Regulatory Public Disclosure

Editorial

Activities around clinical documents disclosure have been slow since September 2018 when I last published this section. As many of you receive emails from the CORE Reference website (sign up at https://www.core-reference.org/subscribe), you have been able to keep up with interim developments. This same information is regularly archived at: https://www.core-reference.org/news-summaries/ and https://www.emwa.org/sigs/regulatory-public-disclosure-sig/ and comes to you in the monthly EMWA Newsblasts, so you have been well supported via multiple open communication channels.

Broadly, the status quo remains… The three main regulators in the ICH family contributing to the disclosure narrative hold completely different positions at present:

A. EMA continues to hold clinical data publication activities (https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/clinical-data-publication/support-industry-clinical-data-publication). There is no indication of when activities may resume, or if public disclosure will apply retrospectively to documents, if or when activities resume. For this reason, we are best advised to maintain our awareness and continue to write our clinical documents in proactively anonymised fashion.
B. Health Canada is actively disclosing clinical documents (https://clinical-information.canada.ca/search/ci-rc) with guidance broadly similar to that of EMA (https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/profile-public-release-clinical-information-guidance/document.html), but with regulators discouraging redaction in favour of proactive authoring (qualitative anonymisation) and ultimately quantitative anonymisation methods
C. FDA is considering its options. After soliciting opinion on how FDA might best support disclosure of clinical documents (https://www.regulations.gov/docketBrowser?rpp=25&so=DESC&sb=commentDueDate&po=0&dct=PS&D=FDA-2019-N-2012) and announcing the conclusion of its Clinical Data Summary Pilot in March 2020 (https://www.fda.gov/news-events/press-announcements/fda-continues-support-transparency-and-collaboration-drug-approval-process-clinical-data-summary?utm_campaign=032620_PR_FDA%20Supports%20Collaboration%20as%20Data%20Summary%20Pilot%20Concludes&utm_medium=email&utm_source=Eloqua), FDA is not currently disclosing clinical documents but has identified a possible approach for disclosing study reports, the framework of which includes the following principles:
    - A centralised international library managed by an independent body would be set up where information is made available to the public, rather than each regulatory authority having its own system
    - An on-demand system would be set up where some documents, e.g., clinical summaries, index of study reports, would be automatically published. The public could request documents and the sponsors would add them to the library
    - Anonymisation and disclosure standards would apply; PHUSE standards are particularly mentioned (https://www.phusewiki.org/wiki/index.php?title=Data_ Transparency)
    - Sponsor commitment to use the international library system would be voluntary.

The trend of the pharmaceutical industry being better at posting summary clinical trial results to public registries than other sections of the clinical trial community continues (https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(19)33220-9.pdf).

Art Gertel (CORE Reference Strategist) and I had planned to present this topic at the cancelled EMWA Conference in Prague planned for May 2020. Due to its time-sensitive nature we have made our slide deck available as an educational resource at: https://www.core-reference.org/publications/

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Other news in brief

CORE Reference

In August 2019, the CORE Reference development team (Budapest Working Group, BWG) published a paper titled: **Critical review of the TransCelerate Template for clinical study reports (CSRs) and publication of Version 2 of the CORE Reference (Clarity and Openness in Reporting: E3-based) Terminology Table** (http://dx.doi.org/ 10.1186/s41073 - 019-0075-5). Our paper includes a detailed assessment of TransCelerate's November 18 CSR template in the form of an "additional file" comprising a 44-page replica of their template marked up with our 69 consolidated comments.

In December 2019, TransCelerate released updated versions of their CSR template and SAP template (referred to as "assets"). These new assets and supporting resources reside at a **new page location** (https://transceleratebiopharmainc.com/assets/clinical-content-reuse-assets/). This relocation of assets has taken place since the publication of our paper. To download the assets, you need to complete an online form.

The December 2019 TransCelerate CSR template is supported by a slide deck titled "Summary of Changes in 2019 Release". This 40-slide deck includes a rationale for each change. From Slide 25 or thereabouts, the rationale for change frequently includes "Feedback from CORE review" or "CORE feedback". TransCelerate notes that this new release brings their template into "alignment with CORE"; however, there are no specifics provided as to how comprehensively the CORE feedback was addressed and incorporated.

TransCelerate have not made any contact with the BWG. The BWG have not reviewed the December 2019 TransCelerate CSR template.

Art Gertel and I had planned to present this topic in May 2020 at the EMWA Conference in Prague that was cancelled. Due to its time-sensitive nature we have made our slide deck available as an educational resource at: https://www.core-reference.org/ publications/

Resources

Two excellent white papers:

- https://cdn2.hubspot.net/hubfs/200783/PC20257%20Clinical%20Data%20Disclosure%202020/Managing%20Privacy%20Risk%20in%20Data%20and%20Document%20Sharing.pdf
  This is a white paper from experts at Astrazeneca and d-wise gets to the nub of what medical writers need to understand around proactive anonymisation of data and documents, and is a great summary of what many of us have been discussing for some years now. In their own words, the authors address: "How should sponsors manage data they share considering what's already been shared? What techniques exist to support sponsors in navigating the reality of human error and the limits of technology?" There are some good screenshots of anonymised and redacted data and documents towards the end of the document.
- https://www.d-wise.com/white-papers/preparing-clinical-study-reports-for-external-sharing?utm_campaign=%5Bobject%20Object%5D%20Transparency-CBI&utm_source=hs_email&utm_medium=email&utm_content=82865504&_hsenc=p2ANqtz—v6Sex-ip2pz9n8murNSD4_pfwcYNoTvViOr EUzKWYSEojKl6EwrPW2P1WKlBbueX4B8gdBhr8x7OdL_UlOPG777QKyNIj49Xf5lY-pyS1aFX2rfo&_hsmi =82865504
  At a recent CBI Clinical Data Disclosure, Transparency & Plain Language Summaries event: "Sharing to Power Innovation", Cathal Gallagher (EMA TAG member) outlined the necessary steps for internal and external sharing in his presentation and white paper, "Preparing CSRs for external sharing". This excellent summary gets to the nub of why industry need to better support medical writers with CSR proactive anonymisation. Also read Cathal's interview with me (on page 58).

Data transparency workshop

On November 11, 2019, a data transparency workshop with EMA was held in Amsterdam as part of the PHUSE EU Connect 2019 event. The event was led by Jean-Marc Ferran of the PHUSE Data Transparency Working Group and EMA representative Anne-Sophie Henry-Eude. They were joined by several TAG members to address questions during the Q&A panel session.

Key topics discussed during the workshop included:

- EMA Policy 0070 Phase 1 and handling of the backlog
- EMA Policy 0070 Phase 2
- EMA – Health Canada Collaboration in data transparency.

Jean-Marc provided a summary of the workshop to the PHUSE community via a webinar on November 20, 2019. View the recording at https://www.youtube.com/watch?v=eQGyL 4SI1K0 (approximately 11 to 25 minutes).

The slides are available here: https://www.phusewiki.org/docs/Working Groups/Webinar/November%202019/EUCon19%20-%20DT%20 Workshop%20-%20Webinar%20Slides%20 -%20v000b.pdf

Recent events impacting transparency and disclosure

EUDAMED delay and the impact on devices transparency

In an article for the Regulatory Affairs Professional Society, Raquel Billiones reviews possible ramifications caused by the delay in launching the European Union's new electronic database, the European Database on Medical Devices (EUDAMED). The article is available at https://www.raps.org/ news-and-articles/news-articles/2020/4/ eudameds-delay-what-happens-to-transparency-for-cl.

COVID-19 impact on clinical trial disclosure and transparency

Regulatory authorities have released guidance documents focusing on the impacts of the COVID-19 pandemic on study start-up activities, changes to ongoing study procedures, and items considered urgent safety matters during this pandemic. This PHUSE blog (https://www.phuse.eu/blog/the-impacts-of-covid-19-on-clinical-trial-transparency-and-document-disclosure-phuse-ctt-project) considers the impacts of COVID-19 on clinical study disclosure and transparency, offering guidance from industry experts on what may require immediate action, as well as consideration of future implications

Health Canada issues notices of nonconformance

In recent months, HC placed identical notices on submissions packages from Lilly, Novartis, Seattle Genetics and Gilead which state that in respect of CSR narratives there are "…extensive redactions to the patient information... redactions do not conform to HC guidance which encourages... other transformation methods…"

Read the full Lilly notice here as an example: https://clinical-information.canada.ca/ci-rc-vu.pdf?file=m1/ca/HC%20STATEMENT%20REDACTED%20PATIENT%20INFORMAOIN%20ENFR.pdf&id=128554

Without a change from retrospective redaction to the proactively anonymised authoring of CSR narratives that is actively encouraged in CORE Reference, we can surely expect to see similar notices on future submissions.