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Clinical Trial Transparency

By Darshan Kulkarni

Most research professionals agree that clinical trial transparency serves important purposes, but progress toward achieving it has been slow. For one thing, many researchers balk at sharing study information due to confidentiality requirements and the consequences of disclosing trade secrets that could benefit competitors. Nevertheless, a consensus is growing among stakeholders — including prescribers, clinicians, patients, ethicists, legislators and some study sponsors — that the benefits of clinical trial transparency outweigh the commercial risks. Proponents argue that data sharing accelerates new treatments, enhances patient safety, and prevents wasteful spending on clinical trials. Responding to this pressure for transparency, government agencies in the U.S. and abroad have implemented various policies to promote data sharing.

In this article, we will discuss the types of transparency that are generating the most discussion and progress toward their adoption.

What Is "Transparency"?

Traditionally, clinical trial "transparency" has referred to (a) registering studies in a public database like clinicaltrials.gov, (b) sharing information with potential study participants during the informed consent process, (c) sharing incidental findings with study participants, and (d) publishing study results in scientific journals. Today, it also refers to (e) reporting study results in a public database like clinicaltrials.gov, (f) providing lay summaries of study results to participants in a study, (g) sharing data about a study participant after the conclusion of a study, and (h) providing redacted versions of the Clinical Study Reports.

U.S. regulations and guidances primarily focus the first five types of transparency but not the last three.

Clinical Trial Registration and Results Reporting

To promote clinical trial transparency, study sponsors are supposed to register their clinical trials when they begin and regularly update their results as the trial moves forward.[1] This practice fulfills a variety of needs, including the company's ethical obligation to study participants and the research community. Making clinical trial registration information and study results publicly available also reduces publication bias and enables more efficient allocation of research funds.[1]

In the United States, clinical trials and results reporting must be performed via the website clinicaltrials.gov. Companies must register phase 2-3 controlled clinical investigations related to FDA-regulated drugs and biologics. Companies must also register clinical trials for medical devices other than small feasibility studies and prototype device testing, including "FDA-required pediatric post-market surveillances of device products."[2] Penalties for failing to register or submit results may include fines or the withholding of grant funds.[3] A recent court decision found that Federal agencies do not have the power to overrule Congressional intent, so registration and results reporting are required for 10 years retroactively.[4] Interestingly, Canada refers to clinicaltrials.gov for clinical trial disclosure and results reporting.[5]

Like the U.S., the European Medicines Agency (EMA) is also pushing for clinical trial registration and results transparency. Due to Brexit, the U.K. has begun its own explorations into clinical trial transparency but has met with difficulty coaxing universities and other academic institutions to comply with trial registration and results reporting. According to one report conducted by the U.K. Parliament's Science and Technology Committee, many universities have neglected to report their trial results and have continuously violated European Union trial reporting rules.[6] To combat this problem, the Committee published a report on clinical trial transparency with strong recommendations and stated that non-compliant companies and institutions would be called before the Committee for disciplinary action.[6] This action has strongly incentivized U.K. study sponsors and institutions to take clinical trial transparency more seriously, resulting in increased trial registration and results reporting.[6]

Nevertheless, few companies are consistently reporting their results at clinicaltrials.gov despite being the threat of a $10,000 per day penalty.[7,8] As a result, important information about the safety and effectiveness of new treatments is not available to the public, despite initiatives by the National Institutes of Health (NIH) and the Food and Drug Administration (FDA).

Scientific Publications: A Dichotomy in Industry Attitudes

Most companies do not even make their official position on scientific publications public. As a consequence, thousands of clinical trials end up unpublished and unreported, leaving patients, clinicians and other researchers in the dark. Some forward-thinking PhRMA and BIO companies have been working to remedy this situation, committing to publish clinical trial data in reputable scientific journals. If those efforts fail, many have even committed to publishing their results in open-access journals.

Patient Confidentiality: A Work in Progress

Finding a way to promote data transparency without sacrificing patient privacy is one of the primary challenges facing study sponsors and health officials. Although data disclosure often benefits doctors and patients, particularly as it concerns new treatment options, it also risks revealing data that patients would rather keep private.

And then, there is the conflict with global privacy laws. The call for protecting personal information embodied in HIPAA, GDPR, PIPEDA (Canada), CCPA (California) and similar laws seems at odds with the spirit of transparency espoused in measures like the EMA's Policy 43 and Policy 70.[11] Nevertheless, EMA and other agencies have required such patient-specific data be made public, limited primarily by certain confidentiality and privacy limitations. Different EMA countries interpret GDPR and the EMA policies differently. Resolution is very much a work in progress.

Lay Summaries: Early Days

The European Union also introduced the "lay summary" in response to pressure from patient organizations to take a more patient-centered approach.[10]

A lay summary is a document explaining the results of a clinical trial in non-technical terms. The EU generally requires such summaries to be published within one year of trial completion.[9] Their main objective is to enhance public understanding of clinical trial data. Although minimal guidelines have been released on how these summaries are to be written, the general recommendations from industry and patient organizations are to keep the document simple and brief (1-2 pages) and use lay language.[9] The document should be

written at the literacy level of a general public audience without assuming any prior knowledge of the study, medical terminology, or clinical research in general.[9] Some stakeholders, including patients and companies, advocate for the use of infographics and cartoons to enhance understanding. These lay summaries will be made available in a new EU database.[9] The requirement that lay summaries be written for all clinical trials conducted in the EU may be fully implemented this year or next.

In the U.S., the FDA conceptually supports lay summaries to participants in clinical studies, but concerns exist that providing such lay summaries may constitute promotion and violate Office of Prescription Drug Promotion (OPDP) requirements.[10] The matter is unresolved at this writing.

Clinical Study Reports (CSRs)

In 2018, the FDA launched a pilot program that involved posting critical portions of some CSRs on its website to enhance data access to researchers and the public.[11] Since the pilot was completed in 2019, the FDA has shown limited interest in pursuing this form of disclosure. In contrast, the EMA and Health Canada require disclosure of redacted CSRs. Such disclosures are subject to appropriate privacy and confidentiality provisions, including compliance with the Protecting Canadians from Unsafe Drugs Act (*"*Vanessa's Law").[12]

Conclusion

Health authorities in the U.S., U.K., EMA and Canada have taken significant steps toward promoting transparency in clinical trials, trying to find the right balance between the disclosure of important information to clinicians, scientific researchers, and patients versus the privacy rights of patients and the trade secret rights that companies need to justify investment in research. Consensus on the right balance has not yet been achieved. Once it has, we can expect rapid expansion of clinical trial transparency.

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Author

Darshan Kulkarni is Principal Attorney at The Kulkarni Law Firm. Contact him at 1.302.252.6959 or Darshan@conformlaw.com.

