From: Hommel, Carolyn - OC on behalf of OC GCP Questions
Sent: Thursday, June 03, 2004 8:54 AM
To: [Redacted]
Subject: RE: telephone consents, fda approved protocol containing regulation violations

Dear Ms. [Redacted] :

In response to your question, FDA would view obtaining consent by telephone only as being contrary to FDA's regulations.

Sincerely,

Carolyn Hommel
Consumer Safety Officer
Good Clinical Practice Program
Office of Science and Health Coordination
Office of the Commissioner
U.S. Food and Drug Administration (HF-34)
5600 Fishers Lane, Room 9C24
Rockville, MD 20857

Phone: 301/827-3340
Fax: 301/827-1169

This communication does not constitute a written advisory opinion under 21 CFR 10.85, but rather is an informal communication under 21 CFR 10.85(k) which represents the best judgment of the employee providing it. This information does not necessarily represent the formal position of FDA, and does not bind or otherwise obligate or commit the agency to the views expressed.

-----Original Message-----
From: [Redacted]
Sent: Wednesday, June 02, 2004 5:46 PM
To: OC GCP Questions
Subject: Re: telephone consents, fda approved protocol containing regulation violations

Dear Ms. Hommel: You do not appear to understand the issue. The clarification is regarding the company's position that obtaining telephone consent ONLY is acceptable. Please refer back to the original email. I am fully aware of the acceptability and circumstances that are appropriate for telephone/fax consent. If you still do not understand the question, I would greatly appreciate contact information for a superior of yours. Thank you for your attention to this matter.
Sincerely, [Redacted]

----- Original Message -----
From: OC GCP Questions
To: [Redacted]
Sent: Wednesday, June 02, 2004 10:41 AM
Subject: RE: telephone consents, fda approved protocol containing regulation violations

Dear Ms. [Redacted]:

In the past, FDA has allowed sites to obtain consent by telephone and fax if, for some reason, consent cannot be obtained in person. For example,

this might be appropriate if the potential subject lives in another state and the study site wants to screen the individual to determine his eligibility for the study before the individual spends a lot of money or time traveling to the study site. In such a situation, FDA would expect the consent form to be faxed to the subject or his legally authorized representative (LAR), discussed by phone, and faxed back to the CI. The purpose is to provide the subject and/or the LAR with an opportunity to discuss the information in the consent form and have their questions answered prior to the subject's enrollment in the study.

It sounds as though the form that you are anticipating using is a "short form" which would require a witness and a written summary of the discussion that has been approved by the IRB (21 CFR 50.27(b)(2)). You mention a witness, but you do not mention the written summary which is a required part of the written information to be provided to the subject.

FDA has said that consent can be obtained by telephone and fax when there is a need to do so. While you have indicated that the subjects may be incapacitated (e.g., sedated), you haven't indicated why enrollment of the subject could not be delayed until the LAR could come and discuss the various options in person. Once that is explained, it would be up to the reviewing IRB to decide whether this type of consent process would be acceptable, and whether it complies with applicable state or local laws.

You may wish to review FDA's "Information Sheets: Guidance for Institutional Review Boards and Clinical Investigators," posted on FDA's Good Clinical Practice website (http://www.fda.gov/oc/gcp ; once on the web page, click on "Guidance and Information Sheets"; it's the first item in the list.) Questions 34, 35, 39, 41, and 44 seem particularly pertinent to your questions. I have pasted them into this e-mail for your convenience, but I would urge you to review the Information Sheets in their entirety.

34. Is getting the subject to sign a consent document all that is required by the regulations?

No. The consent document is a written summary of the information that should be provided to the subject. Many clinical investigators use the consent document as a guide for the verbal explanation of the study. The subject's signature provides documentation of agreement to participate in a study, but is only one part of the consent process. The entire informed consent process involves giving a subject adequate information concerning the study, providing adequate opportunity for the subject to consider all options, responding to the subject's questions, ensuring that the subject has comprehended this

information, obtaining the subject's voluntary agreement to participate and, continuing to provide information as the subject or situation requires. To be effective, the process should provide ample opportunity for the investigator and the subject to exchange information and ask questions.

35. May informed consent be obtained by telephone from a legally authorized representative?

A verbal approval does not satisfy the 21 CFR 56.109(c) requirement for a signed consent document, as outlined in 21 CFR 50.27(a). However, it is acceptable to send the informed consent document to the legally authorized representative (LAR) by facsimile and conduct the consent interview by telephone when the LAR can read the consent as it is discussed. If the LAR agrees, he/she can sign the consent and return the signed document to the clinical investigator by facsimile.

39. Who should be present when the informed consent interview is conducted?

FDA does not require a third person to witness the consent interview unless the subject or representative is not given the opportunity to read the consent document before it is signed, see 21 CFR 50.27(b). The person who conducts the consent interview should be knowledgeable about the study and able to answer questions. FDA does not specify who this individual should be. Some sponsors and some IRBs require the clinical investigator to personally conduct the consent interview. However, if someone other than the clinical investigator conducts the interview and obtains consent, this responsibility should be formally delegated by the clinical investigator and the person so delegated should have received appropriate training to perform this activity.

44. Are there alternatives to obtaining informed consent from a subject?

The regulations generally require that the investigator obtain informed consent from subjects. Investigators also may obtain informed consent from a legally authorized representative of the subject. FDA recognizes that a durable power of attorney might suffice as identifying a legally authorized representative under some state and local laws. For example, a subject might have designated an individual to provide consent with regard to health care decisions through a durable power of attorney and have specified that the individual also has the power to make decisions on entry into research. FDA defers to state and local laws regarding who is a legally authorized representative. Therefore,

the IRB should assure that the consent procedures comply with state and local laws, including assurance that the law applies to obtaining informed consent for subjects participating in research as well as for patients who require health care decisions."

Alternatives 1 and 2 are provided for in the regulations and are appropriate. Alternative 3 allows a designated individual to provide consent for a patient with regard to health care decisions and is appropriate when it specifically includes entry into research. FDA defers to state and local laws regarding substituted consent. Therefore, the IRB must assure itself that the substituted consent procedures comply with state and local law, including assurance the law applies to obtaining informed consent for subjects participating in research as well as for patients who require health care decisions.

41. Must a witness observe the entire consent interview or only the signature of the subject?

FDA does not require the signature of a witness when the subject reads and is capable of understanding the consent document, as outlined in 21 CFR 50.27(b)(1). The intended purpose is to have the witness present during the entire consent interview and to attest to the accuracy of the presentation and the apparent understanding of the subject. If the intent of the regulation were only to attest to the validity of the subject's signature, witnessing would also be required when the subject reads the consent form.

I hope this is helpful.

Sincerely,

Carolyn Hommel
Consumer Safety Officer
Good Clinical Practice Program
Office of Science and Health Coordination
Office of the Commissioner
U.S. Food and Drug Administration (HF-34)
5600 Fishers Lane, Room 9C24
Rockville, MD 20857

Phone: 301/827-3340
Fax: 301/827-1169

This communication does not constitute a written advisory opinion under 21 CFR 10.85, but rather is an informal communication under 21 CFR 10.85(k) which represents the best judgment of the employee providing it. This information does not necessarily represent the formal position of FDA, and does not bind or otherwise obligate or commit the agency to the views expressed.

-----Original Message-----
From: [Redacted]
Sent: Tuesday, June 01, 2004 2:42 PM
To: OC GCP Questions
Subject: Re: telephone consents, fda approved protocol containing regulation violations

Dear Carolyn: Many of the subjects will not be sedated...this was just an example mentioned in the protocol. These are early [Redacted] candidates. The major point is that the fda has already told the company that this drug would not qualify as emergency use as [Redacted] is commercially available. I am not aware that there are any other circumstances that would allow for telephone consent. Please feel free to call me at [Redacted] if I can provide further clarification. Thanks for your attention to this matter. [Redacted]

----- Original Message -----
From: OC GCP Questions
To: [Redacted]
Sent: Tuesday, June 01, 2004 2:19 PM
Subject: RE: telephone consents, fda approved protocol containing regulation violations

Dear Ms. [Redacted] :

There is not enough information in your e-mail to provide a definitive response. Why can't the study be explained to the potential study subjects before they are sedated?

Sincerely,

Carolyn Hommel
Consumer Safety Officer
Good Clinical Practice Program
Office of Science and Health Coordination
Office of the Commissioner
U.S. Food and Drug Administration (HF-34)
5600 Fishers Lane, Room 9C24
Rockville, MD 20857

Phone: 301/827-3340
Fax: 301/827-1169

This communication does not constitute a written advisory opinion under 21 CFR 10.85, but rather is an informal communication under 21 CFR 10.85(k) which represents the best judgment of the employee providing it. This information does not necessarily represent the formal position of FDA, and does not bind or otherwise obligate or commit the agency to the views expressed.

-----Original Message-----
From: [Redacted]
Sent: Wednesday, May 26, 2004 5:14 PM
To: gcpquestions@oc.fda.gov
Subject: telephone consents, fda approved protocol containing regulation violations

Dear Mr. LePay:

I spoke earlier today with Jim McCormick and he suggested that I write you to obtain a written response to the issues we discussed earlier today so that I may pass your response along to a Sponsor regarding my concerns.

We have recently received a protocol from a major pharmaceutical company that within the text of the protocol (which has been reviewed by the FDA) indicates the following:

"It is anticipated that many subjects who will be eligible for this protocol will not be able to give consent themselves due to sedation or other reasons. Therefore, the following options for obtaining consent via a legally acceptable representative are available, subject to local regulations and laws relating to the enrollment of incapacitated adults into clinical trials:-
- Consent from legally acceptable representative in person
-Verbal consent from legally acceptable representative via telephone (at least 2 people from the study site are required, 1 to administer the informed consent and the second as a witness)
-Verbal consent from legally acceptable representative via telephone, confirmed by signed consent form sent by fax

When consent is obtained verbally or by fax via a legally acceptable representative, an original signature should be obtained at the earliest opportunity if possible."

The Sponsor is very clear that their drug does not fit in the emergency use situation. The inclusion of this telephone consent option stems from a planning meeting in which one of their sites indicated that their IRB allows this practice. Additionally the Sponsor template for the informed consent includes this option.

Upon discussion with the Sponsor regarding my concerns it was indicated that there had been numerous discussions regarding this option within the company but that QA/Regulatory Affairs had signed off on it. There have also been several meetings with the FDA re the protocol and apparently no one has questioned the inclusion of this procedure for consent. I have directed the person I spoke with at the Sponsor company to your Q&A site on the internet addressing telephone consent and mentioned a number of other written sources deeming this as an unacceptable practice. I would be most appreciative if you could address this issue in writing so that I may pass the information along to the Sponsor to avoid what I foresee will be future problems. Unfortunately, many assume that if the FDA approves a

protocol including procedures that violate federal regulation, the FDA is waiving applicable regulation.

Thank you for your time and attention to this matter.

Sincerely,

[Redacted]