How the FDA's Proposed Framework for Public Access to Clinical Study Reports Affects Medical Writers and Regulatory Affairs Professionals

As medical writers and regulatory affairs professionals, we understand the challenges of making clinical data publicly available. Sharing data serves the goal of advancing scientific understanding, but also carries with it issues of confidentiality and patient privacy. Regulatory agencies have taken steps to balance public access to data with the need to keep details of that data hidden. There is currently no alignment across regions, however. That is why we took notice when on 26 March 2020 the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA) laid out a framework for making clinical study reports (CSRs) available to the public and supported the goal of regional harmonization[1].

Medical writers and regulatory affairs professionals should be aware of the FDA's proposed framework when working with CSRs.

THE CLINICAL DATA SUMMARY PILOT PROGRAM

The March press release by CDER Director Janet Woodcock marked the conclusion of the Clinical Data Summary Pilot Program[2], which was launched in 2018 with the goal of increasing transparency into the drug approval process. Currently, upon approval of a New Drug Application (NDA), the FDA posts its scientific reviews at Drugs@FDA. Reports include Summary Review along with subject-specific reviews such as clinical pharmacology and statistics.

[1] FDA. "FDA Continues to Support Transparency and Collaboration in Drug Approval Process as the Clinical Data Summary Pilot Concludes." [FDA Statement] 26 March 2020. https://www.fda.gov/news-events/press-announcements/fda-continues-support-transparency-and-collaboration-drug-approval-process-clinical-data-summary

[2] FDA. Clinical Data Summary Pilot Program.

CSRs are available to the public upon a Freedom of Information Act (FOIA) request, although processing these requests may take months or years, delaying public access to the clinical data that informed the FDA decision.

In launching the Pilot Program in 2018, then-FDA Commissioner Scott Gottlieb noted that making CSRs publicly available "will provide stakeholders with more information on the clinical evidence supporting a drug application and more transparency into the FDA's decision-making process."[3]

To launch the pilot program, sponsors of approved drugs were asked to make available the CSRs of pivotal studies, along with the accompanying protocol and statistical analysis plan. One sponsor gave permission for the FDA to publish the CSR for its Phase 3 pivotal trial at Drugs@FDA. The FDA posted the CSR and solicited comments from the public on the pilot program.

COMMENTERS SEEK ALIGNMENT WITH OTHER AGENCIES

The FDA received 21 comments from stakeholders that included industry organizations, patient advocacy groups, and academic researchers[4]. The comments on the program were generally supportive of the goal of increased transparency, although issues were raised about the FDA's approach. In particular, commenters sought greater alignment between the FDA and non-US agencies in the regulations and procedures involved in clinical data publication. Both the European Medicines Agency (EMA) and Health Canada post CSRs, and do so across all phases of development for both approved and rejected/withdrawn drugs (although the EMA has suspended the program since 2018 as its offices move from London to Amsterdam[5]). The FDA program, in contrast, only applied to pivotal studies of approved drugs. Advocacy groups and researchers commented that the public would be served by a broader release of CSRs, rather than the limited approach taken by the FDA.

Industry groups sought clarity on the process of redacting commercially confidential information (CCI) and personal subject data from the CSRs. During the pilot program, the FDA was solely

[3] FDA. "FDA Commissioner Scott Gottlieb, M.D., on new steps FDA is taking to enhance transparency of clinical trial information to support innovation and scientific inquiry related to new drugs." [FDA News Release] 16 January 2018.

[4] "New Drugs Regulatory Program Modernization: Improving Approval Package Documentation and Communication". Docket ID: FDA-2019-N-2012.

[5] EMA. Clinical Data Publication.

responsible for redaction of the CSR, without sponsor involvement. This contrasts with EMA[6] and Health Canada[7], which have processes by which sponsors submit redacted versions of CSRs and other NDA documents, which are reviewed by the agencies. While the agencies have the final say, the sponsor can request a consultation. In its comment, the Biotechnology Innovation Organization wrote that "there is no indication that Sponsors will be given the opportunity to review redactions or justify additional redaction before the documents are made public."[8] PhRMA noted that "FDA did not have a stated policy on the Agency's redaction processes for the documents that were made publicly available."[9]

Several stakeholders wrote about the importance of protecting subject privacy when performing redactions. The FDA's approach of independently redacting subject identifiers to protect privacy produced a document that, according to the PhUSE Data Transparency Working Group, "leaves a number of quasi-identifiers unredacted, which would be anonymized under EMA Policy 0070 and Heath Canada PRCI and could be used for re-identification attacks."[10]

One issue related to privacy that was raised by stakeholders pertained to the inclusion of subject narratives of deaths, serious adverse events, or adverse events of special clinical interest and those leading to permanent discontinuation. In the posted CSR, all narrative information was removed, an approach that contrasts with EMA Policy 0070, which does not allow redaction of entire narratives and instead mandates that narratives be anonymized. The PhUSE working group, which support making subject narratives available, wrote that the FDA's redaction of the narratives "alter[s] data utility"[11].

[6] EMA. "External guidance on the implementation of the European Medicines Agency policy on the publication of clinical data for medicinal products for human use." EMA Policy 0070, Version 1.3, 22 September 2017.

[7] Health Canada. "Public Release of Clinical Information: guidance document". Version 1.0, 12 March 2019.

[8] Biotechnology Innovation Organization. Comment Letter re: Docket No. FDA–2019-N-2012: New Drug Regulatory Program Modernization: Improving Approval Package Documentation and Communication. 25 Aug 2019. 2

[9] PhRMA. Comment Letter re: Docket No. FDA–2019-N-2012: New Drug Regulatory Program Modernization: Improving Approval Package Documentation and Communication. 26 Aug 2019.

[10] PhUSE Data Transparency Working Group. Comment Letter re: Docket No. FDA–2019-N-2012: New Drug Regulatory Program Modernization: Improving Approval Package Documentation and Communication. 25 Aug 2019.

[11] Cancer Support Community. Comment Letter re: Docket No. FDA–2019-N-2012: New Drug Regulatory Program Modernization: Improving Approval Package Documentation and Communication. 26 Aug 2019.

THE PROPOSED FRAMEWORK

The issue of aligning across regions was central to the FDA in proposing a framework for presentation of CSRs. CDER Director Woodcock wrote in the 26 March press release:

> "We found that there are significant inefficiencies in having multiregional disclosure requirements relating to often identical clinical data summaries. These inefficiencies multiply the transactional, administrative and redaction (because there are differing regional disclosure standards) costs, whether the costs are incurred by industry or a regional regulatory authority. These costs create barriers to programs to disclose clinical trial information which might be reduced if a centralized or regional approach could be achieved."

The four elements of the proposed framework are:

1.	**A centralized international library managed by an independent body that makes clinical data available to the public, instead of each regulatory agency having its own procedures.**
2.	**An on-demand system** in which some clinical documents are automatically published and others can be added to the library following public request.
3.	**Anonymization and disclosure standards** would be established that enable synchronization across regions. One example of these efforts is the PhUSE Working Group that is establishing standards for disclosure of CSR information and privacy protection.
4.	**Sponsor use of the international library system would be voluntary**.

WHAT THIS MEANS FOR MEDICAL WRITERS

In emphasizing alignment across regions and the inefficiency of having different standards for clinical data disclosure, the FDA appears to be endorsing a harmonized set of disclosure and redaction standards. It is not clear from the press release if FDA plans to adopt the EMA model in which sponsors are responsible for redacting documents, although they may have opened the door to it, writing in the press release that "the public could request study reports of interest, and the sponsor would then prepare the report, protocol and statistical plan and add it to the library."

Medical writers working on CSRs should be aware of the redaction standards for CCI and anonymization in EMA Policy 0070, and the efforts of the PhUSE Working Group to work with agencies to promote transparency of clinical data while protecting CCI and subject privacy. If medical writers are tasked with performing redactions to CSRs and other reports, they may want to do so using the guidance in Policy 0070. If harmonized standards are to be adopted for an international library of clinical reports, the standards are likely to be based on Policy 0070, which has been in force since 2016. Redacting CSRs is a time-consuming process, and medical writers should seek to avoid duplication of work by adopting the most widely used standards.

Expert Opinion:

"While redaction of clinical information on the back end is almost always involved, it is the responsibility of the regulatory medical writer to properly anonymize clinical reports from the get-go. Not only is writing with anonymity more efficient than redaction alone, but you reduce the risk of losing relevant data when telling the complete story. As regulatory writers, it's vital to have a vision of the content and submission process as a whole."

~Krithi Bindal, MS, PhD, MBA
President and Principal, Regulatory Writing, Aroga Biosciences

SPECIFIC EXPERTISE IN DATA TRANSPARENCY STANDARDS IS CRUCIAL IN THE CURRENT REGULATORY LANDSCAPE

Aroga Biosciences can help keep regulatory departments ahead of the curve with our knowledge and implementation of the most current widely used standards for CSRs. It is our belief that continued data reporting and sharing practices will become increasingly important in today's landscape. Aroga Biosciences can help enhance integrity and trust in research data with regulators, physicians, patients, and the general public.

"Every client's needs are different. What makes it fun to work with our different clients is the chance to develop a strategy tailored to the individual client. We're partners in that process--knowledge experts as well as writers--who will help you navigate the changing regulatory landscape."

~Adam Schindler, MA, PhD
Senior Regulatory Writer, Aroga Biosciences

ABOUT AROGA BIOSCIENCES

Aroga Biosciences is a boutique consulting group that provides regulatory writing services for biotech and pharmaceutical projects. We are a team of scientists with extensive regulatory and medical writing experience in a broad range of therapeutic areas. Our writers have in-depth experience with regulatory and publishing standards so we can ensure each document is submission ready. Our scientific backgrounds allow us to understand content at a fundamental level, which aids us in conveying messaging appropriately for its intended audience.

Regulatory medical writing is our passion. Whether working on large submissions, protocols, or other regulatory documents, our team brings the agility and expertise to successfully and efficiently reach project goals.

We look forward to partnering with you to fulfill your regulatory medical writing needs!