**From:** OC GCP Questions
**To:** [redacted]
**Subject:** a question about illiterate trial subject
**Date:** Wednesday, January 04, 2017 11:08:00 AM
**Attachments:** [redacted]
**Importance:** High

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Good morning -

FDA's regulations on informed consent do not use or define the terms "impartial witness". The regulations require a witness when a "short form" written consent document is used, see 21 CFR 50.27(b)(2), which states:

A short form written consent document stating that the elements of informed consent required by 50.25 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining the consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative in addition to a copy of the short form.

In FDA's "A Guide to Informed Consent - Information Sheet Guidance for Institutional Review Boards and Clinical Investigators", available at www.fda.gov/RegulatoryInformation/Guidances/ucm126431.htm, however, the term "impartial witness" is used in the section on "Illiterate English-Speaking Subjects"; however, no definition of "impartial witness" is provided:

A person who speaks and understands English, but does not read and write, can be enrolled in a study by "making their mark" on the consent document, when consistent with applicable state law.

A person who can understand and comprehend spoken English, but is physically unable to talk or write, can be entered into a study if they are competent and able to indicate approval or disapproval by other means. If (1) the person retains the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is explained verbally (still competent) and (2) is able to indicate approval or disapproval to study entry, they may be entered into the study. The consent form should document the method used for communication with the prospective subject and the specific means by which the prospective subject communicated agreement to participate in the study. An impartial third party should witness the entire consent process and sign the consent document. A video tape recording of the consent interview is recommended.

Another FDA recognized guidance, the ICH "E6 Good Clinical Practice: Consolidated Guidance", available at www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073122.pdf, does include a definition of "impartial witness" in section 1.26:

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.

As you can see, the definition of "impartial witness" includes that the witness be independent.

The E6 guidance also discusses the impartial witness in sections 4.8.6 and 4.8.9:

4.8.6 The language used in the oral and written information about the trial, including the written informed consent form, should be as nontechnical as practical and should be understandable to the

subject or the subject's legally acceptable representative and the impartial witness, where applicable.

4.8.9 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.

By definition, a legally authorized representative means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research (see 21 Code of Federal Regulations (CFR) § 50.3(l)). The regulations for general requirements for informed consent state that no investigator may involve a human being as a subject in research unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative (LAR).

A witness should be a neutral and impartial third party. **When required, a witness should be an impartial adult such as, for example, an adult who is not a member of the study team and who is not a family member of the participant**. A signature of the witness means the requirements for informed consent have been satisfied and consent is voluntary and freely given by the participant, guardian, or legally-authorized representative.

I hope this information is helpful. Please contact us again at gcp.questions@fda.hhs.gov should you have additional questions.

Kind regards,

Doreen M. Kezer, MSN
Senior Health Policy Analyst
Office of Good Clinical Practice
Office of the Commissioner, FDA

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**From:** [redacted]
**Sent:** Wednesday, January 04, 2017 2:43 AM
**To:** OC GCP Questions
**Subject:** a question about illiterate trial subject
**Importance:** High

**Proprietary**

Dear Sir/Madam,

I would like to consult you about illiterate trial subject informed consent process and sign-off.

For an oncology trial, if an illiterate trial subject co visited investigator, his legal representative (husband or son) accompany with him, during the informed consent process, can his legal representative is considered as “an impartial witness”？ Per my understanding, the subject legal representative also has some kind of “potential partiality” with trial subject, e.g. trial subject participates clinical study which may save some medical care cost , so my question is: whether the legal representative or relatives of illiterate trial subject can be considered as “impartial witness” in clinical study ? There are lots of debates and different opinion on it.

Your feedback is highly appreciated.

[redacted]