

## Investigator Signatures on Informed Consent Forms

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FDA's Guidance for Institutional Review Boards and Clinical Investigators (1998 Update) states "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. [However, t]he investigator remains ultimately responsible, even when delegating the task of obtaining informed consent to another individual knowledgeable about the research."

U.S. federal regulations require that investigators "...will inform any potential subjects that the drugs are being used for investigational purposes and will ensure that the requirements relating to obtaining informed consent (21 CFR part 50)... are met." (21 CFR 312.53(c)(vi)(d)) The regulations state that "...informed consent shall be documented by the use of a written consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative at the time of consent." (21 CFR 50.27(a))

In the rarely used short form method of obtaining consent, the regulations go on to state, "...the person actually obtaining the consent shall sign a copy of the summary." (21 CFR 50.27(b)(2)) However, the regulations say nothing specific about any signature by the investigator and nothing about a signature by site personnel on normal informed consent forms (ICFs). This omission is remarkable, given the central role of informed consent in clinical research and the investigator's fundamental responsibilities for subject safety and welfare. Nevertheless, informed consent forms usually require a signature from the person obtaining consent, and often require a signature from the investigator.

ICFs are not legal contracts because they are not binding on the subject. Although the subject signs the ICF, he or she accepts no legal obligations to appear at study visits, take the study drug, etc. However, U.S. courts obviously consider the subject's signature as evidence that the subject read the ICF and gave consent. If a subject signs an ICF that includes a false statement, e.g., pertaining to the subject's good health, the court may consider that statement in subject injury litigation. In contrast, U.S. courts usually interpret ICFs as legally binding on the investigator and research site (and possibly on the study sponsor, depending on the language in the CTA, if the sponsor drafted or approved the CTA, or if the sponsor withheld pertinent information required by the subject to give informed consent).

### What Does the Investigator's Signature Mean?

When an investigator signs an ICF, his or her signature can be taken to mean that he or she is saying that some or all of the following statements are true:

- The subject or authorized representative is competent to give voluntary and informed consent.
- The subject signed the form.
- The subject's signature appears to signify the subject's true wishes, without coercion or undue influence.
- The witness and/or authorized representative, if any, was present and signed the form.
- Consent was obtained in compliance with regulations.

- The subject was adequately informed and all questions were answered to the subject's apparent satisfaction.
- The subject apparently understood the material.
- The subject is qualified for the study and appropriate for enrollment, in the investigator's professional judgment.
- There is no safer and more effective treatment for the subject outside the study.
- The person who explained the study to the subject is qualified and properly delegated for that task.
- The investigator is knowledgeable about the contents of the informed consent form.
- The investigator is knowledgeable about the study and relevant medical practice.
- The investigator will comply with the informed consent form (and protocol).
- The investigator accepts that the subject's signature does not absolve the investigator of any responsibilities.
- The investigator accepts legal liability for himself or herself (and the research site, since he or she is representing the site).

### **Actual Informed Consent Forms**

A sample of 27 unique ICF site signature blocks revealed the following findings:

- One ICF does not require any site signature or even identification of the person who obtained consent.
- Fourteen ICFs require the signature of the person who obtains consent only, three require the signature of the investigator only, five require the signature of the investigator or designee, and four require the signature of both the investigator and the person who obtains consent.
- All signatures require dates. Sixteen signatures require printed names. One signature requires a title.
- The signatory's role is described variously (with consistent capitalization added) as the Doctor/Nurse, Individual Obtaining Consent, Informed Consent Provider, Interviewer, Investigator, Investigator (Study Doctor), Investigator/Delegate, Person Conducting the Informed Consent Discussion, Person Obtaining Consent, Person Administering Consent, Person Administering this Consent, Person Administering Informed Consent, Person Explaining Consent, Person Getting Consent, Person Obtaining the Authorization, Person Who Conducted Informed Consent Discussion, Person Who Explained This, Principal Investigator, Researcher or Designee, or Study Doctor.

Four ICFs set forth the meaning of the site representative's signature:

- I agree that this consent form has been orally presented, the patient has been informed about the study, and the patient and/or legally authorized representative has had an opportunity to ask questions.
- I have explained the purpose of the research, the study procedures, identifying those that are investigational, the possible risks and discomforts, as well as potential benefits and have answered any questions regarding the study to the best of my ability.
- I have fully explained this research study to the subject and have answered any questions (s)he has asked. I believe the subject understands the study and is able to give voluntary consent.

- This is to verify that I have explained to and discussed with the subject, or the subject's Legally Authorized Representative, Legal Guardian, Health Care Agent, or Parent, as appropriate, the following items related to the above procedure(s) before the initiation of the research-related intervention:
  - The nature of the research
  - Potential risks, benefits, drawbacks
  - Potential problems related to recuperation (if applicable)
  - Possible results of research
  - Known side effects or complications of the research
  - The availability of all alternate viable modes of treatment and the benefits and risks of such treatments, if applicable.

### **Conclusions**

Given the central role of informed consent in clinical research and the investigator's fundamental responsibilities for subject safety and welfare, investigators should sign ICFs to signify, at minimum, that they are meeting their regulatory responsibilities for the consented subject.

Investigators who understand the significance of their signature are more likely to meet their study responsibilities. Study sites and sponsors should therefore determine which of the above meanings apply, given their interpretation of the investigator's responsibilities, and explicitly communicate these meanings to investigators.

ICF signature blocks are highly inconsistent. Some blocks are clearly superior to others. At minimum, the blocks should require a signature, date and descriptive role, e.g., "Person Obtaining Consent." A printed name is optional since, in theory, the signature can be matched to the delegation of authority sheet.

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