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White Paper

Regulatory, Ethical and Patient Engagement Considerations for Plain Language Summaries

April 2024

While there is general consensus within the pharmaceutical industry on the importance of providing plain language summaries (PLS) of clinical trial results to participants and the public as a whole, two of the largest regulatory agencies — the European Medicines Agency and the Food and Drug Administration — differ on their approach to the matter.

In Europe, the EMA's EU Clinical Trials Regulation 536/2014 (Article 37 EU CTR) requires sponsors to provide summary results of clinical trials in a format understandable to the general public. In the US, the Multi-Regional Clinical Trials (MRCT) Center of Brigham and Women's Hospital and Harvard, in collaboration with TransCelerate Biopharma, submitted draft guidance on PLS to the FDA in 2017. To date, the FDA has not required sponsors to submit PLS. The guidance remains open for public comment. Table 1 provides a side-by-side comparison of the EU requirement and the proposed US guidance.

Table 1

Elements that should be addressed in plain language summaries:	
EU Regulation	**Proposed US Draft Guidance**
Clinical trial identification	Study title
Name and contact information for sponsor	Study purpose
General information about the clinical trial	Start/end dates, countries where the study took place, type and phase of the study
Population of participants	Study population — demographics, key inclusion/exclusion criteria, number of participants
Investigational medicinal product used	The product being studied
Description of adverse reactions and their frequency	Incidence of serious and non-serious side effects (adverse events)
Overall results of the clinical trial	Primary outcome(s) — describe results for the primary endpoint(s) for each study arm
Comments on the trial's outcome	Comments on study's outcome
Indication if follow-up clinical trials are foreseen	Whether further research is anticipated
Where additional information can be found	Where additional information can be found

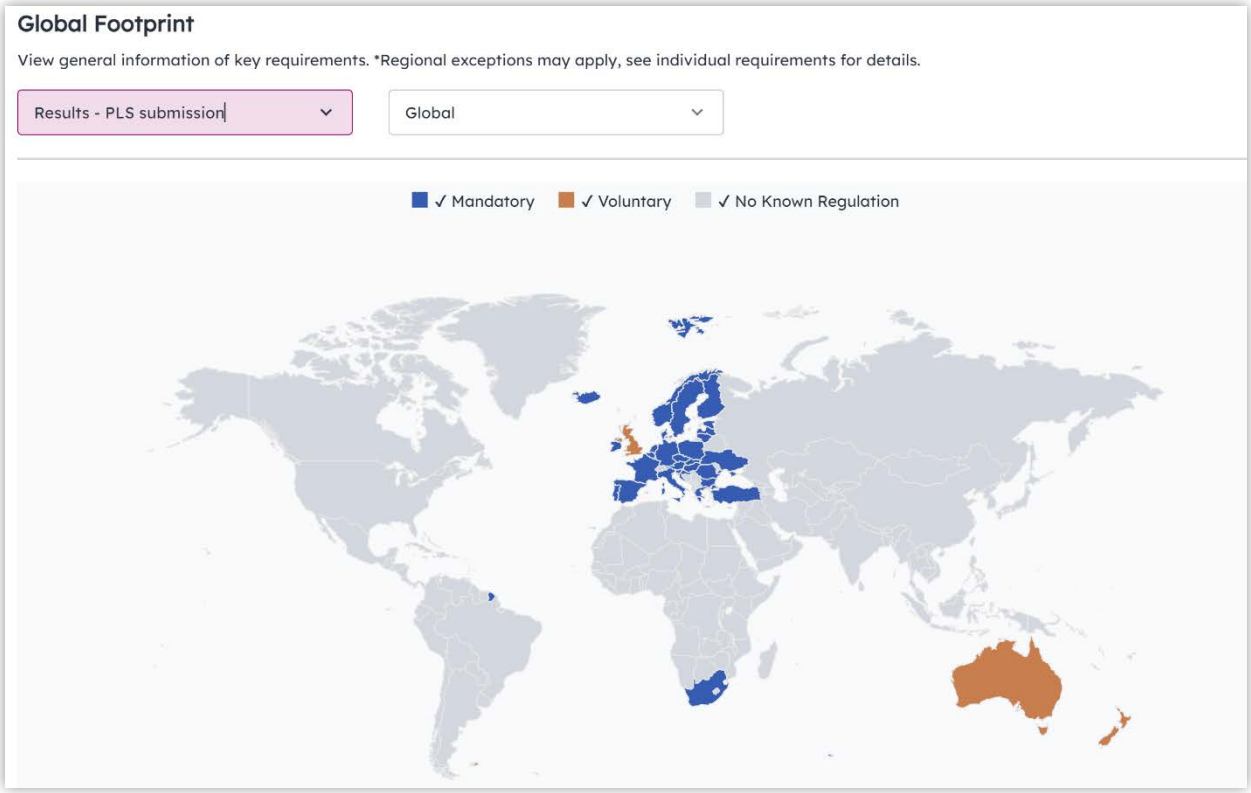
The original EU CTR stipulated that lay summaries, more commonly referred to as plain language summaries, would be made available in a new EU database once it becomes available. That time has come. As of Jan. 31, 2023, all initial clinical trial applications in the EU/EEA must be submitted through the Clinical Trials Information System (CTIS), which launched in January 2022. Protocol synopsis (PLPS) are not a regulatory requirement in EEA/EU member states. However, ethics committees in some countries require them, so they are considered a de facto requirement if not a regulation.

For adult clinical trials, sponsors must post a plain language summary and a technical summary within 12 months of the end of the trial. For non-therapeutic Phase I trials sponsors have up to 30 months after the trial has concluded, and for pediatric trials within six months of the trial's end.

The EU regulations have not changed, they simply became official when the regulation went into effect, explains disclosure and transparency expert Kimberly Green, founder of ClaritiDox. All new studies in the EU fall under the regulation, she says, adding that existing studies must transition by the end of this year. She describes PLPS clause as "a wonderful and meaningful addition, although a bit of a surprise." The fact that the EMA indicated these synopses will be made public "will be really good for patients," she says.

In addition to PLS being easily understood, Green reminds that they must be free of promotional language. This ensures they report on the results with no editorializing, even when comparing one drug to another. The PLS writer must be someone who is objective, and "who knows the science really well," Green says. To underscore objectivity, some sponsors post PLS on a website unaffiliated with their own company, such as TrialSummaries.com.

Although the US has not made PLS mandatory, the FDA has recently emphasized the value of using language easily understood by the public. It encourages sponsors to use plain language in presenting trial information, including informed consent materials, to aid in the decision-making process of whether to join a study. On Feb. 29, FDA and the Office for Human Research Protections (OHRP) at the Department of Health and Human Services (HHS) published draft guidance on best practices.



Source: TrialScope Intelligence

It's the right thing to do

Regulations aside, providing a PLS is simply the ethical choice. However, according to one journal article, even the PLS itself can spur ethical debate. In the article referring to plain language resources (PLR), which include PLS, the authors assert that, while PLR may address many ethical issues, they may potentially exacerbate the following:

- Challenges to fair balanced presentation and interpretation of medical research
- Existing positive publication bias
- Challenges to equitable access to information
- Ambivalent outcomes of patients' autonomy
- Feeding the "info-demic" in medical research literature

To avoid this, the authors recommend there should be standard guidelines for how PLR are developed and shared.

"I think it's important to note that, even when the product didn't do what you hoped it did, it's still advancing research and important to share that," Green says. Whether the study was deemed a success or not, "there's no failure here."

Here's an example of how PLS can take the complex and make it understandable for all:

ICH E3

This is a Phase II, open-label, single-arm study of drug in approximately 65 patients with disease. The primary efficacy endpoint is ORR (CR + PR) in determined by IRC. Efficacy together with PFS, OS, duration of response (DOR), TTR, PRO, and safety of drug.

Clinicaltrials.gov

This is a Phase II study in participants with Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) who have relapsed after at least 1 prior treatment regimen. The study is composed of an initial screening phase, a single-arm treatment phase, and a follow-up phase.

PLS

The patients in your study all had a type of lymphoma. They had all received treatment for cancer at least once before, but their cancer had returned. Everyone in the study received the same kind of medicine. The patients saw their doctors every week to see how the medicine worked.

PLS and patient engagement

It's a bit ironic that, while regulatory agencies tout the benefits of plain language, the data submitted by sponsors to the Clinicaltrials.gov online database, run by the US National Institutes of Health (NIH), is anything but user-friendly. The reviewers engaged by NIH to assess submissions to ClinicalTrials.gov might want to start requiring plain language information for selected information like the brief study title and description. At the recent Summit for Clinical Ops Executives (SCOPE), industry professionals acknowledged that the website is difficult to understand. PLS are designed to combat confusion, promoting health literacy by using language free of jargon and medicalese. To ensure that PLS are patient-friendly, many sponsors enlist the help of a patient panel.

Green notes that having a patient panel review PLS is strictly voluntary. That said, she adds, "I think it's an absolute best practice" to make sure the language is appropriate and can be easily understood by the general population.

Quoting her ClaritiDox colleague Courtneay Parsons, she says, “All of us are patients.”

Patient advocacy groups have done a great job promoting the involvement of patient panels, says Green. “They have been lobbying for this for years, very effectively.”

Green says one organization that has been particularly effective in the use of patient panels is the Center for Information and Study on Clinical Research Participation’s (CISCRP). Its Patient & Care Partner Advisory Boards provide feedback on several areas of the clinical trial process, including study synopses.

Communication between sponsors and participants is important before, during, and after the study to ensure engagement and, in turn, retention. Green says sponsors must show appreciation to the individuals who have “literally put their blood, sweat, and tears into helping others.”

Providing PLS to participants, Green says, is another way of acknowledging “You made a difference. You helped advance research.” This helps build trust in the sponsor, it treatments, and in the pharmaceutical industry.

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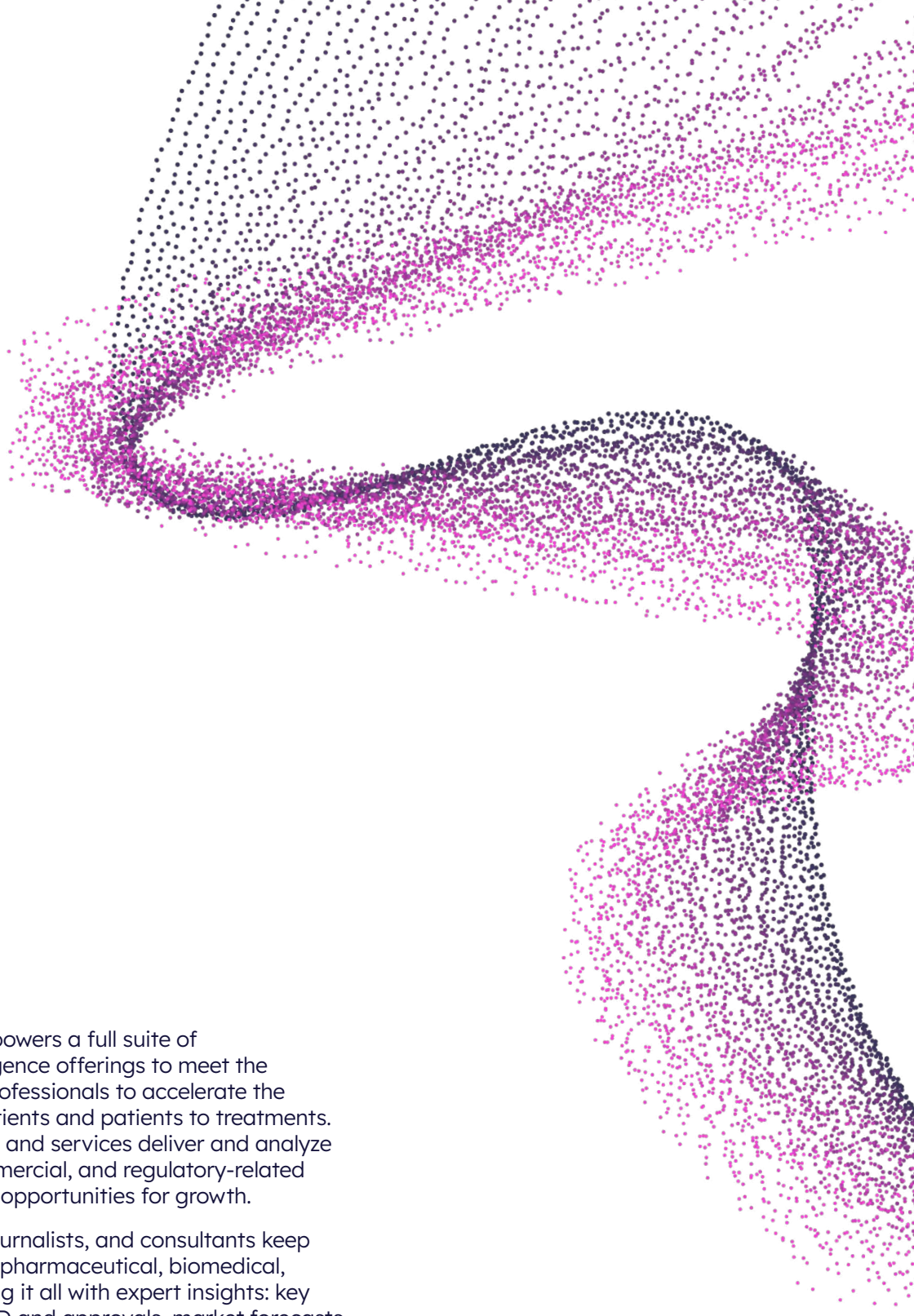

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