From: Hommel, Carolyn - OC on behalf of OC GCP Questions
Sent: Tuesday, January 18, 2005 9:17 AM
To: [purged]
Subject: RE: FDA Form 1572

Dear [purged]:

FDA is often asked if non-U.S. clinical investigators need to sign a Form FDA-1572, "Statement of Investigator" (1572). The 1572 enables a clinical investigator to provide specific information about the study to the study sponsor, for example, the address of all sites at which the research will be conducted, the name and address of any clinical laboratories or other facilities that will be used, the name and address of the ethics committee that will review the study, etc. By signing the 1572, the clinical investigator also provides his personal commitment to comply with FDA requirements for the conduct of the study.

The answer to the question of whether a 1572 is needed for a study conducted outside of the U.S. depends on whether or not the sponsor of the study claims this to be an "IND study" --- that is, conducted under a U.S. IND. Studies conducted in the United States must be conducted under an IND (with certain exceptions listed in 21 CFR 312.2); studies conducted in other countries are not required to be conducted under an IND. However, if/once a sponsor claims a study as an "IND study", then all U.S. IND regulations must be met. (These regulations are contained in 21 CFR Parts 50, 54, 56, 312, 314, 812, and 814) which are accessible from our GCP website (www.fda.gov/oc/gcp; click on "Regulations").

Non-US investigators may be reluctant to sign a 1572 because, for example, they cannot guarantee that the ethics committee that reviews their study will meet all of the requirements for IRBs in FDA's regulations (21 CFR 56). The requirements pertaining to IRB membership (21 CFR 56.107) have proven particularly troublesome for non-US investigators. The 1572, however, requires the clinical investigator to commit to (among other things) ensuring that the IRB that reviews and approves the research study will comply with 21 CFR 56 (See item 9, bullet #8). Because non-US clinical investigators may not be able to guarantee this (due to the differences in US-IRBs and international ethics committees), they consequently do not wish to sign the 1572.

It may be helpful for you to know that under 21 CFR 312.10, sponsors may request waiver of applicable IND requirements. I have pasted the text of the regulation into this e-mail for your convenience:

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]

In other words, the sponsor of an IND study being conducted at a non-US location can request a waiver of this particular requirement. For example, by describing and providing information about the ethics committee that will be reviewing the study, the sponsor can show that although the ethics committee may not meet the membership provisions of 21 CFR 56.107, nevertheless, in all other ways it complies with existing requirements for ethical review of the study and assures the protection of the rights and welfare of the human subjects, etc. FDA can then determine if the information provided by the sponsor is sufficient to grant the waiver.

Please also be assured that FDA is currently evaluating other options to address this particular issue.

More commonly, the sponsor claims that the non-U.S. sites are not operating under a U.S. IND. If it is not under an FDA IND, then no 1572 is required by FDA. (Sponsors may develop their own SOPs and ask for the information in the 1572 for internal purposes, but this is not an FDA requirement unless the study is being conducted under an IND.)

The criteria for FDA acceptance of a non-U.S. drug study not under an IND (for purposes of review, in support of a research or marketing application) are set forth in 21 CFR 312.120 and 21 CFR 314.106. (These regulations are also accessible for the website above.) Among the criteria listed in these regulations is the requirement that the study be well-designed, conducted by qualified investigators, available for FDA inspection, and conducted in conformance with the Declaration of Helsinki (older versions as listed) or national/local requirements if the latter provide greater protection that Helsinki. In general, most regulatory authorities in developed countries have established legislation/regulations that provides greater protection than Helsinki, and so we expect these national laws/regulations to be adhered to. Furthermore, in most developed countries, these national/local regulations closely parallel provisions of the International Conference on Harmonization Good Clinical Practice guideline (and/or some other internationally accepted GCP guideline --- e.g., the WHO GCP guideline which is currently under revision to even more closely parallel ICH provisions). ICH GCP is officially recognized guidance in the U.S. and is accessible from the FDA GCP website above (link to Guidances). I

This is a rather long response to your inquiry, but I hope it answers your questions.

Carolyn
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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: Sunday, January 16, 2005 11:09 PM
To: GCPQuestions@OC.FDA.GOV
Subject: FDA Form 1572

Dear Carolyn,

Are investigators required to complete Form 1572 for IND/NDA studies' participation? According to some local monitors, Form 1572 could be waived as local investigators are non-US citizens; they are not bound by US laws/regulations. Does it make sense to you?

Regards,

[purged}