

Regulatory Public Disclosure

SECTION EDITOR



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Editorial

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

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

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

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

Kind regards,
Sam

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

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

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

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

Tracy confirmed that with the fast changing environment of RPD, CORE Reference can also act as a useful resource. Within this user manual

guidance information is provided to help medical writers navigate public disclosure “hotspots” (<http://www.core-reference.org/>). Sam confirmed that CORE Reference is a “living document” and she is gathering information affecting CORE Reference such as disclosure references including the FDA pilot scheme and Health Canada guidance.

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

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



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

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

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

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

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

A request was made to provide a bullet point summary of Policy 0070 content. Discussions determined that as data anonymisation is a complex and new area for medical writers it will require some changes in working practices, as well as the development of new processes. If a medical writer is involved in this area they must become familiar with the practical aspects of data anonymisation. The EPDP offers several workshops to support medical writers with this topic. To develop processes addressing Policy 0070

requirements, there is a need for individuals to become knowledgeable about the relevant guidance and other associated supporting information to enable appropriate processes to be developed. It was thought that Policy 0070 requirements could not be summarised in a bulleted format. However, there was a request for a simple decision tree, or flow chart-type of representation of disclosure for clinical trials and

this will be investigated further.

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

Status updates ... from the regulators

Canada and the US

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

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

The first published clinical study report (pivotal study report for Erleada: https://www.accessdata.fda.gov/zdrugsatfda_docs/nda/2018/Erleada_210951_toc.cfm) does not have the names of sponsor staff, including the names of medical writers, redacted, but does have the details for local sponsors redacted; does have selected formulation and other product-related information redacted; has sensitive information in patient narratives redacted; does have site ID, subject ID, date of death redacted from death listings; and does have site ID, subject ID, assessment date redacted from abnormal laboratory and other similar listings.

Europe

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

EMA Brexit preparedness (http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2018/08/news_detail_002999.jsp&mid=WC0b01ac058004d5c1) is impacting broadly across EMA activities and this will specifically impact clinical data publication “...for which the launch of new procedures will be temporarily suspended as of August 1, 2018; data packages submitted for medicines until the end of July 2018 will be processed and finalised”.

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

... from peer-review journal editors

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

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

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

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

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

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

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References

1. Cuadrado Lafoz M, Ramirez-Soriano A, Richardson S. Anonymisation: A new challenge for medical writers. *Med Writ.* 2018;27(3):31–6.
2. Billiones R. Anonymisation reports from 2016 to 2017: A preliminary analysis. *Med Writ.* 2018;27(2):22–6.



CORE Reference

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

EMWA workshops on regulatory public disclosure and disclosed clinical documents

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

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

Resources

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

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

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

TransCelerate’s Common Protocol Template. Protocols are disclosed clinical documents. If you are using TransCelerate’s December 2017 version (current) of their Common Protocol Template, (<http://www.transceleratebiopharmainc.com/assets/common-protocol-template/>), remember to consider including “estimand” in your protocol. Estimand is explained in ICH E9(R1), which is currently at Step 2 (draft guidance). http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E9/E9R1EWG_Step2_Guideline_2017_0616.pdf.

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

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