From: OC GCP Questions
To: [redacted]
Subject: RE: Principal Investigator as the Chairman of IRB
Date: Thursday, February 19, 2015 5:50:00 PM

Dear [redacted]

Thank you for your questions. If I understand your questions correctly, you have a situation where the IEC Chairman is also the Principal Investigator of a study being reviewed and overseen by the IEC. Your questions cover both regulatory and administrative issues, so I will try to address both.

If the study is subject to the FDA regulations, then the regulations at 21 CFR 56.107(e) (see http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=56.107) 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.

A conflicted IRB member of the IRB may not participate in the initial or continuing review so they may not vote, or count towards quorum for that study. FDA recommends that IRB members with a conflicting interest in a project recuse themselves by leaving the meeting room when the IRB conducts initial or continuing review of that project, except when requested by the IRB to be present to provide information.

A conflicted member has a conflict that should prevent him/her from being involved in the review of any information about the project for which they are conflicted. This includes any expedited review of information related to that project. Because of the conflict, a conflicted IRB member is not eligible to perform a review of such information on behalf of the IRB.

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 relevant information in sections 3.2.1 and 3.2.5 (copied here for reference):

> 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. [emphasis added]**
>
> A list of IRB/IEC members and their qualifications should be maintained.
>
> **3.2.5 The investigator may provide information on any aspect of the trial, but should not participate in the deliberations of the IRB/IEC or in the vote/opinion of the IRB/IEC. [emphasis added]**

FDA also has Information Sheet Guidance for Institutional Review Boards (IRBs), Clinical Investigators, and Sponsors (see http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidancesInformationSheetsandNotices/ucm113709.htm). Question #12 under the Frequently Asked Questions section reads:

> II. IRB Membership
>
> 12. May a clinical investigator be an IRB member?
>
> Yes, however, the IRB regulations [21 CFR 56.107(e)] prohibit any member from participating in the IRB's initial or continuing review of any study in which the member has a conflicting interest, except to provide information requested by the IRB. When selecting IRB members, the potential for conflicts of interest should be considered.

> When members frequently have conflicts and must absent themselves from deliberation and abstain from voting, their contributions to the group review process may be diminished and could hinder the review procedure. **Even greater disruptions may result if this person is chairperson of the IRB. [emphasis added]**

As far as the administrative actions you mentioned (e.g., signing meeting minutes, receipt of submission letter), the regulations do not specifically address these tasks. The regulations provide flexibility and when the regulations are silent, IRBs, institutions, sponsors, investigators are free to develop their own procedures and practices as long as applicable regulatory requirements are met.

You should discuss this particular issue and how the IEC should handle it with the appropriate individuals at your company as well as the IEC and institutional officials at the site in question. You may want to discuss whether there is another representative of the IEC that can serve as Chairman on any matters related to the study for which the IRB Chairman is conflicted. The IEC may also want to consider including how these situations are handled in their IEC written procedures. If this situation occurs regularly, the IEC and institution also may wish to reassess the role of the IEC Chairman.

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, CIP
Policy Analyst, Office of Good Clinical Practice
Office of Special Medical Programs, Food and Drug Administration

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From: [redacted]
Sent: Tuesday, February 17, 2015 4:19 AM
To: OC GCP Questions
Subject: Principal Investigator as the Chairman of IRB

Dear Sir or Madame,

I would like kindly ask your advice regarding the situation when Principal Investigator is the Chairman of Independent Ethics Committee at site.

I clearly understand that In this case it is not possible for him to vote but is it possible for him to provide the signature under the protocol of meeting minutes?

Moreover, is it possible for him to receive information as Chairman (for ex. Submission of SUSARs where the quorum is not required)?
In this case submission letter should be addressed to him as Chairman from him as by Principal Investigator? Or information for clinical studies where the Chairman is PI should be addressed to another member of IRB for example to Deputy Chairman or to Secretary?

Thank you very much in advance!

Sincerely,
[redacted]