From: Hommel, Carolyn - OC on behalf of OC GCP Questions
Sent: Tuesday, November 22, 2005 4:12 PM
To: [purged]
Cc: [purged]
Subject: RE: Drugfo/o Comment Form FDA/CDER Site

Dear Ms. [purged]:

Your questions about the circumstances under which a 1572 is required to be signed by a foreign clinical investigator, were forwarded to me for a response.

Question 1. You indicated that you have noticed that sites sometimes "cross out the reference to the CFRs on the 1572, as they consider that Australian regulations should apply instead." You asked if this invalidates the 1572 or would cause problems with the IND.

Answer 1. The short answer is, if a non-US study is conducted under an Investigational New Drug Application (IND), then ALL FDA IND regulations, including the requirement to obtain a signed 1572, must be met.

We are aware that a non-US investigator may be reluctant to sign a 1572, because the investigator cannot commit to all of the requirements on the form (for example, institutional review board (IRB) membership requirements as outlined in 21 CFR 56.107)). If there is a specific requirement in the IND regulations which the investigator cannot comply with, the sponsor may request a waiver of the specific requirement from FDA. (See 21 CFR 56.105 (for waiver of IRB requirements) and 21 CFR 312.10, for waiver of applicable requirements under 21 CFR 312.) [I have pasted the text of 312.10 into this e-mail for your convenience, but all of FDA's regulations may be viewed on FDA's good clinical practice website at http://www.fda.gov/oc.gcp..]

PART 312--INVESTIGATIONAL NEW DRUG APPLICATION

Subpart A--General Provisions

Sec. 312.10 Waivers.

(a) A sponsor may request FDA to waive applicable requirement under this part. A waiver request may be submitted either in an IND or in an information amendment to an IND. In an emergency, a request may be made by telephone or other rapid communication means. A waiver request is required to contain at least one of the following:
(1) An explanation why the sponsor's compliance with the requirement is unnecessary or cannot be achieved;
(2) A description of an alternative submission or course of action that satisfies the purpose of the requirement; or
(3) Other information justifying a waiver.
(b) FDA may grant a waiver if it finds that the sponsor's noncompliance would not pose a significant and unreasonable risk to human subjects of the investigation and that one of the following is met:
(1) The sponsor's compliance with the requirement is unnecessary for the agency to evaluate the application, or compliance cannot be achieved;
(2) The sponsor's proposed alternative satisfies the requirement; or
(3) The applicant's submission otherwise justifies a waiver.

[52 FR 8831, Mar. 19, 1987, as amended at 52 FR 23031, June 17, 1987; 67 FR 9585, Mar. 4, 2002]

Question 2: You said, "Secondly, some companies have taken the approach of collecting a signed 1572 form from sites, even if the site is not participating in a study conducted under the IND. In these cases, data may be submitted to the FDA in support of a registration of a new drug or a change in labelled product information. These studies would be conducted in accordance with appropriate local and international GCP and ethical requirements. The belief is that having the 1572 will smooth the passage of the data with the FDA, even if the study is not under the IND. Is this an appropriate thing to do? Does a 1572 in these circumstances have any meaning? Also, is it then appropriate to cross out reference to the CFRs for a 1572 collected in a study not conducted under an IND, as the CFRs will definitely not be applied in such a case?"

Answer 2: If a study is conducted outside of the U.S. and it is NOT conducted under an IND, then the investigator would NOT be required by FDA to sign a 1572, nor would having the form in the file have any effect on FDA's consideration of the data. Sponsors may ask investigators to sign a 1572 for some other reason, for example, to obtain assurance that the investigator will conduct the study according to good clinical practice, but as I said above, the form is NOT required for studies that are NOT conducted under an IND.

The criteria for accepting data from non-US studies NOT conducted under an IND are set forth in 21 CFR 312.120. FDA proposed to revise this regulation in June 2004 (http://www.fda.gov/oc/gcp/draft.html). The notice proposes replacing the requirement that non-US studies be conducted in accordance with ethical principles stated in the Declaration of Helsinki with a requirement that the studies be conducted in accordance with good clinical practice (GCP), including review and approval by an independent ethics committee (IEC). The proposed rule is intended to update the standards for the acceptance of non-IND foreign studies and to help ensure the quality and integrity of data obtained from such studies. You might want to check our website periodically to see if the final rule has been published.

I hope this answers your questions.

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

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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: [purged]
Sent: Monday, November 21, 2005 2:59 PM
To: OC GCP Questions
Subject: FW: Drugfo/o Comment Form FDA/CDER Site

I have tried to provide this person with an adequate answer but apparently it is beyond my scope. Can someone provide me with more detail or the emailer? Thank you!

Christine Oliver

-----Original Message-----
From: [purged]
Sent: Tuesday, November 01, 2005 2:39 PM
To: "CDER DRUGINFO"
Subject: RE: Drugfo/o Comment Form FDA/CDER Site

Thank you for the information, however, it still leaves two key parts of my question unanswered. If the study is NOT being conducted under the IND (an international study with no US sites), is there any advantage to getting investigators to sign the 1572?

Is it acceptable to amend the 1572 by crossing out reference to the CFRs in this case?

I appreciate because these situations are not of the norm, it is difficult for you to provide advice. If you could give me your opinion on the practice, that would be helpful.

Many thanks

[purged]

-----Original Message-----
From: CDER DRUGINFO [mailto:DRUGINFO@cder.fda.gov]
Sent: Wednesday, 2 November 2005 3:47 AM
To: [purged]
Subject: RE: Drugfo/o Comment Form FDA/CDER Site

Dear [purged],

Thank you for your message to the Division of Drug Information in the Center for Drug Evaluation and Research (CDER).

If a multinational or non-U.S. study is conducted under a U.S. IND as you describe (which presumes that the sponsor of the study has indicated that all sites, both U.S. and non-U.S., will be operating under the IND), then the Form FDA 1572 is required from all investigators (U.S. and non-U.S.) in accordance with FDA IND requirements.

The 1572 has two important functions. First of all, the 1572 is intended to provide the sponsor with information about the clinical site and investigator qualifications that will enable the sponsor to establish and document that the investigator and site are qualified to conduct the study. The second important purpose of the 1572 is to obtain the clinical investigator's commitment that he/she will conduct the study in accordance with the approved protocol, and will comply with all of the requirements for conducting such studies as set forth in 21 CFR 312, 50, and 56.

Many people are don't realize that the 1572 itself is not required to be submitted to FDA, although in practice, sponsors often submit the 1572 to the IND as an efficient means to provide the information required under 21 CFR 312.23(a)(6)(iii)(b):

"(b) The name and address and a statement of the qualifications (curriculum vitae or other statement of qualifications) of each investigator, and the name of each subinvestigator (e.g., research fellow, resident) working under the supervision of the investigator; the name and address of the research facilities to be used; and the name and address of each reviewing Institutional Review Board."

Thank you again for your message. We hope that the above information will help answer your question.

Sincerely,
Cdrdrugfo/o

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: [purged]
Sent: Sunday, October 30, 2005 5:43 PM
To: drugfo@cder.fda.gov
Subject: Drugfo/o Comment Form FDA/CDER Site

Name: [purged]

E-Mail: [purged]
Comments: Hi

I was wondering if you could help with some questions regarding the 1572 form. Statement of Investigator.

I work in Australia and conduct training courses and clinical trial audits and one of the questions I get commonly is "When is a 1572 required and when is it not required?" I understand that if sites are included under the IND then a 1572 should be completed by each Principal Investigator. In some cases, I have noticed that sites cross out the reference to the CFRs on the 1572, as they consider that Australian regulations should apply instead. What is your opinion on doing this and does it invalidate the 1572 and cause problems with the IND?

Secondly, some companies have taken the approach of collecting a signed 1572 form from sites, even if the site is not participating in a study conducted under the IND. In these cases, data may be submitted to the FDA in support of a registration of a new drug or a change in labelled product information. These studies would be conducted in accordance with appropriate local and international GCP and ethical requirements. The belief is that having the 1572 will smooth the passage of the data with the FDA, even if the study is not under the IND. Is this an appropriate thing to do? Does a 1572 in these circumstances have any meaning? Also, is it then appropriate to cross out reference to the CFRs for a 1572 collected in a study not conducted under an IND, as the CFRs will definitely not be applied in such a case?

Your advice regarding these matters would be much appreciated.

With best wishes

[purged]