Regulatory Public Disclosure

Editorial

Keeping up with regulatory public disclosure (RPD) globally is a challenge for us all. This regular RPD section of *Medical Writing* and EMWA's RPD Special Interest Group (SIG) help you stay ahead of the game through information sharing.

Although the EU lull in RPD continues with clinical data publication activities suspended since October 2018 (https://www.ema.europa. eu/en/human-regulatory/marketing-authorisation/clinical-data-publication/ support-industry-clinical-data-publication), RPD activities elsewhere have gained pace.

Health Canada (HC) concluded their "Public Release of Clinical Information" consultation and issued a final regulation with final guidance on March 12, 2019 (see box for links). Broadly, the HC guidance is aligned with EMA Policy 0070 guidance with the intention of streamlining sponsor effort. Clinical information is now publicly available via the HC Clinical Information Portal (see box for link). The portal contains clinical information on a few products from volunteer organisations in advance of the March 12 "in force" date, and afterwards, drug submissions data will be posted as each review is completed. Proactive device data disclosure will start in 2021, aligning with EMA's intended timetable. Further, drug and device data that is already "available on request" will be publicly posted. A MEW open access feature article – a deeper dive into the HC guidance – is planned for the second half of 2019. In the meantime, Christopher Marshallsay neatly summarises the take-home points for us in his short "nutshell guide" to the Health Canada guidance.

Vivli – a platform offering clinical trial data sharing management capability and functionality – is spotlighted by Raquel Billiones. If you know of other such platforms, please be in touch.

This quarter, we are incredibly lucky to have two excellent feature articles. In the first, Sybille Eibert explains the FDA final rule requirements for publication of protocols and statistical analysis plans on ClinicalTrials.gov. Sybille navigates the limited guidance on redaction of personally identifiable information and confidential commercial information prior to publication, and highlights some key questions (p. 81). Our second feature article, brought to us by Raquel Billiones and Kathy Thomas, is a bold challenge to the idea that the drug products and devices worlds are vastly different. The two worlds collide when the Clinical Trial Regulation (CTR) and Medical Device Regulation (MDR) are interrogated in the context of clinical studies and public disclosure (p. 74). The authors tenaciously support the case for medical writers interchanging between the regulatory drug and device arenas.

In March 2019, the Budapest Working Group (BWG) – the developers of CORE Reference – concluded a line-by-line review of the November 2018 TransCelerate clinical study report (CSR) template – i.e., the template that cites CORE Reference and ICH E3 as key developmental resources. Following the BWG's preliminary higher-level review findings (https://www.core-reference.org/news-summaries/core-reference-statement-on-transcelerate-csr-template/), the team submitted a paper describing more detailed

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findings to an open access peer-review journal in May 2019. We hope to have our work published later in 2019. A summary of and link to our article will appear in *Medical Writing*.

Finally, it was a pleasure to meet those of you who came to the RPD SIG meeting at EMWA's May 2019 conference in Vienna. We are delighted to welcome Miriam Kremser who kindly volunteered to join the RPD SIG Committee and help out with resource management. We also discussed ideas that we hope to develop into articles and resources in the coming months. There is an easy way for you to help with written content…if you plan to attend a relevant conference – for example, DIA's December 2019 Clinical Trial Disclosure and Data Transparency Conference (https:// www.diaglobal.org/conference-listing/ meetings/2019/12/clinical-trial-data-transparency-conference) – consider contributing a short article about your conference experience and what you learned.

As usual, relevant clinical trial transparency and disclosure information will be shared via multiple outlets – this regular RPD section, through www.core-reference.org emails (sign up at: http://www.core-reference.org/subscribe), and through EMWA News Blasts.

Kind regards, Sam

A nutshell guide to the Health Canada guidance on public release of clinical information

- Clinical information released for drugs will be:
  - Clinical overviews (M2.5), clinical summaries (M2.7.1 - 2.7.4), and CSRs
  - CSRs = single report with the protocol, sample case report forms, investigator related information, information related to the test drugs/investigational products, technical statistical documentation, related publications, patient data listings, and technical statistical details such as derivations, computations, analyses, and computer output.
- Clinical information released for devices will be:
  - Summaries and detailed information of all clinical studies and investigational testing that provided evidence of safety and effectiveness for medical devices.
- Individual patient records will not be publicly released with other clinical information.
- The publication process has five phases – initiation, submission, review, finalisation, and publication

- Health Canada targets uploading of the redacted and anonymised package within 120 calendar days of process initiation
  - Issuance of the positive regulatory decision triggers the publication process
  - Issuance of negative decision triggers publication 31 calendar days after the date of the notice, but may be halted if a Letter of Intent for Reconsideration is submitted.
- Redacted documents that were previously accepted by EMA Policy 0070 may be submitted.
- Use of the EMA specifications on redacted text are permissible in finalised documents. (See Box for links).

Christopher Marshallsay

An introduction to the vivli.org data sharing platform

Vivli.org is one of a number of platforms offering an alternative to the perhaps more widely known CSDR (clinicalstudydatarequest.com). The National Academy of Medicine recently wrote about the launch of the Vivli platform (https://nam.edu/moving-data-sharing-forward-the-launch-of-the-vivli-platform/).

Vivli hosted a meeting in Tokyo on May 13, 2019, that included roundtable discussion with experts in privacy and transparency of clinical trials on the theme "One Year On: GDPR and Its Implications for Data Disclosure and Data Sharing".

Raquel Billiones

Status updates – from regulatory regions

Canada
Public disclosure guidance and portal:
- Health Canada released final guidance on the "Public Release of Clinical Information": https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/profile-public-release-clinical-information-guidance/document.html.
- Clinical information on drugs and medical devices is publicly available via the HC Clinical Information Portal: https://clinical-information.canada.ca/search/ci-rc
  The HC "Public Release of Clinical Information" consultation is concluded: https://www.canada.ca/en/health-canada/programs/consultation-public-release-clinical-information-drug-submissions-medical-device-applications.html

Europe
1. The role of big data for evaluation and supervision of medicines in the EU is being assessed (https://www.ema.europa.eu/en/news/role-big-data-evaluation-supervision-medicines-eu). Stakeholders are invited to submit feedback and observations on the recommendations to inform the upcoming work of the group.
2. Opinion 3/2019 (January 23, 2019) (https://edpb.europa.eu/sites/edpb/files/files/file1/edpb_opinionctrq_a_final_en.pdf) concerning the "Questions and Answers on the interplay between the Clinical Trials Regulation (CTR) and the General Data Protection regulation (GDPR) (art. 70.1.b))" by the European Data Protection Board is a legal "opinion" that should be shared widely in the clinical research industry, including amongst legal departments. Review of standard Informed Consent Template and Protocol Template texts for appropriate wording is recommended.

United Kingdom
4. In the event of a "no-deal" Brexit, the UK Government's "Guidance on the registration of clinical trials for investigational medicinal products and publication of summary results" (https://www.gov.uk/guidance/guidance-on-registration-of-clinical-trials-for-investigational-medicinal-products-and-

publication-of-summary-results) published March 20, 2019, will become applicable.

This guidance contains information about registration of clinical trials, publishing trial results and future requirements if the UK leaves the EU without a deal. Remember that until the UK's exit from the EU is clearer (date and manner of exit), this guidance represents the UK's preparedness position in the event of a "no deal" only.

4. The UK government has announced that a national clinical trial transparency strategy will be published before the end of 2019. The statement marks a significant step towards ensuring that all clinical trials conducted in Britain will be registered and will publish their results. Read TranspariMED's summary report on the status of the strategy (https://www.transparimed.org/single-post/2019/02/25/UK-government-promises-national-strategy-to-boost-clinical-trial-reporting).

... from the journals

In this IAPP article (https://iapp.org/news/a/does-anonymization-or-de-identification-require-consent-under-the-gdpr/), experts Khalid El Amam and Mike Hintze article, make the case that consent is NOT required to anonymise or de-identify clinical trial data.

CORE Reference

- 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 approach 20,000 (June 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

Resources

1. EMA's invaluable reference to describe their end-to-end process for the journey of a centrally-authorised EMA medicine from lab to patient
https://core-reference.us13.list-manage.com/track/click?u=c2b68d727a3b5cd76327cee23&id=d989b6ae35&e=79858c7e19.
On page 14, there is a great summary titled: "What information is publicly available during the evaluation of a new medicine and once a decision has been made?" complete with relevant web links.

2. Read EMA's EudraCT and EU Clinical Trial Regulation (CTR) Q & A document https://eudract.ema.europa.eu/docs/guidance/EudraCT%20FAQ_for%20publication.pdf
The 32-page long 84 Q & A covers general, protocol, and results information, the EU CTR, and paediatric clinical trial information (protocol and results).

3. PhUSE White Paper (March 14, 2019) titled "Retrospective versus proactive anonymization of narratives": https://www.phusewiki.org/docs/Deliverables/Narratives%20White%20Paper%20Version%202.pdf
This 17-page PhUSE White Paper by Rashmi Dodia and Gregory Campbell focuses on two approaches to produce anonymised narratives – retrospective and proactive. The retrospective section addresses challenges faced with qualitative methods (e.g., redaction) and the impact on data utility. Desirable features of a tool or software solution for redaction are included on page 10. In the proactive section, the needs for modern solutions and skills enhancement in order to meet Policy 0070 requirements are discussed. Suggestions on how to operationalise proactive anonymisation are also offered on page 15. All PhUSE white papers are available at: https://www.phuse.eu/white-papers

4. EMWA RPD SIG members' page: https://www.emwa.org/members/special-interest-groups/regulatory-public-disclosure-sig/
Subpage for disclosure-related regulatory news updates: https://www.emwa.org/members/special-interest-groups/regulatory-public-disclosure-sig/regulatory-news-emwa-newsblast/.