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Providing Research Participants with New Information: Is “Re-Consent” Always Necessary?

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Obtaining informed consent—providing information to people about clinical trials and obtaining their willingness to participate in them—is a cornerstone of conducting research with human research participants. Sometimes information or study procedures change while the study is in process, and when this happens, it is important to confirm that participants want to continue. But how is that best done? Revised consent forms and the formal collection of signatures will document the participant's agreement and protect the participant and researchers, but the management of multiple consent versions adds administrative burdens and can be confusing for participants. Initial consent discussions may be formal and can take substantial time, but does having the same process for every subsequent consent interaction serve the participants or the researchers?

This white paper will discuss a reasoned approach to applying the right amount of consent discussion for the right situation when there is new information in ongoing research.

BACKGROUND

Federal regulations require that the consent form notify participants that they will be informed of 'significant new findings developed during the course of the study'.[1] While it is clear that participants need to be provided with significant new findings and be advised of changes that affect them, (which we will refer to as "new information,") during the study, the details of how this information is provided and documented is not defined. While the default approach is that the new information is included in a revised consent form and the participants are formally "reconsented" in a process similar to the initial consent discussion, it can be more effort than is necessary.

The regulations do not mention reconsent or what this process should look like. The FDA Information Sheet – A Guide to Informed Consent[2] (1998) only provides the following information:

> *When it is anticipated that significant new findings that would be pertinent to the subject's continued participation are likely to occur during the subject's participation in the study, the IRB should determine that a system, or a reasonable plan, exists to make such notification to subjects.*

FDA Information Sheet - A Guide to Informed Consent

The FDA Draft Guidance – Informed Consent Information Sheet[3] (2014) also does not provide guidance on how new information should be provided.

> *The consent process must, when appropriate, include a statement that significant new findings that may relate to the subject's willingness to continue participation, such as new risk information, will be provided to the subject. (21 CFR 50.25(b)(5).) Significant new findings may include an unexpected adverse event or an adverse event occurring at greater frequency or severity than previously stated in the consent process. FDA encourages the inclusion of this statement in the consent form for clinical investigations where knowledge of risk is limited, for example, clinical investigations of the first use in humans, novel therapies, and new molecular entities, or complex clinical investigations that involve significant risk.*

FDA Draft Guidance - Informed Consent Information Sheet

RECOMENDATIONS

Recently the Secretary's Advisory Committee on Human Research Protections (SACHRP) provided recommendations[4] to the Office of Human Research Protections (OHRP) on the issue of providing new information to research participants. These recommendations draw a distinction between providing new information to participants, and a formal re-consent process. The recommendations

use re-consent to mean "subjects will go through a complete consent process that supersedes the original consent using a document that contains all required elements of consent and is documented in accordance with the federal regulations." In contrast, the recommendations recognize that there may be other mechanisms of providing new information to participants, such as the use of information sheets and consent form addenda that would not be considered legal informed consent. Furthermore, it indicates that there are many ways new information could be provided to participants so they can "reaffirm their willingness to continue to participate in the research."

We agree that IRBs, sites, and sponsors should consider the new information to be provided to participants and determine what approach could be used to satisfy the regulatory requirement to provide the participants significant new information, but in the least burdensome way. "Burdensome" in this case refers both to the inconvenience for the participant, and for the administrative and logistic burdens on research sponsors and clinical site study teams. Unnecessarily burdensome approaches do not provide more protections for participants and thus are a burden without benefit. A reasoned approach will allow a maintained respect for persons while ensuring appropriate protections when they are needed. The options on how to provide new information to participants should be based on the kind of information to be provided and if participants need to document that they wish to remain in the study.

OUR PROPOSED HIERARCHY

Our proposed hierarchy for the provision of new information, which is consistent with the SACHRP recommendations, is:

Verbal Discussion
Providing information to participants verbally may be sufficient if the information is simple, not likely to change the individual's decision to remain in the study and doesn't require the participants to document that they want to remain in the study. Examples include informing participants that certain procedures are no longer necessary without changes to the visit schedule (e.g., "We won't need to do an eye exam when you come for your Week 12 study visit").

Letter
It may be appropriate to send a letter to the participants to provide new information when the information is simple and self-explanatory, but it is important for the participants to have something in writing for future reference. The new information likely will not impact a participant's decision to remain in the study. Examples include informing participants that they can use a commercial lab to have blood samples drawn or informing the participants of a change of investigator.

Addendum

This is an in-between step, when information may be somewhat complex or important, but not to the level of needing full reconsent and discussion of the entire study. Examples include new safety information, the addition of a single new study procedure, or changes to how the participant's information will be kept confidential. The new information may impact a participant's decision to remain in the study, and there should be documentation (by signature) that the participant agrees to remain in the study. The benefit of using a consent form addendum is that it can provide a focused discussion of the new information and will be more efficient that a full reconsent process.

Note that a verbal discussion also may be the initial step of providing participants with new information if it is urgent to provide that information while the written information is being created.

Reconsent

Due to the time and effort involved, this is best for situations where there is no time pressure and there is complex information to be conveyed. Participants will have not started or will still be undergoing research procedures and having regularly scheduled study visits. Sites and sponsors should reconsent participants when the changes are so significant or pervasive that it would require a thorough consent discussion to re-explain the study and that the participants will need to document their agreement to remain in the study. Examples include situations where participants are moving into a new cohort or phase of the study that is very different from what they are currently doing, when an adaptive study design may be changing, or when there are multiple changes being made to the study and it would be impractical to provide the new information in any other way.

IN CLOSING

In line with the guidance provided by SACHRP, we want to encourage investigators and sponsors to consider approaches other than a full reconsent process for providing new information to currently enrolled participants. Using mechanisms that are the least burdensome approach is based in ethical principles. As such, there should be a hierarchy of providing participants new information that ranges from verbally notifying the participants of the changes, to using letters, consent form addenda, and finally a complete consent discussion based on a revised consent form. In situations in which the approach to providing new information may not be clear, both sponsors and researchers can talk to the IRB to help determine the most appropriate pathway.

REFERENCES

1. 21 CFR § 50.25(b)(5) and 45 CFR § 46.116(c)(5).
2. FDA Information Sheet – A Guide to Informed Consent: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guide-informed-consent
3. FDA Draft Guidance – Informed Consent Information Sheet: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/informed-consent
4. Attachment A – New Information Provided to Previously Enrolled Research Subjects: https://www.hhs.gov/ohrp/sachrp-committee/recommendations/april-7-2020-attachment-a/index.html

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