Returning Study Results to Research Participants: Best Practices for Preparation and Institutional Review Board Oversight

David Forster, JD, MA, CIP, Lindsay McNair, MD, MPH, MSB, Brandis Pickard

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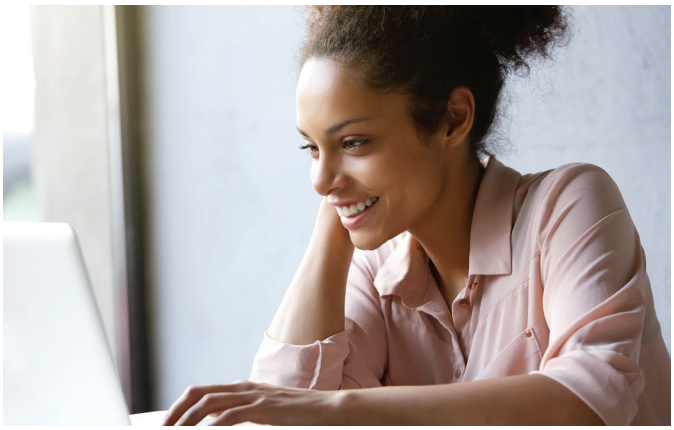

When a clinical trial is completed, the research community can access the results through several outlets. For the trial participants, though, the same has not always been true. Studies have shown that most clinical trial participants want to know what was learned from their involvement[1] , yet most don't hear from the sponsor or site staff once the trial is over. ClinicalTrials.gov, while a legitimate resource for industry professionals, is designed for the "educated reader of the medical literature"[2]—not for patients or other lay audiences. Even those participants who are able to navigate the website are unlikely to decipher the posted trial results. A growing number of sponsors are implementing an important practice to close this communication gap: delivering plain language summaries to trial participants. This paper will discuss the current best practices for the content and preparation of plain language summaries, and the current guidance for how sponsors should work with Institutional Review Boards (IRBs) which have oversight of the clinical trials for which the summaries are provided.

Plain Language Summaries

Plain language summaries (also known as lay language summaries) are significant not only in content, but also in style and format. Usually written at a 6th-8th grade reading level, a lay summary is designed for a general audience. It segments key information about the trial into reader-friendly sections, while remaining non-promotional. It provides trial participants with an objective description of the overall results of the trial, focusing on those pieces of information that are most relevant to the reader. Importantly, the lay summary should also thank clinical trial participants for being part of the research.

Not only is it ethically responsible to provide trial results to participants—it will soon be mandatory for studies conducted in the European Union. The EU Clinical Trials Regulation (EU) No 536/2014 will come into effect in 2019, and will require sponsors to provide trial results for laypersons through the European Medicines Agency (EMA) portal and database. As this becomes standard practice for sponsors with trial sites in the EU, and as patient advocacy groups continue to encourage providing lay language summaries, it may be in sponsors' best interest to create a dedicated patient engagement function within their organization.

The current US Health and Human Services (HHS) and Food and Drug Administration (FDA) regulations on IRBs and informed consent, at 45 CFR 46 and 21 CFR 50 and 56, respectively, neither require nor prohibit the

return of research results to participants. However, there is a revision coming to 45 CFR 46 (which applies to the oversight of federally-funded research), currently scheduled to go into effect on January 21, 2019. The new regulation requires that the consent form disclose "a statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions." It is expected that FDA will also adopt this regulatory requirement at some point. The Secretary's Advisory Committee on Human Research Protections (SACHRP) has issued a recommendation regarding the return of general research results to subjects.[3]

A study conducted by the Center for Information and Study on Clinical Research Participation (CISCRP) found that before reviewing the lay language summary, only about 11% of participants understood basic facts about the trial (such as why the research had been conducted). After reading the summary, participants' understanding of these basic facts improved by as much as 65.6 percentage points. Further, most trial participants felt appreciated, valued and connected to the site staff and the research after receiving the lay language summary.[4]

Other feedback collected by CISCRP after summary distribution showed that of those participants polled, slightly over 90% were satisfied with the lay language summary process and were pleased with their experience.[5]

CISCRP's 2017 Perceptions and Insights Study confirmed that participants want to be more involved in the research process, and that most—91% of those polled—think it is "somewhat or very important" to receive a summary of the results.[6]

Best Practices for Returning Results

All stakeholders in the clinical research process can benefit from communicating trial results to participants. The process of creating a plain language summary usually begins when the research sponsor has analyzed the study data and prepared trial results. These results may also be posted in online registries, published in medical literature or presented at medical meetings. Because it is imperative that these summaries remain non-promotional and objective, it is usually considered important to use sponsor-independent medical writers to create the summary. Once the summary is drafted, the sponsor reviews and confirms that the scientific and technical content is correct and no meanings or implications from the data have been changed by the translation to lay language.

While there are no specific regulatory requirements around the preparation of plain language summaries, the following factors are considered to be best practices in this process:

- Utilize medical writers who are trained in health communication to a lay audience

- Review, proofread and perform quality/content compliance checks throughout the development of the summary
- Incorporate graphics where helpful to represent data and break up text
- Collect sponsor feedback on the summary's scientific/technical accuracy and adherence to any applicable sponsor policies/guidances
- Meet with the sponsor to discuss study team feedback on the summary
- Engage an editorial panel- an independent group of volunteers made up of patients, patient advocates, and health professionals- to assess the summary for readability, transparency, and non-biased language
- Render the final summary in high resolution for web posting, printing and distribution purposes

When the summary is final, the summary will need translation into participants' native languages. While the method of distribution (print, electronic, or both) is up to the sponsor, it is recommended to provide a printed copy to the participants. Surveys have found that participants prefer receiving a tangible copy of the results.[7]

Requirements for IRB Oversight of Plain Language Summaries

As the practice of providing plain language summaries to research subjects has become more common, one of the frequently asked questions is whether the summaries need to have review and approval by the IRB that reviewed and approved the research. Because the return of results is not addressed in the current IRB regulations, the answer to this question is not completely clear.

The general opinion on this question is that the need for review depends on the status of the study. In its report on the return of general research results to subjects, SACHRP recommended that if the research site at which the participants are enrolled is still open with the IRB and under IRB oversight, the summary should be submitted for IRB review, as it is new information to be provided to subjects. However, if the study is closed with the IRB (as will most often be the case, by the time study results have been analyzed and are ready to be reported), then SACHRP recommended that IRB review should not be required. Most IRBs appear to be comfortable with following this recommendation, although some IRBs may not be aware of the SACHRP recommendations, and may want to follow a different plan for review. While anecdotally some IRBs have based their decisions about review on factors such as whether the return of plain language summaries are mentioned in the protocol, the consent, or even in the sponsor-site contract, none of these factors create

a regulatory requirement for the IRB review of plain language summaries.

As noted previously, when the new regulations for federally-funded research come into effect in January of 2019, sponsors will be required to disclose any plans to provide plain language summaries in the consent form; it is expected that FDA will harmonize their requirements with this at some point.

Conclusions

As the recommendations of multiple extra-regulatory committees and advisory groups have made clear, returning study results to research participants is a best practice, which should become standard practice. An important part of this effort is the provision of plain language summaries, written to describe the study outcomes in a way that is understandable and relevant to the research participants. While return of plain language summaries is still a relatively new practice, there are organizations which have been on the forefront of this movement and have developed best practices that are essential knowledge for any sponsors who are considering moving toward this goal.

About the Authors

David Forster, JD, MA, CIP is the chief compliance officer with WIRB-Copernicus Group (WCG)

Lindsay McNair, MD, MPH, MSB is the chief medical officer with WIRB-Copernicus Group (WCG)

Brandis Pickard is a project manager with the Center for Information and Study on Clinical Research Participation (CISCRP)

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