From: OC GCP Questions
To: [redacted]
Subject: RE: Question on complying to 21CFR 56.107 (e) Conflict of Interest
Date: Thursday, December 17, 2015 3:41:00 PM

Dea [redacted] -

Thank you for your question. As you know, the FDA regulations at 21 CFR 56.107(e) state:

> Sec. 56.107 IRB membership.
> (e) No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

The FDA regulations found at 21 CFR 312.66 state:

> Sec. 312.66 Assurance of IRB review.
>
> 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.

And, the regulations at 21 CFR 312.50 state:

> Sec. 312.50 General responsibilities of sponsors.
>
> Sponsors are responsible for selecting qualified investigators, providing them with the information they need to conduct an investigation properly, ensuring proper monitoring of the investigation(s), ensuring that the investigation(s) is conducted in accordance with the general investigational plan and protocols contained in the IND, maintaining an effective IND with respect to the investigations, and ensuring that FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug. Additional specific responsibilities of sponsors are described elsewhere in this part.

The ICH GCP E6 Good Clinical Practice: Consolidated Guidance, (which is recognized as official FDA guidance - see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073122.pdf), addresses the composition, functions and operations of IRBs/IEC/s in section 3.2. Section 3.2.1 states:

> 3.2 Composition, Functions, and Operations
>
> 3.2.1 The IRB/IEC should consist of a reasonable number of members, who collectively have the qualifications and experience to review and evaluate the science, medical aspects, and ethics of the proposed trial. It is recommended that the IRB/IEC should include:
>
> (a) At least five members.
> (b) At least one member whose primary area of interest is in a nonscientific area.
> (c) At least one member who is independent of the institution/trial site.
>
> Only those IRB/IEC members who are independent of the investigator and the sponsor of the trial should vote/provide opinion on a trial-related matter.
>
> A list of IRB/IEC members and their qualifications should be maintained.

Neither the regulations nor the guidance are specific about what kind of "proof" a sponsor or investigator is required to maintain to ensure the IRB's compliance with its written procedures. When the regulations are silent, sponsors, CROs, investigators, institutions and IRBs are free to develop their own procedures and practices as long as applicable regulatory requirements are met.

I am not familiar with IRB's providing "recusal letters" to sites, however, this might be a practice your company follows. The decision about whether or not a copy of the IRB policy is enough for the TMF is really up to you and your company. On inspection of an IRB, FDA would review the IRB's records to determine that no IRB member participates in the deliberation or

voting during the initial or continuing review of any study in which that IRB member has a conflicting interest except to provide information requested by the IRB in accordance with 21 CFR 56.107(e).

If your company has any concerns about whether or not the IRB followed its IRB member COI policy for your particular study, you may consider discussing this concern with the investigator and the IRB and obtaining some form of confirmation that you and your company decide is appropriate for the files.

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

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From: [redacted]
Sent: Tuesday, December 15, 2015 7:55 PM
To: OC GCP Questions
Subject: Question on complying to 21CFR 56.107 (e) Conflict of Interest

Hello,

We have a site that has several of their study team members being IRB members. The IRB does not provide recusal letters to the site instead it provided a copy of its IRB policy indicating that IRB members with COI do not participate in the review and approval of the study. There is a debate ongoing on whether it is sufficient to just file a copy of the policy in the site TMF in support of 21CFR56.107 (e). I say "no" because the policy is not sufficient evidence to proof that the 21CFR56.107 (e) is met. I believe obtaining a documentation from IRB that the members had abstain or a redacted meeting minutes to proof the compliance.

Who is correct (just filing a policy in TMF or obtaining more documented evidence - redacted minutes or IRB documentation)?

You are advice is greatly appreciated.

Thanks,
[redacted]