question regarding consent of illiterate volunteersFrom: Lee, Bonnie on behalf of OC GCP Questions
Sent: Thursday, May 02, 2002 12:49 PM
To: [purged]
Subject: RE: question regarding consent of illiterate volunteers

[purged], I think that the only thing missing from your summary is my colleague's suggestion that when subjects are illiterate, then the short form ought to be used, because one is relying on a verbal explanation.

Bonnie

Bonnie M. Lee
Associate Director for Human Subject Protection Policy
Office for Good Clinical Practice
Office of Science Coordination & Communication, HF-34
Food and Drug Administration
5600 Fishers Lane, Parklawn, Room 9C24
Rockville, MD 20857
Telephone: 301-827-1259
Fax: 301-827-1169
E-Mail: BLee@oc.fda.gov

-----Original Message-----
From: [purged]
Sent: Tuesday, April 30, 2002 7:18 PM
To: 'OC GCP Questions'
Subject: RE: question regarding consent of illiterate volunteers

Dear Bonnie,

I greatly appreciate your help and patience with my questions. Your colleague is correct in assuming that both US and in-country IRBs with assurances on file with OHRP review our research I do not want to belabor this matter further, but just to be absolutely sure that I understand you, let me repeat my understanding of what you have said.... As long as the alternative approach is a) approved by both the relevant in-country and US IRBs and b) adheres to 21 CFR parts 50 and 56 and 45 CFR part 46 (the latter of which refers to a witness to the oral presentation only in the context of using a short form, which we do NOT use), it would be considered acceptable. Therefore, with these conditions met, an alternative to the to Section 4.8.9 of the Guideline for GCP, (which I believe is the only place that it is specifically stated

that a witness must be present for the entire consent process), would be acceptable. Please let me know if I have misunderstood this.

Your suggestion of having a designated subject advocate is very helpful and would be a good approach.

Thank you very much for your help.

[purged]
-----Original Message-----
From: OC GCP Questions [mailto:GCPQuestions@OC.FDA.GOV]
Sent: Thursday, April 25, 2002 11:20 AM
To: [purged]
Subject: RE: question regarding consent of illiterate volunteers

[purged], As to your latter point, I think that this is one reason why the regulations state that the IRB has the authority to monitor the consent process. Also, there is nothing to preclude the IRB--who may have greater knowledge of the subject population--from requiring a witness or third party for "naive" but literate subjects. Remember, the regulations only establish a minimum standard.

I shared what I sent to you with my colleague, who wrote back: "What you wrote looks fine. Under 50.27, because the subject cannot read...the short form and witness method should be used for documentation (although the subject should be given all of the relevant info that would be in the long version)--also note this research doesn't qualify for one of the exceptions in 56.109(c). And, like you implied, the purpose of having the witness is to make sure the oral presentation is accurate and comprehensive.

I think she said the study is federally funded (45 CFR 46 applies)--and her phone has a 919 area code--so her US institution's IRB would review the study along with the in-country IRB. Plus, they'll need to have an assurance filed with OHRP for the African IRB/institution... I think all of these folks will review the consent process--and determine what is appropriate."

Thus, I'd modify your conclusion by saying that both the U.S. and local IRB would need to agree to the alternative method, and that alternative would need to be consistent with our requirements (if it is FDA-regulated, then it would need to comply with 21 CFR parts 50 and 56; if it is federally funded, then it would need to comply with 45 CFR part 46; and if both are true, then

it would need to comply with all cited regulations). Hope this helps.

Bonnie

Bonnie M. Lee
Associate Director for Human Subject Protection Policy
Office for Good Clinical Practice
Office of Science Coordination & Communication, HF-34
Food and Drug Administration
5600 Fishers Lane, Parklawn, Room 9C24
Rockville, MD 20857
Telephone: 301-827-1259
Fax: 301-827-1169
E-Mail: BLee@oc.fda.gov

-----Original Message-----
From: [purged]
Sent: Tuesday, April 23, 2002 6:09 PM
To: 'OC GCP Questions'
Subject: RE: question regarding consent of illiterate volunteers

Dear Bonnie,

Thank you very much for your response. If I understand correctly, an alternative approach would be acceptable, IF (and only if) the local IRB agreed to it. If I have misunderstood you in this regard, please let me know.

This issue is rather complex in general and further complicated by confidentiality issues associated with HIV-related research. One question we face over and over from investigators and study staff is how we can trust the person conducting the consent discussion to do it completely and well when the subject is in some [perhaps subjective and/or arbitrary] way deemed to be "literate" and yet not when the subject is in some way deemed "illiterate", when that distinction is very difficult to make and possibly meaningless with regard to someone's ability to comprehend concepts that are in all likelihood quite complicated or foreign to them. In other words, if the presence of a second person really ensures thoroughness and adequacy of the consent discussion and indeed does not hinder the process in any way, why is it not required across the board for all potential study subjects? I am not posing this question to you specifically - only sharing some of the thoughts behind a proposal for an alternative approach.

Thanks again for your help. I look forward to any further advice from you or your colleagues on this matter.

[purged]

-----Original Message-----
From: OC GCP Questions [mailto:GCPQuestions@OC.FDA.GOV]
Sent: Tuesday, April 23, 2002 2:26 PM
To:[purged]
Subject: RE: question regarding consent of illiterate volunteers

[purged],

Please consider this an interim reply because I would like to talk with one of my colleagues to get her thoughts, and she's out of the office for a few days. However, because you indicated that you "urgently" needed some clarification, I will provide what I can now.

First, it is the responsibility of the IRB to review and determine the adequacy of the proposed informed consent process. I think that the questions that you have asked could best be addressed by an IRB in the country where the research will be conducted. That IRB would be the most knowledgeable of whether, as you assert, the presence of an observer would be "intimidating and inhibiting" or whether, through the choice of an appropriate individual, such a person might be supportive and helpful.

I do not think that an "impartial" witness necessarily needs to be someone who is totally unaffiliated with the study. It may be possible, for example, to designate a "subject advocate" who would be available at each site for subjects--both as a witness as well as as an individual available throughout the trial to answer questions and be supportive of the subjects. I agree with you that "impartiality" can be interpreted differently and approached in practice in different ways.

My concern with your alternative approach is that if the "second person" is not present during the entire consent process, I do not see how that individual would be able to attest that "the information in the consent form was accurately explained." I agree the individual may, through questions and answers, determine whether the subject understood the information covered by the specific questions; but it would be difficult

to ask enough questions to cover all information conveyed during the consent process.

I do not know whether it would be inhibiting to have a stranger--described as a subject advocate--present during the consent process; or whether, in fact, it might be more inhibiting to have an observer the subject knows. It may be more inhibiting to have the latter. I think this is where the views of the local IRB could be very useful.

I believe you can apply the GCP standards without compromising the consent process. I do not think, however, that the alternative approach that you described is consistent with the GCP guidelines.

If my colleague has additional thoughts on this matter, I will let you know. I hope this is somewhat helpful to you. I'm sorry that I can't in good conscience simply bless your alternative approach.

Bonnie
Bonnie M. Lee
Associate Director for Human Subject Protection Policy
Office for Good Clinical Practice
Office of Science Coordination & Communication, HF-34
Food and Drug Administration
5600 Fishers Lane, Parklawn, Room 9C24
Rockville, MD 20857
Telephone: 301-827-1259
Fax: 301-827-1169
E-Mail: BLee@oc.fda.gov

-----Original Message-----
From: [purged]
Sent: Thursday, April 18, 2002 9:30 AM
To: 'gcpquestions@oc.fda.gov'
Subject: question regarding consent of illiterate volunteers
Importance: High

Dear Madame or Sir,
I urgently need clarification on application of Section 4.8.9 of the Guideline for GCP, which states that 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" and then signs the consent form attesting that the

information in the consent form was accurately explained to and understood by the subject and that the subject freely agreed to participate.

The organization for which I work is involved in the planning and implementation of federally funded clinical trials among HIV infected and HIV uninfected men and women in developing countries - primarily in Africa - where there is a high rate of illiteracy and where the stigma associated with HIV infection remains high, particularly for women. This cultural environment and the nature of the studies (HIV-related) makes strict application of the above requirement problematic for several reasons. Therefore, I am seeking clarification from you about whether alternative approaches to ensuring appropriate informed consent for illiterate subjects would be considered acceptable and, if so, what specific documentation would be required.

The requirement that a second person be present for the entire consent process may introduce a situation in which true informed consent may not be achieved, for example, if an HIV infected woman does not feel comfortable asking questions about the study or does not feel free to talk about her infection status. Having an observer present, particularly if not known to the subject, can be intimidating and inhibiting, especially in the context of HIV-related research.

In addition, in populations in which the illiteracy rate is very high, the need for an "impartial" witness to be present during the entire consent process becomes difficult to arrange, as this could mean having someone unaffiliated with the study "on call" or busy all day, every day of the accrual period, which is not typically feasible. And of course, it is not helpful to have someone who may not fully understand the study him/herself in this role. "Impartiality" of the witness, can be interpreted differently and approached in practice in different ways. Any advice you can give on this aspect of the requirement would be appreciated, however, my larger, more immediate question follows:

Would the following alternative approach be considered acceptable, and if so, what level of approval and documentation would be required?

Instead of being present for the entire consent process, a second person (e.g. a nurse/counselor, perhaps affiliated in some way with the study) would talk with the subject and ask her questions (i.e. conduct a short interview) after the investigator or designee has completed the informed consent discussion with him/her and s/he has verbally agreed to participate. If the subject demonstrates understanding and willingness to participate, the second person would sign the consent form as the witness (along with the subject and

investigator), attesting that the information was accurately explained to and apparently understood by the subject and that she freely agrees to participate in the study (the same attestation as called for in the cited Guideline above).

Can you please confirm whether this alternative approach would be considered acceptable? Would it need to be approved by the relevant IRB before implementation? What other documentation would be required?

I wish to acknowledge that in 21 CFR 50.27, the issue of a witness to the consent process is mentioned, though only in the context of using a "short form" (which does NOT apply to our research as we use the full consent form) and does not explicitly refer to the context of consenting illiterate volunteers. Because there is obviously a continuum of literacy and recognizing that just because someone can read a little does not mean that s/he can fully comprehend the content of an informed consent form regarding a clinical drug trial, we emphasize the need for the person conducting the informed consent discussion to carefully read each paragraph of the entire written consent to and review the information thoroughly with each potential subject, encouraging him or her to ask questions and so forth. In other words, because of the low level of literacy in the population in general, the study investigators/staff typically err on the conservative side in administering the consent process.

Please let me know if there is a more appropriate email address or phone contact for this question.

Thank you in advance for your prompt reply.

[purged]