From: OC GCP Questions
To: [redacted]
Cc: CDER SBIA; CDER DRUG INFO
Subject: RE: Declaration of Helsinki (DoH) Version
Date: Monday, December 03, 2018 2:55:00 PM
Attachments: [redacted]

Dear [redacted] -

I'm not sure I understand what you mean by "relevant to cite for the US clinical trials". Where are you citing the DoH? Are you referring to documenting the description of ethical considerations relating to the study in the protocol as suggested in section 6.12 of the ICH GCP E6(R2) guidance (see https://www.fda.gov/downloads/Drugs/Guidances/UCM464506.pdf)?

Studies that are conducted under an IND or IDE must adhere to the applicable US FDA regulations (e.g, 21 CFR 312, 21 CFR 812, 21 CFR 50, 21 CFR 56, etc.). Whether or not a sponsor decides to additionally follow other relevant standards for a study (e.g., ICH GCP E6(R2)) is up to the sponsor.

I hope this information is useful.

Best Regards,

Janet
Janet Donnelly, RAC
Policy Analyst

Office of the Commissioner
Office of Good Clinical Practice
U.S. Food and Drug Administration

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.

From: [redacted]
Sent: Friday, November 30, 2018 4:57 PM
To: OC GCP Questions <gcpquestions@fda.hhs.gov>
Cc: CDER SBIA <CDERSBIA@fda.hhs.gov>; CDER DRUG INFO <DRUGINFO@fda.hhs.gov>
Subject: RE: Declaration of Helsinki (DoH) Version

Dear Janet,

Thank you for the information.

Just to confirm – is it correct to state that DoH will not be relevant to cite for the US clinical trials conducted under an IND and/or an NDA/BLA/PMA?

Best Regards,

[redacted]

[redacted]

From: OC GCP Questions <gcpquestions@fda.hhs.gov>
Sent: Friday, November 30, 2018 1:44 PM
To: [redacted]
Cc: CDER SBIA <CDERSBIA@fda.hhs.gov>; CDER DRUG INFO <DRUGINFO@fda.hhs.gov>
Subject: FW: Declaration of Helsinki (DoH) Version

Dear [redacted] -

Thank you for your question, which was forwarded to my office for a response. The information provided below represents FDA requirements.

Prior to the regulatory revisions in 2008 and 2018 described below, FDA regulations relating to studies that were used to support marketing applications that were conducted outside the United States (OUS) and not under an investigational or marketing application required conformance with the Declaration of Helsinki. The 2008 and 2018 revisions to these regulations updated the standards for the acceptance of OUS studies. The revised regulations replaced the requirement for conformance with the Declaration of Helsinki with a requirement to conduct such studies in accordance with good clinical practice (GCP), as defined in the revised regulations (see 21 CFR 312.120 at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.120 and 21 CFR 812.28 at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.28).

On April 28, 2008, the FDA amended its regulations on the acceptance of foreign clinical studies not conducted under an investigational new drug application (IND) ("non-IND foreign clinical studies") as support for an IND or a new drug application (NDA), abbreviated new drug application (ANDA), or a biologics license application (BLA) (collectively known as "marketing applications" or "applications for marketing approval"). The final rule requires that such studies be conducted in accordance with good clinical practice (GCP), including review and approval by an independent ethics committee (IEC) and informed consent from subjects. The GCP requirements in the final rule encompass both ethical and data integrity standards for clinical studies. This final rule, which took effect on October 27, 2008, is codified at 21 CFR 312.120. It is intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies as well as the quality and integrity of the resulting data.

FDA issued guidance titled, "*Guidance for Industry and FDA Staff – FDA Acceptance of Foreign Clinical Studies Not Conducted Under an IND – Frequently Asked Questions*" that can be found at https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM294729.pdf. This guidance document is intended to clarify for sponsors and applicants how they can demonstrate compliance with the requirements of 21 CFR 312.120. It provides recommendations for the submission of information, whether in an IND or application for marketing approval for a drug or biological drug product, to demonstrate that a non-IND foreign clinical study was conducted in accordance with GCP.

On February 21, 2018, FDA amended its regulations on the acceptance of data from clinical investigations for medical devices. Under the new rule, FDA is requiring that data submitted from clinical investigations conducted outside of the United States (OUS) intended to support an investigational device exemption (IDE) application, a premarket notification (510(k)) submission, a request for De Novo classification, a premarket approval (PMA) application, a humanitarian device exemption (HDE) application, or a product development protocol (PDP) application, be from investigations conducted in accordance with good clinical practice (GCP), which includes review and approval by an independent ethics committee (IEC) and informed consent from subjects. The GCP requirements in the final rule encompass both data quality and integrity and ethical standards for device clinical investigations.

FDA also issued guidance titled, "*Acceptance of Clinical Data to Support Medical Device Applications and Submissions – Frequently Asked Questions – Guidance for Industry and Food and Drug Administration Staff*" that can be found at https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM597273.pdf. This guidance document is intended to help sponsors and applicants understand and comply with the new requirements of 21 CFR parts 807, 812 and 814. It provides recommendations for the submission of information, whether in an IDE or marketing application or submission for a device, to demonstrate that when clinical data from investigations conducted within the US or OUS are submitted to support such application or submission, the investigations conformed with FDA's regulations in 21 CFR parts 50 (human subject protection), 56 (institutional review boards), and 812 (investigational device exemptions), or GCP, as applicable.

It would be appropriate to reference Good Clinical Practice (GCP), instead of the Declaration of Helsinki, as discussed above for such OUS studies. Studies that are conducted under an IND or IDE would need to adhere to the applicable regulations under 21 CFR 312 and 812.

I hope this information is useful. If you need further information and/or have additional questions, please feel free to contact us at the official GCP mailbox, gcp.questions@fda.hhs.gov. You may also find it useful to access the set of redacted GCP e-mails found at http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/RepliestoInquiriestoFDAonGoodClinicalPractice/default.htm since we find that many questions and concerns are repeated over time.

Best Regards,

Janet
Janet Donnelly, RAC
Policy Analyst

Office of the Commissioner
Office of Good Clinical Practice
U.S. Food and Drug Administration

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.

From: [redacted]
Sent: Tuesday, November 27, 2018 6:46 PM
To: CDER SBIA <CDERSBIA@fda.hhs.gov>
Subject: Declaration of Helsinki (DoH) Version

Dear CDER SBIA,

My question is regarding the relevant version of *Declaration of Helsinki (DoH)* to be referred and cited, for the conduct of clinical trials in the United States (US) and outside-the-US (OUS).

Question: What is the specific version of the DoH that is to be followed for conducting clinical trials in (1). US, and (2). OUS? Thank you.

Best Regards,

[redacted]