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33 Questions an IRB Should Ask about the Research Informed Consent Process

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Informed consent is not just a document; it is a process that begins with a patient's first contact with a study, e.g., seeing an advertisement, and ends when the study concludes for that patient.

IRBs are responsible for ensuring that the consent process is adequate and properly documented per 21 CFR 50.20 and 45 CFR 46.116:

> Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with and to the extent required by part 50. (21 CFR 56.111(a)(4))
>
> Informed consent will be appropriately documented, in accordance with and to the extent required by §50.27. (21 CFR 56.111(a)(5))

Applicable regulations, guidances and guidelines are below.

Questions about the Research Informed Consent Process

The following 33 questions can assist IRBs in determining whether the consent process for a study is adequate:

1. Does the investigator understand that informed consent is a process?
2. How will it be determined that the correct version of the consent form is being used?
3. Who will give the consent form to the prospective study participant?
4. Where will the consent form be given to the prospective study participant (e.g., by mail, in a physician office, in a quiet exam room, or in a busy waiting room)?
5. What information will the prospective study participant receive prior to and when receiving the consent form?
6. How much time, when and where will the prospective study participant have to read and deliberate about the consent form (e.g., overnight at home after the consent visit)?
7. How will the consent visit proceed? For example, the prospective study participant may be invited into a quiet clinic office or exam room, given a brief verbal introduction, be given adequate time to read the consent form, and have the key points verbally explained, with the opportunity to ask and discuss any questions.
8. How much time will the typical discussion take?
9. How will the consent process, e.g., the setting and the dress of the person(s) obtaining consent, minimize the therapeutic misconception?
10. Who will explain the study to the prospective study participant? For example, the study coordinator might review the study, followed by the principal investigator discussing it further.
11. What training and experience will the person(s) obtaining consent have about the study in particular and clinical research and human subjects protection in general?
12. Who will train the person(s) obtaining consent (e.g., an IRB staff member, the study sponsor, the principal investigator, or a study coordinator)?

13. Does a person obtaining consent have a relationship with the prospective study participant, e.g., as his or her primary care physician, that might create undue influence? If so, how would the potential undue influence be mitigated?
14. How will it be determined whether the prospective study participant has the cognitive capacity to give consent?
15. If a Legally Authorized Representative is required, how will the person(s) obtaining consent determine whether the person is qualified to serve in that capacity?
16. If an impartial witness is required, how will that person qualify to serve in that capacity?
17. Will the person(s) obtaining consent verify that the prospective study participant understands the important points? If so, how? For example, the person(s) obtaining consent might ask a prepared set of questions or use the teach-back method.
18. Will the prospective study participant be encouraged, allowed or forbidden to write on the consent form? (A clean copy can be signed later.)
19. Will the prospective study participant have the opportunity — and be encouraged — to share the consent form and ask for advice from family members, friends, healthcare providers, or a patient advocate? If so, what, if any, guidance, will the prospective study participant and those people receive?
20. Will family members, etc., be invited or allowed to accompany the prospective study participant to the consent visit(s)?
21. How will the person(s) obtaining consent follow up after the visit on open questions and issues?
22. If the prospective study participant is not able or willing to make a decision after the initial visit, what will be the subsequent process?
23. If the prospective study participant states that he or she is leaning against participation in the study, to what extent may the person(s) obtaining consent attempt to persuade him or her to participate?
24. How much time will the prospective study participant have to decide whether to participate in the study (e.g., overnight)?
25. If the prospective study participant states that he or she has decided against participation, what will be the subsequent process?
26. How will the presence of the prospective study participant's signature, initials and signature date on the consent form be verified?
27. How will consent or refusal to consent be documented, and how will the documentation be verified?
28. How will it be verified that the consent process has been followed correctly?
29. If, during the consent process or prior to the first study visit, a study participant is judged to be unsuitable for the study, what will be the subsequent process?
30. How and when will the consent process continue during the study?
31. Does the site have a standard operating procedure (SOP) that answers the above questions?
32. Should the IRB observe a mock or actual consent discussion, as permitted by federal regulation (46 CFR 109(e))?

Regulations, Guidances and Guidelines on the Consent Process

Federal regulations, federal guidances, and ICH guidelines place the following principal requirements on the consent process:

Code of Federal Regulations

…no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. (21 CFR 50.20 and 45 CFR 46.116)

FDA Informed Consent FAQs

The informed consent process involves three key features: (1) disclosing to potential research subjects information needed to make an informed decision; (2) facilitating the understanding of what has been disclosed; and (3) promoting the voluntariness of the decision about whether or not to participate in the research. (See Reference section)

FDA Guidance for Institutional Review Boards and Clinical Investigators

Informed consent is more than just a signature on a form, it is a process of information exchange that may include, in addition to reading and signing the informed consent document, subject recruitment materials, verbal instructions, question/answer sessions and measures of subject understanding. Institutional Review Boards (IRBs), clinical investigators, and research sponsors all share responsibility for ensuring that the informed consent process is adequate. Thus, rather than an endpoint, the consent document should be the basis for a meaningful exchange between the investigator and the subject.

The clinical investigator is responsible for ensuring that informed consent is obtained from each research subject before that subject participates in the research study. FDA does not require the investigator to personally conduct the consent interview. The investigator remains ultimately responsible, even when delegating the task of obtaining informed consent to another individual knowledgeable about the research.

In addition to signing the consent, the subject/representative should enter the date of signature on the consent document, to permit verification that consent was actually obtained before the subject began participation in the study. If consent is obtained the same day that the subject's involvement in the study begins, the subject's medical records/case report form should document that consent was obtained prior to participation in the research. A copy of the consent document must be provided to the subject, and the original signed consent document should be retained in the study records. Note that the FDA regulations do not require the subject's copy to be a signed copy, although a photocopy with signature(s) is preferred.

The IRB should be aware of who will conduct the consent interview. The IRB should also be informed of such matters as the timing of obtaining informed consent and of any waiting period (between informing the subject and obtaining the consent) that will be observed.

The consent process begins when a potential research subject is initially contacted. Although an investigator may not recruit subjects to participate in a research study before the IRB reviews and approves the study, an investigator may query potential subjects to determine if an adequate number of potentially eligible subjects is available.

Impartial Witness: A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject. (ICH (E6) 1.26)

Informed Consent: A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form. (ICH (E6) 1.28)

Neither the investigator, nor the trial staff, should coerce or unduly influence a subject to participate or to continue to participate in a trial. (ICH (E6) 4.8.3)

Before informed consent may be obtained, the investigator or a person designated by the investigator should provide the subject or the subject's legally acceptable representative ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial should be answered to the satisfaction of the subject or the subject's legally acceptable representative. (ICH (E6) 4.8.7)

Prior to a subject's participation in the trial, the written informed consent form should be signed and personally dated by the subject or by the subject's legally acceptable representative, and by the person who conducted the informed consent discussion. (ICH (E6) 4.8.8)

If a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any other written information to be provided to subjects is read and explained to the subject or the subject's legally acceptable representative, and after the subject or the subject's legally acceptable representative has orally consented to the subject's participation in the trial, and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally acceptable representative, and that informed consent was freely given by the subject or the subject's legally acceptable representative. (ICH (E6) 4.8.9)

Prior to participation in the trial, the subject or the subject's legally acceptable representative should receive a copy of the signed and dated written informed consent form and any other written information provided to the subjects. During a subject's participation in the trial, the subject or the subject's legally acceptable representative should receive a copy of the signed and dated consent form updates and a copy of any amendments to the written information provided to subjects. (ICH (E6) 4.8.11)

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