From: OC GCP Questions
Sent: Friday, July 17, 2015 4:02 PM
To: [redacted]
Subject: RE: Question Foreign clinical study and form 1572

Dear [redacted]–
The Statement of Investigator, Form FDA 1572 (1572), is an agreement signed by the investigator to provide certain information to the sponsor and assure that he/she will comply with FDA regulations related to the conduct of a clinical investigation of an investigational drug or biologic. The most recent version of the 1572 is available online at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM074728.pdf.

Whenever a sponsor selects a new investigator to participate in a clinical investigation that is being conducted under an investigational new drug application (IND), the sponsor must obtain a completed and signed 1572 before permitting the investigator to begin participation in the clinical investigation (21 CFR 312.53(c)). Although the sponsor is required to collect the 1572 from the investigator, FDA does not require the form to be submitted to the agency.

Regarding foreign studies, the 1572 form guidance (link below) http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM214282.pdf states --

10. Must investigators who conduct studies outside of the United States sign a 1572?
If a foreign clinical study is conducted under an IND, then all FDA IND regulations, including the requirement to obtain a signed 1572, must be met. If a clinical study is conducted outside of the U.S. and is not conducted under an IND, then the investigator need not sign a 1572. If local laws or regulations prohibit the signing of a 1572, FDA would expect the sites to operate as non-IND sites and the study conducted as a non-IND study. If the study data is to be submitted to support a marketing application (e.g., a new drug application (NDA)), the study must be conducted in compliance with 21 CFR 312.120.

11. If a foreign clinical study is being conducted under an IND, what are the investigator's responsibilities with respect to local laws and regulations?
Investigators are responsible for complying with the applicable laws and regulations of the country in which the study is being conducted, regardless of whether the study is being conducted under an IND. We recommend that sponsors obtain signed, written statements from investigators acknowledging their commitment to comply with local laws and requirements. In addition, if a foreign clinical study is being conducted under an IND, the investigator must sign Form FDA 1572 (investigator statement) and ensure that the study is conducted in accordance with the investigator statement and all other applicable regulations under 21 CFR Part 312.

12. For foreign clinical studies conducted under an IND, how can an investigator sign the 1572 when the investigator knows he/she cannot commit to all of the requirements on the form, specifically IRB membership (21 CFR 56.107)?
IRB review and approval is required before a clinical study can be initiated under an IND (21 CFR 56.103(a)). FDA may waive any of the IRB requirements for specific research activities or for classes of research activities otherwise covered by the IRB regulations (21 CFR 56.105), but FDA uses the waiver provision only when alternative mechanisms for ensuring protection of the rights and welfare of human subjects are acceptable. The most common circumstance for which FDA receives a waiver request is when a sponsor

Investigators conducting studies outside of the U.S. may want to consult with local regulatory authorities for additional guidance when considering whether to conduct studies under an IND
wishes to conduct a foreign clinical study under an IND. In this case, typically an Independent Ethics Committee (IEC) that operates in accordance with Good Clinical Practice (GCP) is utilized instead of a U.S. IRB. Although its membership and functions for assuring human subject protection are comparable to an IRB, an IEC may not meet all of the IRB requirements contained in 21 CFR Part 56.

For a foreign study, an IRB waiver request should contain a description of alternative mechanisms for assuring human subject protection. It would generally be acceptable for a waiver request to state the intention to use an IEC that complies with GCP (e.g., ICH E6) instead of an IRB that complies with 21 CFR Part 56.
The sponsor should submit the waiver request to the IND under which the study will be conducted. The IND will have been submitted to the appropriate review division in either the Center for Drug Evaluation and Research (CDER) or the Center for Biologics Evaluation and Research (CBER).
The sponsor will be informed by the agency in writing whether the waiver request is denied or granted. If a waiver is granted, the sponsor should have investigators attach a copy of the letter granting the waiver to the signed 1572 in the investigator's record.

Please see the 312.120 regulations as well as the 312.120 FDA guidance.

CFR - Code of Federal Regulations Title 21

http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM294729.pdf

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

Sincerely,

Bridget A. Foltz, MS, MT(ASCP)
Policy Analyst, Office of Good Clinical Practice
Office of the Commissioner, Food and Drug Administration

From: [redacted]
Sent: Thursday, July 16, 2015 2:43 PM
To: OC GCP Questions
Subject: RE: Question Foreign clinical study and form 1572

Hi,

A sponsor who is conducting a foreign clinical study under an IND has an additional question regarding 1572s. Since the study will not being prior to IND submission, is it acceptable to submit just one 1572 with the IND and follow-up with subsequent 1572s once the study is underway at the various foreign sites?

Thank you so much,

[redacted]

From: OC GCP Questions
Sent: Friday, May 29, 2015 1:53 PM
To: [redacted]
Subject: RE: Question Foreign clinical study and form 1572

Dear [redacted],

Thank you for your inquiry. I am not sure if I completely understand your question. I believe that you may find the relevant information in the FAQ Guidance on the Statement of Investigator/Form FDA 1572 (http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM214282.pdf) :

10. Must investigators who conduct studies outside of the United States sign a 1572?[3]
If a foreign clinical study is conducted under an IND, then all FDA IND regulations, including the requirement to obtain a signed 1572, must be met. If a clinical study is conducted outside of the U.S. and is not conducted under an IND, then the investigator need not sign a 1572. If local laws or regulations prohibit the signing of a 1572, FDA would expect the sites to operate as non-IND sites and the study conducted as a non-IND study. If the study data is to be submitted to support a marketing application (e.g., a new drug application (NDA)), the study must be conducted in compliance with 21 CFR 312.120.

11. If a foreign clinical study is being conducted under an IND, what are the investigator's responsibilities with respect to local laws and regulations?
Investigators are responsible for complying with the applicable laws and regulations of the country in which the study is being conducted, regardless of whether the study is being conducted under an IND. We recommend that sponsors obtain signed, written statements from investigators acknowledging their commitment to comply with local laws and requirements. In addition, if a foreign clinical study is being conducted under an IND, the investigator must sign Form FDA 1572 (investigator statement) and ensure that the study is conducted in accordance with the investigator statement and all other applicable regulations under 21 CFR Part 312.

12. For foreign clinical studies conducted under an IND, how can an investigator sign the 1572 when the investigator knows he/she cannot commit to all of the requirements on the form, specifically IRB membership (21 CFR 56.107)?
IRB review and approval is required before a clinical study can be initiated under an IND (21 CFR 56.103(a)). FDA may waive any of the IRB requirements for specific research activities or for classes of research activities otherwise covered by the IRB regulations (21 CFR 56.105), but FDA uses the waiver provision only when alternative mechanisms for ensuring protection of the rights and welfare of human subjects are acceptable. The most common circumstance for which FDA receives

a waiver request is when a sponsor wishes to conduct a foreign clinical study under an IND. In this case, typically an Independent Ethics Committee (IEC) that operates in accordance with Good Clinical Practice (GCP) is utilized instead of a U.S. IRB. Although its membership and functions for assuring human subject protection are comparable to an IRB, an IEC may not meet all of the IRB requirements contained in 21 CFR Part 56.
For a foreign study, an IRB waiver request should contain a description of alternative mechanisms for assuring human subject protection. It would generally be acceptable for a waiver request to state the intention to use an IEC that complies with GCP (e.g., ICH E6) instead of an IRB that complies with 21 CFR Part 56.
The sponsor should submit the waiver request to the IND under which the study will be conducted. The IND will have been submitted to the appropriate review division in either the Center for Drug Evaluation and Research (CDER) or the Center for Biologics Evaluation and Research (CBER).
The sponsor will be informed by the agency in writing whether the waiver request is denied or granted. If a waiver is granted, the sponsor should have investigators attach a copy of the letter granting the waiver to the signed 1572 in the investigator's record.

Additionally, if there are sites outside of the Unites States that will not be conducted under an IND, you may also wish to reference the guidance on FDA Acceptance of Foreign Clinical Studies Not Under an
IND: http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM294729.pdf

I hope that this information is helpful. Please contact us at gcp.questions@fda.hhs.gov if you have further questions. Since many questions and concerns regarding good clinical practices have been addressed over time, some individuals may find it useful to access a set of redacted GCP inquiries found at the following web address: http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/RepliestoInquiriestoFDAonGoodClinicalPractice/default.htm .

Sincerely,

Bridget A. Foltz, MS, MT(ASCP)
Policy Analyst, Office of Good Clinical Practice
Office of the Commissioner, Food and Drug Administration

From: [redacted]
Sent: Tuesday, May 26, 2015 3:05 PM
To: OC GCP Questions
Subject: Question Foreign clinical study and form 1572

Hi,

A sponsor is conducting a clinical trial, but will not have any US sites. They have the following question, ".. since we will not have any US sites, can we submit the 1572s for the foreign investigators, not with the IND, but post the IND going into effect, because our IND will be our first filing before we file any clinical trial applications in our other targeted countries?"

Please let me know.

Thank you,

[redacted]