document/download/13c622d1-6aef-4d54-b41d-b60dd2e 1e0a9_en?filename=Guidance%20for%20applicants%20S AWP%20CTCG%20pilot%20on%20scientific%20advice.pdf **Pilot 2 Guidance:** https://accelerating-clinical-trials.europa. eu/ document/download/741d2c8d-3a99-48e1-ab51-2bec3e cf3277_en?filename=Guidance%20for%20applicants %20pre-CTA%20advice%20pilot.pdf
Phase 2 of the Declaration of Helsinki Revision Process	To maximise input by all stakeholders and the public, two separate public comment periods are held. Phase 1 public comment period was held earlier in 2024, and a Phase 2 comment period was open June 4–24, 2024.	https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/public-consultation-on-a-draft-revised-version-of-the-declaration-of-helsinki-2/
July 2024 highlights		
EMA released an ICH reflection paper on pursuing opportunities for harmonisation in using real-world data to generate real world evidence, with a focus on effectiveness of medicines.	The paper outlines a strategic approach to address challenges and discusses how to enable the integration of RWE into regulatory submissions and timely regulatory decision-making. The authors state that the reflection paper represents the initial step of an incremental approach towards harmonisation of regulatory RWE guidance.	https://www.ema.europa.eu/en/documents/other/ich-reflection-paper-pursuing-opportunities-harmonisation-using-real-world-data-generate-real-world-evidence_en.pdf
FDA released finalised guidance "Real-World Data: Assessing Electronic Health Records and Medical Claims Data to Support Regulatory Decision-Making for Drug and Biological Products"	The guidance offers clarification of study design elements including on selecting study variables and validation.	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/real-world-data-assessing-electronic-health-records-and-medical-claims-data-support-regulatory
Webinar "Utilizing the Digital Protocol): Collaborating to Accelerate ICH M11 and End User Value	This provides an update to the challenge of defining, adapting, and releasing a fully utilisable digital protocol template. The Webinar included representatives from FDA, EMA, CDISC, TransCelerate and Vulcan. **Of note, ICH M11 Step 4 is planned for autumn 2025.**	**Recording**: https://www.youtube.com/watch?v=E72Dc6ib7Q **Slides**: https://www.transceleratebiopharmainc.com/wp-content/uploads/2024/07/TCB-CDISC-and-Vulcan-Webinar_July24.pdf

Disseminated Information July 2024 highlights	Brief description	Link
The WHO has introduced an online platform called MeDevIS (Medical Devices Information System), the first global open access clearing house for information on medical devices.	A webinar was held on July 8 titled "Nomenclature of medical devices: EMDN & GMDN"	**Recording and slides:** https://www.who.int/news-room/events/detail/2024/07/08/default-calendar/webinar—nomenclature-of-medical-devices—emdn—-gmnd **The WHO announcement:** https://www.who.int/news/item/08-07-2024-medevis-platform-announced-to-boost-access-to-medical-technologies-and-devices#:https://www.raps.org:text=The%20MeDevIS%20platform%20became%20operational,00%2D15%3A00%20CEST.

Abbreviations: ACT-EU, Accelerating Clinical Trials in the EU; AI, artificial intelligence; CCI, commercially confidential information; CIOMS, Council for International Organizations of Medical Sciences; CTA, clinical trial application; CTIS, Clinical Trials Information System; CTR, clinical trial regulation; EMA, European Medicines Agency; FDA, Food and Drug Administration; HMA, Heads of Medicines Agencies; ICMJE, International Committee of Medical Journal Editors; MAA, marketing authorisation application; MDR, Medical Device Regulations; MeDevIS: Medical Devices Information System; MHRA, Medicines and Healthcare products Regulatory Agency; NCA, National Competent Authorities; PD, personal data; PRCI, Public Release of Clinical Information; PRS, Protocol Registration and Results System; RWD, real-world data; RWE, real-world evidence.

Sign up to the CORE Reference email list using this email: https://www.core-reference. org/subscribe to receive the bimonthly email updates, with current information on regulatory reporting and public disclosure which support the continuing professional development (CPD) needs of medical and regulatory writers. The topics covered include FDA and EMA guidance and news, real-world data, transparency and disclosure resources and news, development strategy news, AI in the regulatory arena, the intersection of drugs and devices including in vitro devices (IVDs), transparency in relation to medical devices, news from Asia regulators, and regulatory guidances open for public consultation. The emailed information is collated monthly and archived here: https://www.core-reference.org/news-summaries/

Table 2 (above) provides a selection of key information disseminated by the CORE Reference Project Team between April and July 2024.

Don't miss!

The March 2025 edition

Rare Diseases

Although rare diseases are individually uncommon, there are more than 7000 rare ("orphan") diseases affecting around 300 million people globally. Rare diseases are incredibly diverse and often life-threatening. Long diagnostic delays, termed a diagnostic "odyssey", are common, and many have no effective treatments. Rare diseases offer unique challenges and opportunities that are not seen in other therapeutic areas.

This issue of *Medical Writing* spotlights the evolving regulatory landscape, the nuances of unmet medical needs, the importance of the patient voice, and the key role of medical writers in the orphan disease space.

Guest Editors: Sarah Milner and Heather Mason
The deadline for feature articles is December 1, 2024.

In the Bookstores

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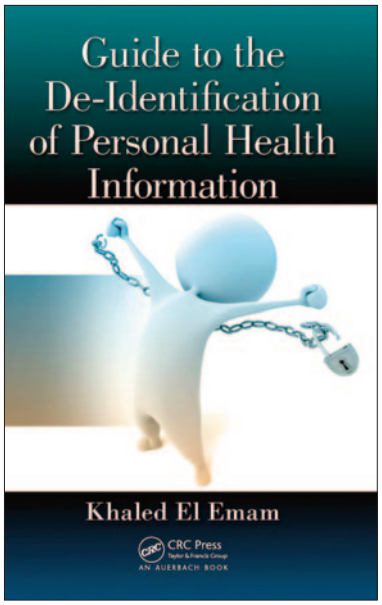
Guide to the De-Identification of Personal Health Information

Written by Khaled El Emam
ISBN-10: 466579064
Publisher: Auerbach Publications (T&F)
414 pages
Paperback: £42.66

Reviewed by Alison McIntosh
AAG Medical Writing

doi: 10.56012/hbvt6966



Increasingly, regulatory authorities require sponsors to publish clinical documents to increase transparency and openness and improve public trust in clinical research. In doing so, the sponsor has a responsibility to ensure that personal data that might allow individuals to be identified is not released in the published version.

Alongside regulatory public disclosure, de-identified clinical data can be made available for secondary health-related research purposes. A third party may submit a request to a sponsor to perform secondary analysis or research of patient clinical trial datasets. Again, prior to release for secondary purposes the sponsor must ensure that the identity of a trial participant is not inadvertently revealed. The amount of de-identification required to ensure anonymisation then has to be balanced against preserving data utility for the researcher.

Regulatory medical writers have an important role to play in the process of preparing clinical documents suitable for public disclosure, and separately can also have involvement in the process of preparing clinical trial datasets suitable for data sharing. There is overlap in the methodology used to manage the risk of de-identification of individuals in both processes.

Guide to the De-Identification of Personal Health Information provides information on the different methodologies that can be employed to manage the risk of reidentification of personal health information. The author, Professor El Emam, is a true expert in the field and is a member of the European Medicines Agency Technical Anonymization Group (https://www.ema.europa.eu/en/human-regulatory-overview/marketing-authorisation/clinical-data-publication/technical-anonymisation-group). Over many years, he has been influential in advocating and developing practical methodology and software tools that allow health data to be accessible whist importantly maintaining patient privacy. He also promotes the idea that when properly applied, de-identification of personal health information can allow the use of health data for important secondary reasons, including health-related research.

For those working in the transparency and disclosure arena this book is a practical guide designed to provide "a valuable and much needed resource for all data custodians who use or disclose personal health information for secondary purposes." Professor El Emam defines secondary purposes as "non-direct care use of personal health information including, but not limited to, analysis, research, quality/safety measurement, public health, payment, provider certification or accreditation, and marketing and other business including strictly commercial activities."

> This book is a valuable and much needed resource for all data custodians who use or disclose personal health information for secondary purposes.

The book has 28 chapters and hence can be a little daunting at first view. However, to help the reader it is organised into four main sections covering: 1. The case for de-identifying personal health information (Chapters 2-9); 2. Understanding disclosure risks (Chapters 10-15); 3. Measuring re-identification risk (Chapters 16-19); and 4. Practical methods for de-identification (Chapters 20-21). A fifth section entitled "End Matter" provides appendices with supporting materials (Chapters 22-28).

Although the book is written principally with disclosure of personal health information for secondary purposes as the main thrust, there is much that is useful to those medical writers working in the regulatory transparency and disclosure arena. Early chapters provide a useful background to the topic and the later chapters provide in-depth methods for managing reidentification risk.

A general background to the Health Insurance Portability and Accountability Act (HIPAA) is provided together with a discussion around HIPAA Safe Harbor principles. The author argues that the Safe Harbour approach, upon which much of the de-identification methodologies employed in regulatory public disclosure are currently based, "does not provide adequate protection". Rather, he recommends the statistical method as a better risk-based de-identification method to apply (Chapter 1). The chapter entitled "Scope, Terminology and Definitions" provides an introduction to identifiers and their classification. Applicable rules to help determine if a variable is a direct identifier or a quasi-identifier are presented and illustrated in a useful in-text table (Chapter 10).

Although as medical writers we do not need a full understanding of the statistical concepts behind data anonymisation, it is useful for us to have a working knowledge of them. A thorough review of the types of statistical approaches that can be implemented together with measuring the probability of re-identification risks are covered in later chapters.

While quite complicated, explanations of how data utility loss can be mitigated and risk assessed, together with any limitations of the approaches being used, will be of help to medical writers working as a subject matter expert (SME) in the transparency and disclosure arena. Taken

together they offer extra insight on how best to achieve de-identification of personal health information using risk-based approaches.

The general summary of commonly used and recommended data masking includes descriptions of suppression, randomisation, irreversible and reversible coding (Chapter 14). Explanations of why other techniques are generally not to be recommended are also presented, including constraining names, adding noise, character scrambling, character masking, truncation, and encoding. For non-statisticians this chapter provides detailed explanations of statistical terminology that, in my experience, is not always well-defined. Specifically, this chapter will allow medical writers working as SMEs in this area to have a better grasp of the approaches that statistical colleagues implement when a quantitative anonymisation strategy is used.

El Emam suggests that generalisation (e.g., generalising date of birth to a five-year age interval) and suppression (e.g., removing a patient or a visit from the data set) methods "have the most acceptability" and both are discussed in much detail in Chapter 20 "De-identification Methods".

Although this book was first published in 2013, even now there is no single method recommended for de-identification of health information. The book provides an in-depth and detailed background to the statistical concepts that can be applied to de-identify clinical datasets. As you grapple with preparing clinical documents suitable for public disclosure, my personal view is that although this book is quite technical, and may not answer all the questions you have about data anonymisation, it provides you with an appreciation of the complex methodologies involved.

Professor El Emam has published more recent books and journal articles. A full list of his publications, including book titles, can be found on the Electronic Health Information Laboratory website: https://www.ehealthinformation.ca/publications where you can also sign up to receive monthly newsletter updates.

Publications

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Preprints: Why and how to use them

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doi: 10.56012/nwco8539

A preprint is a preliminary version of a manuscript that is posted on an open access server without peer review.[1,2] Preprints are intended to precede, not replace, peer-reviewed publications. Example preprint servers are medRxiv (pronounced "med-archive") for health sciences,[3] bioRxiv for biology and life sciences,[4] and PsyArXiv for psychology.[5]

Preprint posting is increasing in medicine, life sciences, and psychology.[6-8] However, few preprints are pharmaceutical industry-authored. For example, between January 2014 and January 2018, only 1% of approximately 19,000 preprints posted on bioRxiv reported industry-authored research.[9] This matches my personal experiences: when I worked in academia, it was common practice to post a manuscript as a preprint before submitting the manuscript to a journal. However, since working in medical writing, I have noticed that pharmaceutical industry researchers are less familiar with the practice.

Preprints are a key part of science communication and publication strategy. Medical writers should therefore help inform authors about preprint options. In this article, I present the arguments for and against using preprints and provide practical considerations when posting, disclosing, updating, and citing them.

For more information on preprints:

- Joint position statement on medical publications, preprints, and peer review from the American Medical Writers Association (AMWA), EMWA, and the International Society for Medical Publication Professionals (ISMPP).[10]
- International Committee of Medical Journal Editors (ICMJE) Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (Section III.D.3).[11]

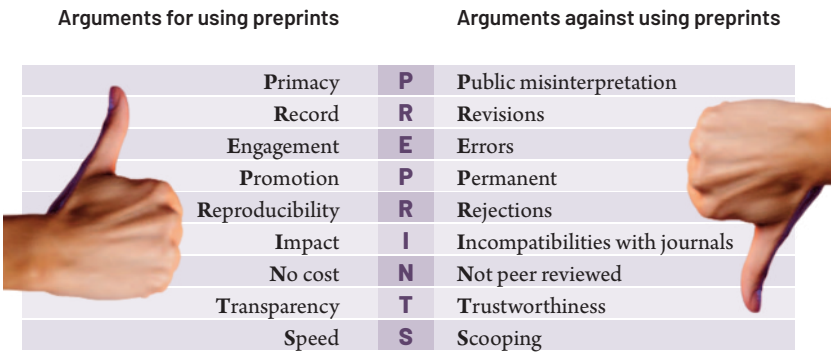


Figure 1. Common arguments for and against using preprints

Should we use preprints?

Arguments for and against using (i.e., posting and citing) preprints are summarised in Figure 1.

Arguments for using preprints

One of the main arguments for posting preprints is its speed in making information available to authors, other researchers, and the wider public. Preprints can be available within hours or days of posting, whereas peer-reviewed publications may take months or years to be available. Therefore, although essential, peer review can slow medical and scientific communication.[12] "The sooner a piece of work can be read, evaluated, and built upon, the faster science moves."[7] For example, authors can self-cite a preprint before the peer-reviewed publication is available. Citing a preprint is preferable to citing a conference abstract because the full-text manuscript is available to readers. Further, while authors wait for the peer-reviewed publication to become available, preprints can be listed on grant, promotion, and job applications.[13,14]

Preprints are also free to post and free to read, which again benefits everyone. Typically, preprints are assigned a unique digital object identifier (DOI), making them traceable, citable, and part of the scientific record.[10,15,16] Authors can openly share the preprint with a wider audience, which increases engagement, inclusivity, and transparency.[12,13,17] Authors can also obtain feedback on a preprint from the scientific community and wider public and then implement that feedback before submitting the manuscript to a journal.[4,7,18] This additional scrutiny may improve the quality of the manuscript, which in turn may help to address the reproducibility crisis.[19,20] However, preprint comments sections and social media posts of preprints may attract "trolls",[21] who deliberately try to offend people or cause trouble. Authors need to consider how comments will be tracked and appropriately addressed,[22] and they should be prepared to handle the (sometimes challenging!) discourse.

> Preprints are a key part of science communication and publication strategy.

Preprints can increase research impact. For example, peer-reviewed publications with a preprint posted on bioRxiv had, on average, a 49% higher Altmetric Attention Score and 36% more citations than peer-reviewed publications without a preprint.[23] Preprints do not appear to impede scholarly metrics. For example, if a study has both a preprint and a peer-reviewed publication, the peer-reviewed publication is preferentially cited in subsequent publications.[14]

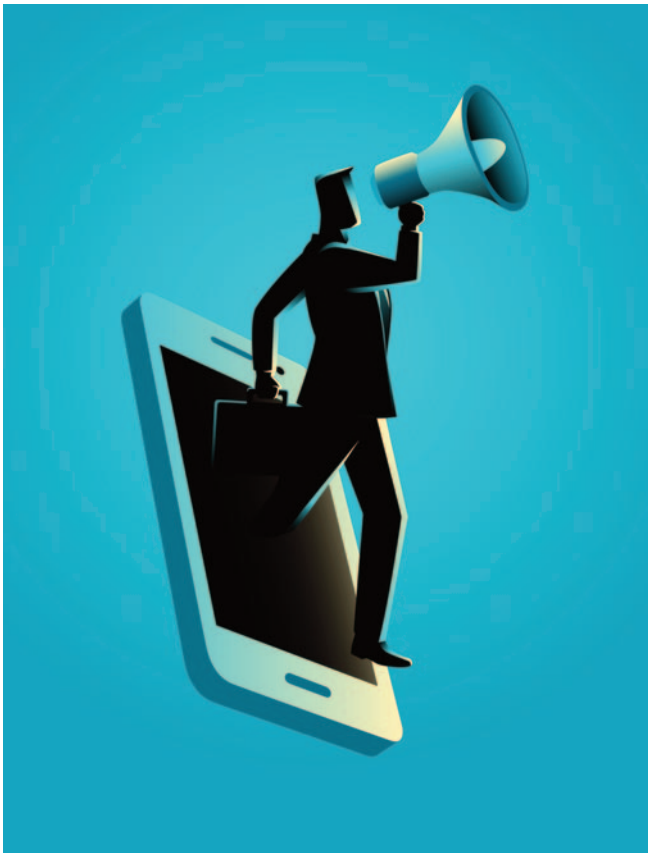
Arguments against using preprints

The main argument against citing and sharing preprints is that they are not peer reviewed and therefore they are not trustworthy.[24] Further, journal reputation, which helps authors and medical writers to determine what to read or cite, is missing from preprints.[24] Some are concerned that the press and the public may fail to differentiate preprints from peer-reviewed publications and may consider them equally credible sources.[6] Consequently, poor quality, misleading, or biased information could be shared via the media and social media, causing harm to patients.[10,21]

A barrier to posting preprints is a fear of being "scooped", which is when a competitor publishes research on the same topic first or without citing the authors of the original research.[7] However, because preprints have a public timestamp, they allow authors to claim primacy of their ideas and results.[12,16,25] Although, this point of contention may be redundant, as some argue that claims to primacy or priority in publications are unnecessary and inappropriate.[26]

Further, posting preprints may be incompatible with peer-reviewed journals – journal policies should always be checked. Some journals use double-blind peer review, meaning authors' and peer reviewers' identities are hidden from each other, but this may be undermined because, in preprints, the identities of the authors are public.[27]

Another concern for some is that preprints are permanent. MedRxiv's policy, for example, is that preprints cannot be removed, but authors may withdraw their preprint if they no longer stand by their findings and conclusions or discover fundamental errors in the research.[15] In these cases, the original preprint will remain accessible but with a "withdrawn" watermark along with a statement explaining the reason for the withdrawal.[15]



Posting preprints on a preprint server

Check the journal's policy

Before posting a preprint, check the preprint policies of the target journal and any alternatives. These can be found on the journal's website or on Sherpa Romeo (https://www.sherpa.ac.uk/romeo/), an online resource that aggregates publisher policies. Most journals and publishers consider manuscripts that have been previously posted as preprints, and many actively promote preprints. For example, Springer states, "Springer journals encourage posting of preprints of primary research manuscripts on preprint servers, authors' or institutional websites, and open communications between researchers whether on community preprint servers or preprint commenting platforms… Posting of preprints is not considered prior publication and will not jeopardise consideration at Springer journals."[28]

Choose a preprint server

When choosing a preprint server, consider its scope. For example, medRxiv does not accept case reports, narrative reviews, editorials, or opinion pieces.[3] According to the International Committee of Medical Journal Editors (ICMJE) recommendations:

- "[Preprint servers should] clearly identify preprints as work that is not peer reviewed; require authors to document disclosures of interest; require authors to indicate funding source(s); have a clear process for preprint archive users to notify archive administrators about concerns related to posted preprints – a public commenting feature is desirable for this purpose; maintain metadata for preprints that are withdrawn from posting and post withdrawal notices indicating the timing and reason for withdrawal of a preprint; and have a mechanism for authors to indicate when the preprint article has been subsequently published in a peer-reviewed journal."[11]

Some journals invite authors to post a preprint in their publisher-owned preprint servers concurrently when submitting the manuscript to the journal.[16] Other journals are integrated with external preprint servers. For example, over 100 journals are integrated with medRxiv accepting "medRxiv-to-journal" or "journal-to-medRxiv" options.[15] However, a disadvantage of concurrently posting a preprint and submitting the manuscript to a journal is that feedback on the preprint cannot be incorporated in the manuscript.

Write a preprint disclosure statement

Before posting the preprint, write a preprint disclosure statement on the first page of the manuscript reminding readers that caution is required when interpreting and sharing the results.[10] For example:

"This manuscript is a preprint. A preprint is a preliminary version of a manuscript that has not yet been peer reviewed. Peer review is the standard procedure used by scholarly journals to assess the quality of a manuscript and its suitability for publication. Preprints should not be relied on to guide clinical practice and should not be reported in news media as established information."

This helps readers to not confuse preprints with peer-reviewed publications when they are downloaded or taken out of context.[29]

Post the preprint

Post the preprint to one preprint server only and before submitting the manuscript to a journal. For medRxiv, the process is similar to journal submission and involves:

- Creating an account and signing in;
- Selecting the subject area;
- Entering the title and abstract, author approval statement, competing interests statement, declarations (author assent, ethical declarations, participant consent, trial registry, legal responsibilities, and reporting guide-

lines), data availability statements and link, funding statement, and clinical protocol link;
- Completing the author information and distribution/reuse options (license option);
- And uploading the manuscript file. Upon approval by medRxiv, the preprint will be timestamped and assigned a DOI.

Share the preprint and incorporate feedback

Authors can share the preprint via social media, email, and other channels, and they can invite feedback. If authors receive constructive feedback, the manuscript can be updated before journal submission.

Disclosing preprints to the journal

Check the journal's policy

When submitting a manuscript, the target journal should be informed that the manuscript has been posted on a preprint server, and the DOI should be provided.[11] Check the target journal's instructions to authors for how and where preprints should be disclosed. Journals usually require a clear statement with the preprint DOI in the cover letter, the online submission system, or the manuscript itself. To improve transparency, the DOI should link to the full history of the preprint, even versions that were previously rejected by another journal.

Updating preprints

Add new versions

New versions of a preprint may be posted if the original manuscript was previously rejected by a journal. However, the final published version and interim versions that are produced during peer review should not be posted on a preprint server.[11]

Link the preprint to the publication

Once a manuscript is published, the preprint should be linked to the peer-reviewed publication via a DOI.[10] Directing readers to the peer-reviewed publication helps ensure that they are cited in subsequent publications instead of the preprint and increases transparency. On some preprint servers (e.g., medRxiv), the link is automatically generated.[10] On others (e.g., PsyArXiv), the publication DOI needs to be manually added to the preprint. Some journals also expect the peer-reviewed publication to be linked to the preprint via a statement in the manuscript. For example, "A preprint of this article before peer review by *Addiction* can be found at [URL and DOI]."[29]

Citing preprints in a manuscript

Identify preprints

Preprints are indexed in various places such as Google, Europe PubMed Central, and OSF preprints.[15,25]

Cite preprints

Although a joint position statement by the American Medical Writers Association (AMWA), the EMWA, and the International Society for Medical Publication Professionals (ISMPP), and the ICMJE recommendations agree that the word "preprint" and the DOI should be included when citing preprints, they disagree on whether preprints should be included in the reference list. The AMWA-EMWA-ISMPP position statement states: "Preprints should not be used as references in any medical publication unless these are cited in the manner of a personal communication, that is, as an in-text reference (using the preprint link, DOI, or both) rather than as bibliographic references. It should be clearly disclosed that the source is a preprint."[10]

The ICMJE recommendations, in contrast, state: "When preprints are cited in submitted manuscripts or published articles, the citation should clearly indicate that the reference is a preprint … Journals should include the word "preprint" following the citation information in the reference list and consider indicating that the cited material is a preprint in the text. The citation should include the link to the preprint and DOI if the preprint archive issues DOIs."[11]

The AMWA-EMWA-ISMPP position statement was challenged by Richard Sever, co-founder of bioRxiv and medRxiv, who argued that preprints should be "included in the reference list as this is essential for citation indexing by services such as Google Scholar."[30] AMWA-EMWA-ISMPP's response can be found online.[31]

If a preprint is cited in a manuscript draft, authors and medical writers need to keep an eye on when the preprint article gets published. As recommended by the ICMJE, "When a preprint article has been subsequently published in a peer-reviewed journal, authors should cite the subsequent published article rather than the preprint article whenever appropriate."[11] Usually, the last opportunity to update a citation is when the manuscript is accepted and the corresponding author receives the proofs.

Conclusions

Posting and citing preprints have pros and cons, which should be weighed up. Medical writers should make authors aware of preprints so that authors can make informed decisions. If authors choose to use preprints, medical writers can support them with the processes of posting, disclosing, updating, and citing preprints.

Acknowledgements

The author would like to thank Phil Leventhal for providing feedback on this article.

Disclaimers

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

Disclosures and conflicts of interest

The author is employed by PPD, a Thermo Fisher company.

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The Crofter: Sustainable Communications

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Editorial

Greetings from the croft. As a UN Sustainability Partner Organisation, EMWA supports the two UN Sustainable Development Goals (SDGs) SDG 3 – Good Health and Wellbeing and SDG 12 – Responsible Consumption and Production. Both are linked to the concept of a circular economy, in which products and materials are designed to be reused, remanufactured, recycled, or recovered and thus maintained in the economy for as long as possible. Waste generation is avoided or minimised, and greenhouse gas emissions are prevented or reduced.[1]

In recent years, the unintended negative impact of healthcare on the environment – and thus on human health – has gained attention.[2] Implementing circular economy principles can help tackle the healthcare industry's waste generation and make its procurement policies more sustainable.[3]

In this issue, Crofter co-section editor Louisa Ludwig-Begall shares her experience as part of a research team that developed a low-tech, low-cost, low-energy method for decontaminating single-use face masks and respirators.

Louisa's article briefly touches on an important tool in environmental impact research – the Life Cycle Assessment (LCA), a top-to-bottom analysis of the environmental impact of a given product throughout its entire "life". To illustrate the complexities and benefits of LCAs, Sofia Polcowñuk from the EMWA graphics team and co-section editor Sarah Kabani have created an amazing LCA infographic. This is an essential resource for medical writers working in sustainability. We recommend keeping it handy for future reference!

Best, Louisa and Sarah

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The virologists in the reusable masks

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doi: 10.56012/fusu7803

Introduction

Everyone in the Sustainability Special Interest Group (SUS-SIG) has a different story of what first sparked their interest in sustainability. My story involves a pandemic.

Recent history has seen a steady rise of throwaway culture within the healthcare sector, and disposable healthcare consumables have progressively replaced reusable staples since the 1960s.[1–3] This evolution went largely unremarked or may even have been feted by harassed healthcare professionals who no longer needed to bother sterilising much of their kit: don, doff, discard, done.

However, as the COVID-19 pandemic accelerated in 2020, it unmasked the unsustainable nature of such a generalised single-use-only approach. In early 2020, the global demand for personal protective equipment (PPE) far exceeded manufacturing capacities: the World Health Organization (WHO) anticipated a global monthly requirement of 89 million masks, 76 million gloves, and 1.6 million goggles.[4]

To combat critical shortages, the WHO issued interim guidance on PPE rationing and recommended PPE reuse in March 2020.[5] On the face of it (pun intended), a measure to augment the availability of surgical masks and respirators during the COVID-19 crisis, this call heralded an important step towards a more sustainable circular healthcare economy. It also galvanised virologists worldwide into action, since, if an item of PPE is to be safely reused, it must first be decontaminated, i.e., rid of such dangerous germs as SARS-CoV-2, the virus that causes COVID-19.

At the time, I was part of a team of virologists at the University of Liège in Belgium. Ours was one of many groups to begin trialling PPE decontamination techniques. In delving deeper into the subject matter, we increasingly prioritised sustainable and equitable methods of readying masks and respirators for reuse beyond the immediate emergency. We had been drawn to sustainability by some worrying trends.

The unsustainable face of disposable masks and respirators

The carbon footprint of a single mask has been calculated in life cycle analyses (which take into account greenhouse gas emissions from production to disposal) to lie between 32.7g – 65.5g of CO_2 equivalents per item.[6–9] The total global warming potential of all disposable surgical masks supplied in a single year of the COVID-19 pandemic has been calculated as 1.1 megatons of CO_2 equivalents.[10]

Incorrect disposal poses an additional environmental burden. Since the beginning of the pandemic, discarded single-use items have led to widespread environmental pollution [11,12] and a "shadow pandemic" of plastic PPE rubbish.[13] In 2020 alone, an astounding 1.56 billion surgical masks were reported to have entered the world's oceans.[14] There, they degrade into micro- and nano-plastics, leach toxic heavy metals, and pose significant dangers to flora and fauna.[15]

Finding masks or respirators in unusual places is now unfortunately commonplace. I have found masks in soggy little piles amongst the cobbles of my hometown, garlanding the hedgerows of the

surrounding countryside, and – most bizarre of all – secreted under a rock on a mountaintop.

Meanwhile, depending on the reprocessing method used, reusing a mask or respirator reduces its carbon footprint by 58%–85%[6,8] and may help alleviate the burden of illegal – if often inventive – PPE fly-tipping.

Rendering masks and respirators reusable

Rendering a SARS-CoV-2-contaminated mask or respirator reusable requires prior decontamination. Figuring out what decontamination technique gets the job done requires a virologist (or rather a whole lot of virologists). Early in the pandemic, little was known of SARS-CoV-2, and even tried and tested techniques had to be re-tested against this new foe.

Tried and tested techniques

We initially trialled fairly traditional methods of ridding items of infectious viruses: we baked artificially contaminated masks and respirators in an oven (dry heat decontamination), exposed them to UV light (germicidal irradiation), and steamed them with bleach (hydrogen peroxide vaporisation). All these methods successfully inactivated not only a porcine coronavirus (standing in for its more dangerous relative SARS-CoV-2) but also a norovirus, the *bête noire* of all those attempting decontamination.[16,17] Noroviruses are notorious for their hardiness, and it is a fairly safe bet that any treatment able to inactivate one of their ilk will make short work of most other viruses.

Baked, irradiated, and oxidised – perhaps those viruses never stood a chance. But what of the hapless PPE simultaneously being exposed to these aggressive treatments? A disintegrated mask is no more useful than a contaminated one. To make sure the PPE was able to resist the onslaught, we teamed up with textile researchers who performed breathability and filtration efficiency tests; these showed that even thrice-decontaminated masks and respirators allowed wearers to breathe easily and protected them from airborne pathogens.[18] This was excellent news for all three traditional methods.

However, depending on both expensive equipment and a stable energy supply, traditional decontamination methods are costly and may not be feasible in low-resource settings. Electricity remains unavailable to nearly 16% of the world population and electricity prices have fluctuated greatly in recent years.[19] Equitable and *truly* sustainable PPE decontamination must be cheap and energy-independent.

Back to the future

In 2020, our team thus joined an interdisciplinary consortium of researchers pioneering a novel low-tech, low-cost, low-energy PPE decontamination technique. Supported by the WHO and the research and grantmaking foundation Open Philanthropy, this group united researchers from academia and industry to study antimicrobial photodynamic inactivation (aPDI). aPDI combines light with colourants (photosensitisers) to rout germs. The colourants transfer energy from light to oxygen in the air, thereby generating reactive singlet oxygen. Singlet oxygen, in turn, inactivates viruses and other pathogens by breaking apart their chemical bonds.[20] From the photosensitiser paintbox, the team chose methylene blue. Both a venerable textile dye used since the 1870s and a WHO-listed essential drug,[21] it was time for methylene blue to show its mettle: was it also a decontaminant?

The decontamination procedure itself was simple: we sprayed contaminated masks and respirators with a methylene blue solution and exposed them to light for half an hour. One gram of methylene blue is enough to spray over 3000 masks or respirators, so that a single item can be decontaminated for less than €0.01. Initially, the light was generated in custom-built LED light boxes, but we later found that sunlight does the job just as well. In fact, aPDI efficiently decontaminated our PPE even when the light emanated from a cloud-shrouded sun on an overcast day[22–24] – we had plenty of opportunity to test this in Belgium in 2022! After three years of research, we had found a near-energy-independent way to decontaminate masks and respirators.

Research into aPDI PPE decontamination continues.[25] I, however, have hung up my lab coat. After the conclusion of my postdoc in 2023, I pursued my dream of becoming a medical writer. I went to my first ever EMWA conference in Prague and, at the conference dinner, told this story to SUS- SIG members…

Lessons learned – sustainability for medical writers

I am convinced that the various decontamination projects and – in a wider sense – working in the field of sustainability helped prepare me for the challenges of medical writing. Acting throughout as the team's unofficial medical writer, I learned to tackle and write about new, hitherto unfamiliar, topics. Working with interdisciplinary and international teams was an object lesson in adapting your message to your audience. Sustainability ties many disciplines together; this opened up new collaborations with other teams, new funding options, and new journals to publish in – an excellent way to broaden a writing portfolio. Finally, I met a fantastic group of sustainability enthusiasts and continue to learn more about sustainability and medical writing from them.

I am sharing this experience in the hope that it may embolden other medical writers to explore sustainability. Perhaps someone reading this article will join the SUS-SIG and share their origin story.

Acknowledgements

I am grateful to all my colleagues at the University of Liège and beyond for their support during our interdisciplinary decontamination adventure. I would like to thank Sarah Kabani and Kimi Uegaki for encouraging me to write up my story, and Kimi Uegaki and Stephen Gilliver for their valuable input in developing this article.

Disclaimers

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

Disclosures and conflicts of interest

The author declares no conflicts of interest.

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Life Cycle Assessment (LCA)

LCAs are powerful tools in healthcare sustainability research, assessing the environmental impact of products such as medications and medical devices. They can take a "cradle-to-grave" approach considering every step of the manufacturing, use, and disposal.

Use of LCAs in healthcare

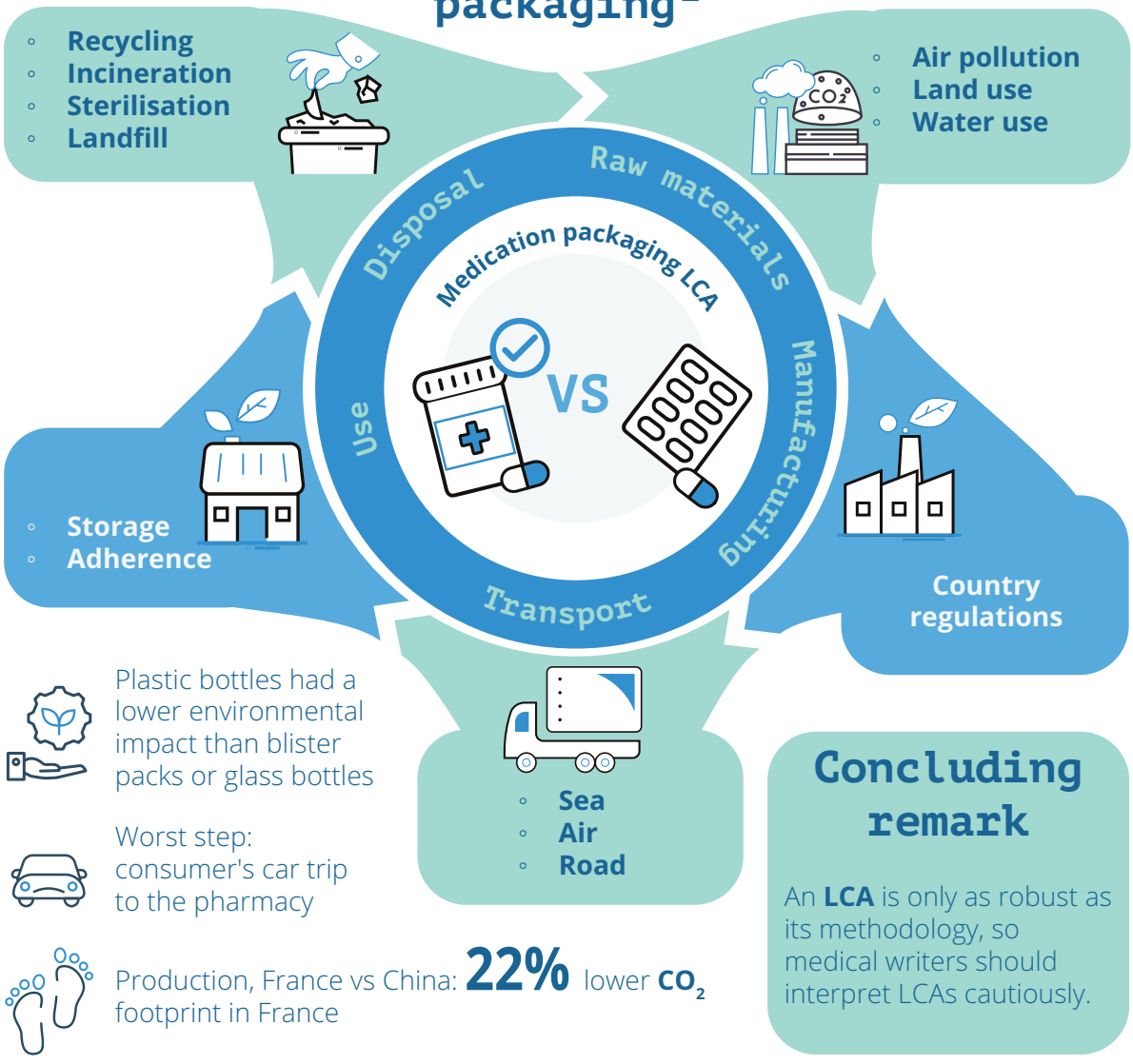
Comparing products

- Reusable vs. single use
- Different packaging
- Different sterilisation processes

Weaknesses of LCAs

- Need extensive data
- Suppliers often reluctant to share information
- Rely on assumptions – remedy with sensitivity analysis
- Rapidly become outdated

Example LCA: Comparing medication packaging[1]



Plastic bottles had a lower environmental impact than blister packs or glass bottles

Worst step: consumer's car trip to the pharmacy

Production, France vs China: **22%** lower CO_2 footprint in France

Concluding remark

An **LCA** is only as robust as its methodology, so medical writers should interpret LCAs cautiously.

Sofia Polcowñuk@@SketchLab

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Good Writing Practice

Results section of a journal article

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Introduction

In the sequence of journal article writing, the Results section is third after Title (the shortest) and Methods (uncomplicated chronologic order). This sequence is directed to graduate students familiar with a research project. To start, the sequence is focused on one set of data for which pertinent methods were written. As additional sets of data and their pertinent methods are written, the whole journal article will take shape guided by the following Results section-specific conceptional components:

1. Context re-orientation,
2. Data presentation, and
3. Result statement + data-based preliminary interpretation.

There are two further considerations when writing the Results section:

4. Tense, and
5. Premature inference.

1. Context re-orientation

Context re-orientation can be expressed minimally as a subheading and a sentence. Such re-orientation enables the Results section to be self-sufficient, minimising the necessity to reread the Introduction and Methods section.

Example
Relative Molecular Weight Determination
To determine the relative molecular weights of proteins A and B in order to ascertain their structural relation, the purified proteins ***were*** *electrophoresed on polyacrylamide.*

2. Data presentation

A table or figure is usually the focus of the Results section. Thus, excessive repetition of the data as data verbalisation is verbose and unsophisticated to an insightful reader, who would view the repetition as a ploy to increase (pad) article length.

Example
The movement of protein A ***corresponded*** *to a marker with a molecular weight twice that of protein B (Fig. 3).*

3. Result statement plus data-based preliminary interpretation

Results are data-based observations, trends, comparisons.

As shown by electrophoresis (Fig. 3), the molecular weight of protein A ***was*** *twice that of protein B,* ***an observation consistent with protein A as a dimer of protein B****.*

4. Tense

Being a retrospective, the tense in a journal article is primarily past which conventionally conveys an observation of past information, not a current observation of the visual (graphical) data. Also, the past tense conveys understatement. *Something was* as opposed to the time-independent, over-stated truism *something is*.

5. Controversial inference of data-based preliminary interpretation

Placing preliminary interpretation statements in the Results section is controversial because of a resemblance to Discussion section components. However, the Discussion extends the Results into the following four types of paragraphs: conclusions-support, limitation – counterargument, recommended future research, and conclusion-consequence – all of which are based on already expressed result statements in the Results section. Not one of these conceptual paragraphs appears in the Results section.

Conclusion

Each component of the Results section should be oriented to the relevant Method description. Data presented in tables and figures conveys more information than descriptive text, which should be used for observations – not data repetition.

CONTACT US

If you have ideas for themes or would like to discuss any other issues, please write to mew@emwa.org.

Upcoming issues of **Medical Writing**

December 2024:

Medical Writing Around the World

Medical writing transcends geography, demography, language, and culture. To date, EMWA has over 1400 members from 48 countries on 6 continents, and we want to celebrate the diversity and global presence of the medical writing community. In this issue, we will focus on medical writing activities around the world and will delve into topics like the benefits of having geographically diverse teams, translation and language-specific challenges, the landscape of global freelance medical writing, etc. We hope that these insights will assist the medical writing community in strengthening interactions and collaboration with teams and freelancers spread across the world.

Guest Editors: Asha Liju and Evguenia Alechine
The deadline for feature articles has now passed.

March 2025:

Rare Diseases

Although rare diseases are individually uncommon, there are more than 7000 rare ("orphan") diseases affecting around 300 million people globally. Rare diseases are incredibly diverse and often life-threatening. Long diagnostic delays, termed a diagnostic "odyssey", are common, and many have no effective treatments. Rare diseases offer unique challenges and opportunities that are not seen in other therapeutic areas.

This issue of *Medical Writing* spotlights the evolving regulatory landscape, the nuances of unmet medical needs, the importance of the patient voice, and the key role of medical writers in the orphan disease space.

Guest Editors: Sarah Milner and Heather Mason
The deadline for feature articles is December 1, 2024.

June 2025:

Communicating with the Public

When we communicate effectively with patients and the public, we empower them to make informed decisions about their health. This issue will cover the latest guidelines and standards to be considered when writing and designing information for patients and the public. It will also feature articles from thought leaders on plain language writing, inclusive communication, and patient involvement in research. With this issue, we hope to provide insights that will strengthen the role of medical writers as advocates for the patient voice, and as powerful and effective communicators of understandable science.

Guest Editors: Sampoorna Rappaz and Lisa Chamberlain James
The deadline for feature articles is March 1, 2025.

http://journal.emwa.org/