Regulatory Public Disclosure

Editorial

Regulatory public disclosure (RPD) is the subject of this regular MEW section, and EMWA's RPD Special Interest Group (SIG) – together, we help you develop your understanding and maintain your knowledge.

In the EMA region, we find ourselves in a lull with clinical data publication, ostensibly because EMA is focussing on their relocation from London to Amsterdam. By the end of October 2018, EMA had published all submitted clinical data, had cancelled new submissions due after August 1, 2018, and had suspended all new activities relating to the publication of clinical data. There is no timetable for the lifting of this suspension. EMA's web page "Support for industry on clinical data publication" (https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/clinical-data-publication/support-industry-clinical-data-publication) is a valuable resource – check it regularly. In Q4 2018, I asked EMA if they could confirm if submissions made between Aug 2, 2018, and the (future) date of the lifting of the suspension - will or will not be subject to retrospective publication? EMA responded: "EMA is only processing applications adopted by CHMP up to the first quarter of 2017 and which were submitted to the Agency by July 31, 2018, (upon receipt of an Invitation letter). We cannot currently comment on how the process will be resumed and whether clinical data will be published retrospectively. EMA will contact concerned applicants/MAHs prior to the restart of clinical data publication, once its relocation to Amsterdam is completed. We appreciate any preparatory work done by companies regarding their upcoming CDP package submissions, however, and EMA is asking companies simply to pause any ongoing work until further notice."

When the suspension is lifted, Policy 0070 implementation guidance Version 1.4 dated October 15, 2018 (https://www.ema.europa.eu/documents/regulatory-procedural-guideline/external-guidance-implementation-european-medicines-agency-policy-publication-clinical-data_en-3.pdf) will apply. As we need to be working towards this latest guidance, I summarise the changes from Version 1.3 below. I also spotlight EMA's first report on the Policy 0070 publication of clinical data, and in particular the commercially confidential information (CCI) redacted and the anonymisation techniques used. In doing so, I hope to help you carefully consider CCI presentations in your documents.

Our feature article this quarter, brought to us by Hiroko Ebina and Jocelyn Coquhoun of Envision Pharma Group, is a status update about the growing awareness of the clinical trial disclosure landscape in Japan (see page 74). The authors describe current disclosures and commitments to clinical trial data sharing in Japan, and explain the effect of the Common Technical Document on CSRs used for Japanese New Drug Applications. In short, understanding in Japan of the importance of preparing disclosure-ready CSRs to meet global requirements is growing.

The developers of CORE Reference are pleased that the developers of the TransCelerate clinical study report (CSR) template used CORE Reference and ICH E3 extensively during their template development process. Read the CORE Reference Press Release about this (https://www.core-reference.org/news-summaries/core-reference-statement-on-transcelerate-csr-template/), which includes links to all relevant materials.

In many ways, EMA's lull in clinical data publication allows time to reflect, fine-tune our disclosure processes, and consider what we would like to improve upon – in time for the lifting of the suspension.

Please continue to approach me with your articles and tips to optimise disclosure writing. I will continue to information share via this MEW regular section, through www.core-reference.org emails (sign up at: http://www.core-reference.org/subscribe), and through EMWA News Blasts.

Sam

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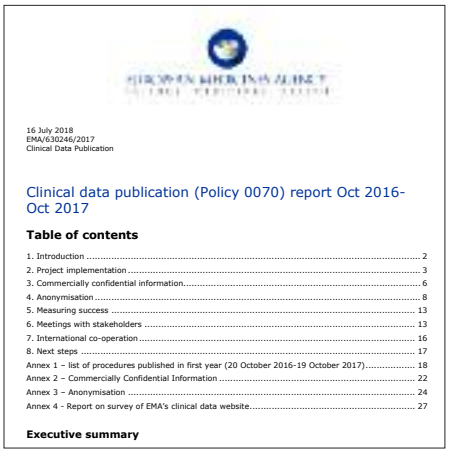
Commercially confidential information in clinical reports

EMA published their first report on the Policy 0070 publication of clinical data (July 16, 2018): https://www.ema.europa.eu/documents/report/clinical-data-publication-policy-0070-report-oct-2016-oct-2017_en.pdf. Over the period October 2016 to October 2017, EMA's report provides information on the total number of documents published, the amount of commercially confidential information (CCI) redacted and the anonymisation techniques used.

By gaining understanding about the types of information that might be accepted for redaction in clinical documents under the auspices of CCI, we can better judge the types of CCI that if included in our reports, might reasonably be expected to be accepted for redaction. Annex 2 of EMA's report reveals that a quarter of CCI proposals made by applicants were accepted by EMA, hence redaction of that information was allowed. All accepted CCI was related to pharmaceutical development; reasons for acceptance of CCI were broadly categorised as "Quality" (49 instances accepted) and "Clinical" (60 instances accepted). Detailed reasons for CCI acceptance within these two broad categories are illustrated in EMA's report (Figures 1 and 2).



16 July 2018
EMA/630246/2017
Clinical Data Publication

Clinical data publication (Policy 0070) report Oct 2016-Oct 2017

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Executive summary

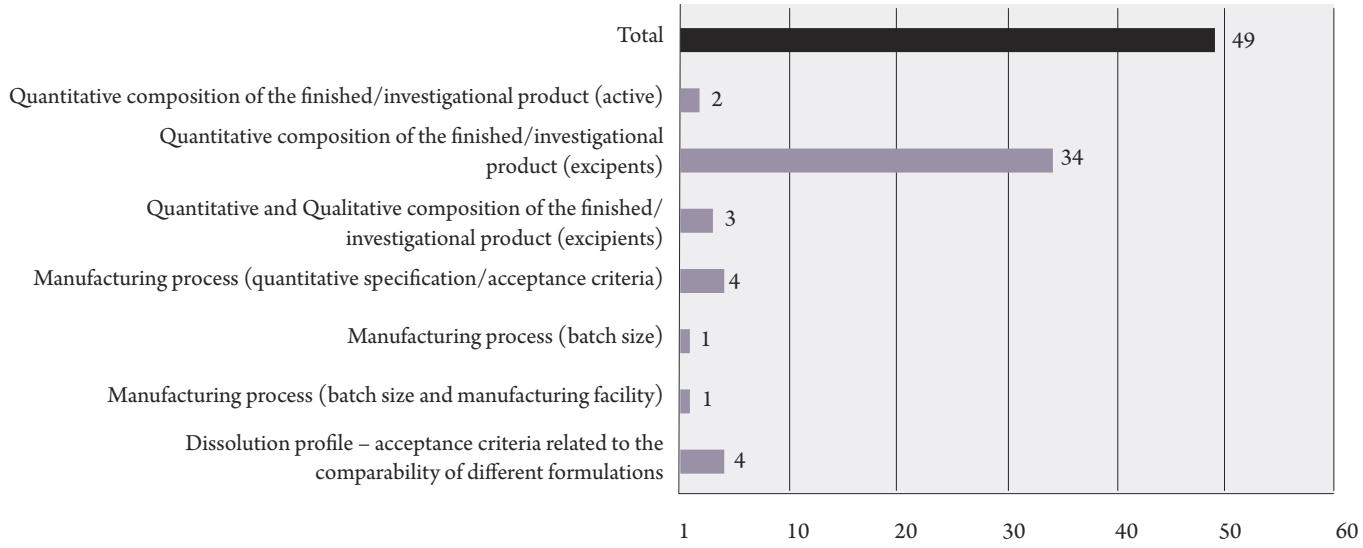

Figure 1. Quality CCI accepted – pharmaceutical development – detailed reasons

Source: European Medicines Agency. Clinical data publication (Policy 0070) report Oct 2016-Oct 2017. Annex 2, Figure 12
https://www.ema.europa.eu/documents/report/clinical-data-publication-policy-0070-report-oct-2016-oct-2017_en.pdf

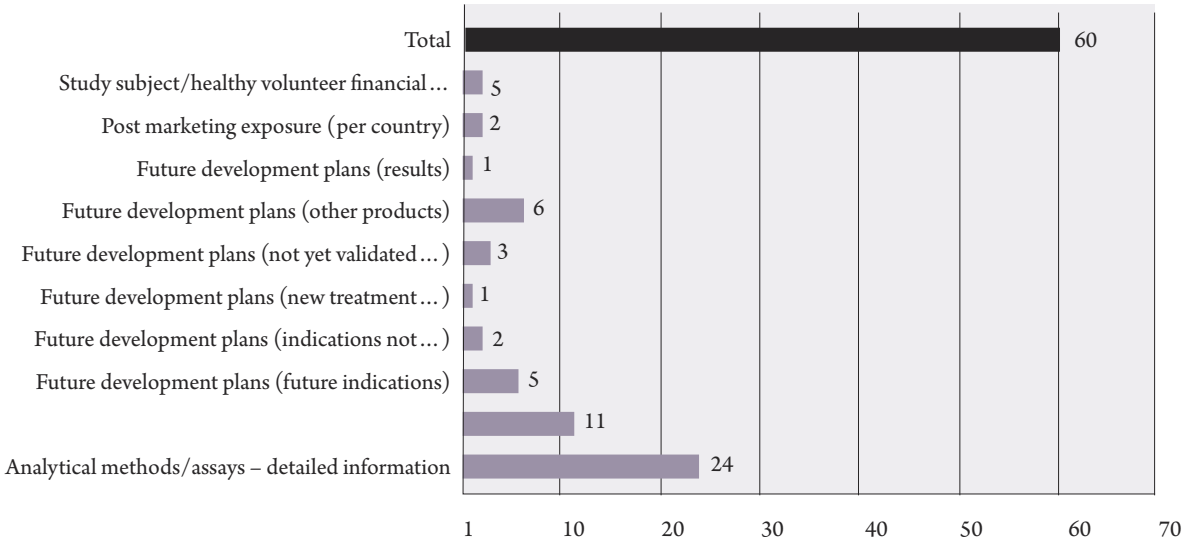

Figure 2. Clinical CCI accepted – detailed reasons

Source: European Medicines Agency Clinical data publication (Policy 0070) report Oct 2016 - Oct 2017. Annex 2, Figure 13
https://www.ema.europa.eu/documents/report/clinical-data-publication-policy-0070-report-oct-2016-oct-2017_en.pdf

CORE Reference

Read our Press Release on TransCelerate's CSR template and use of CORE Reference in its development: (https://www.core-reference.org/news-summaries/core-reference-statement-on- transcelerate-csr-template/)

CORE Reference (available for download from http://www.core-reference.org/core-reference/) identifies each point in an ICH E3-compliant CSR where anonymisation considerations should apply. Downloads stand at 17,000+ (March 2019).

CORE Reference has a News Summaries page: https://www.core-reference.org/news-summaries where relevant regulatory and disclosure news is posted periodically. Stay one step ahead and receive these updates in "real time" by signing up at: http://www.core-reference. org/subscribe.

Summary of Changes – EMA Policy 0070 Implementation Guidance Version 1.4

The following major changes to guidance are effective when clinical data publication by the EMA resumes:

1. Clarification has been provided on the publication of withdrawn applications in cases where the application has been re- submitted or has an agreed re-submission date
2. Clarification has been added on the publication of clinical studies where the main period/phase of a clinical study is still ongoing at the time of publication
3. Timetable of the main steps of the end-to-end process for the publication of clinical reports has been added
4. Wording has been added to reflect the review of the anonymisation report that takes place during the consultation phase
5. Wording has been added on the potential need to submit an updated anonymisation report and/or written responses to the comments transmitted by EMA on the anonymisation report before the submission of the Final Redacted Document package
6. Wording has been added flagging the availability of a checklist to assist applicants/ marketing authorisation holders with the preparation of the Final Redacted Document package
7. Template paragraphs and use instructions within the cover letter regarding studies already published previously under Policy 0070 have been included
8. In addition to the checklist for the Redaction Proposal Document package, a new checklist for the Final Redacted Document package has been added.

Several minor changes are also detailed. For EMA's complete Summary of Change document, see https://www.ema.europa.eu/documents/other/summary-changes-external-guidance-implementation-european-medicines-agency-policy-publication_en-2.pdf.

Status Updates – from Regulatory Regions

Europe

1. Clinical data disclosure is suspended until further notice from EMA. Check EMA's web page 'Support for industry on clinical data publication' (https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/ clinical-data-publication/support-industry-clinical-data-publication) regularly
2. On 04 Dec 2018, EMA published a 32-page data anonymisation workshop report (https://www.ema.europa.eu/documents/report/report-data-anonymisation-key-enabler-clinical-data-sharing_en.pdf) on the 30 Nov – 01 Dec 18 workshop "Data anonymisation – a key enabler for clinical data sharing" held jointly between EMA and the US-based Multi Regional Clinical Trials Center covering:

- The global landscape for clinical data sharing
- The foundations of data anonymisation
- The mechanics of anonymisation – meeting the challenge of different types of data
- Balancing access and data utility
- Future challenges for data anonymisation.

Canada

The Health Canada regulation on public access to clinical information on drugs and medical devices will finally be published on March 20, 2019. Press release: https://www.canada.ca/en/health-canada/news/2019/03/health-canada-finalizes-regulations-to-provide-public-access-to-clinical-information-on-drugs-and-medical-devices.html

– from the Journals

Hendrick Schmidt and Boehringer Ingelheim (BI) colleagues wrote a collaborative 'Corre-spondence' piece in the New England Journal of Medicine with the University of Basel. The article titled "An Industry Experience with Data Sharing" (https://www.nejm.org/ doi/full/10.1056/NEJMc1805610) describes BI's experience – as a member sponsor – in listing studies on https:// ClinicalStudyDataRequest.com

Resources

1. Visit the RPD SIG members' page: https://www.emwa.org/members/special-interest-groups/regulatory-public-disclosure-sig/ and the subpage for disclosure-related regulatory news updates: https://www.emwa.org/members/special-interest-groups/regulatory-public-disclosure-sig/regulatory-news-emwa-newsblast/.
2. "Anonymizing Health Data: Case Studies and Methods to Get You Started" by Khaled El Emam and Luk Arbuckle, ISBN number 978-1-449-36307-9, is available as an eBook. Précis: "Updated as of August 2014, this practical book will demonstrate proven methods for anonymizing health data to help your organization share meaningful datasets, without exposing patient identity. Leading experts Khaled El Emam and Luk Arbuckle walk you through a risk-based methodology, using case studies from their efforts to de-identify hundreds of datasets."
3. "Guide to the De-identification of Personal Health Information" by Khaled El Emam, ISBN number 978-1-4665-7906-4, is available as an eBook. Précis: "Offering compelling practical and legal reasons why de-identification should be one of the main approaches to protecting patients' privacy, the Guide to the De-Identification of Personal Health Information outlines a proven, risk-based methodology for the de-identification of sensitive health information. It situates and contextualizes this risk-based methodology and provides a general overview of its steps."