**From:** Brown, Sheila (OGCP)
**To:** [redacted]
**Subject:** RE: PI responsibilities
**Date:** Friday, April 21, 2017 9:19:00 AM

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Dear [redacted],

I believe the sponsor may be thinking of 21 CFR 312.66, Assurance of IRB review, which is reproduced here for your convenience:

> An investigator shall assure that an IRB that complies with the requirements set forth in part 56 will be responsible for the initial and continuing review and approval of the proposed clinical study. The investigator shall also assure that he or she will promptly report to the IRB all changes in the research activity and all unanticipated problems involving risk to human subjects or others, and that he or she will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

There is similar language in 21 CFR 312.53(c)(vii):

> A commitment by the investigator that, for an investigation subject to an institutional review requirement under part 56, an IRB that complies with the requirements of that part will be responsible for the initial and continuing review and approval of the clinical investigation and that the investigator will promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects or others, and will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to the human subjects.

Also, in ICH E6, which is a guidance recognized by FDA, Section 5.11, Confirmation of Review by IRB/IEC, states, in part,

> 5.11.1 The sponsor should obtain from the investigator/institution:
>
> (a) The name and address of the investigator's/institution's IRB/IEC.
>
> (b) A statement obtained from the IRB/IEC that it is organized and operates according to GCP and the applicable laws and regulations.

The ICH E6 guidance can be found on FDA's website at
https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073122.pdf

The regulations do not specify how a sponsor or investigator should determine that a reviewing IRB complies with the requirements in 21 CFR Part 56. When the regulations are not specific, sponsors may develop their own SOPs to meet the regulatory requirements.

When an investigator signs an FDA-1572 form, the investigator provides assurance that the study will be reviewed by an IRB that complies with the requirements of 21 CFR 56, which may be sufficient for this sponsor. The following statement is included on the FDA-1572:

> I will ensure that an IRB that complies with the requirements of 21 CFR Part 56 will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects or others. Additionally, I will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

Please note that, while an investigator may ask for a statement of compliance from the IRB, there are no regulatory requirements that require an IRB to supply this type of documentation. However, some IRBs may be willing provide a statement of compliance. We recommend that the investigator discuss with the sponsor what their documentation requirements are, specifically, and then ask the IRB to provide the necessary information. It may be helpful to have a conversation between the sponsor, investigator, and IRB staff if

clarifications are needed.

I hope this information is helpful to you. If you need further assistance, please feel free to contact the GCP mailbox at gcp.questions@fda.hhs.gov .

Best regards,

Sheila

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-----Original Message-----
From [redacted]
Sent: Wednesday, April 19, 2017 12:12 PM
To: OC GCP Questions
Subject: PI responsibilities

A sponsor just informed our PI ( over 400 trials so very experienced in GCP) that it is his responsibility to call and inquire if the IRB is following operational requirements and he should ask for the meeting minutes. There is no issue of the IRB that brought this on so we are very confused about this instruction and never heard of any other PI doing this oversight  they claim its in the regs????

Regards

[redacted]