From: OC GCP Questions
To: [redacted]
Subject: Ref- Urgent Question about Clinical trial and local IRB mandatory requirement
Date: Thursday, September 01, 2016 8:30:00 AM

Good morning –

Many of your questions are answered in the guidance document below. IRB regulations require the IRB to "be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards or professional conduct and practice" (21 CFR 56.107(a)). As stated, the responsibilities of a central IRB for consideration of local concerns are discussed in FDA's Guidance for Industry, Using a Centralized IRB Review Process in Multicenter Clinical Trials:

http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm127013.pdf. Specifically, please see sections III and IV.

When a central IRB is used for a multisite study and a site has a local IRB available that it would normally use for study review and approval, an agreement should be made regarding who is responsible for what. In some cases, a local IRB may relinquish all oversight to the study's central IRB. In other cases, they may share responsibilities. In the latter case, just who has responsibility for what and how any changes are handled should be agreed upon from the start, so there are no disagreements that could potentially hold up the initiation of an approvable study.

A centralized IRB review process involves an agreement under which multiple study sites in a multicenter trial rely in whole or in part on the review of an IRB other than the IRB affiliated with the research site. Because the goal of the centralized process is to increase efficiency and decrease duplicative efforts that do not contribute to meaningful human subject protection, it will usually be preferable that a central IRB take responsibility for all aspects of IRB review at each site participating in the centralized review process. Other approaches may be appropriate as well. For example, an institution may permit a central IRB to be entirely responsible for initial and continuing review of a study, or apportion IRB review responsibilities between the central IRB and its own IRB.

As you can see, the intent of cooperative review is to reduce duplicative review efforts. Therefore, when a cooperative agreement exists, both IRBs would not be expected to fully review the study. The actual cooperative agreement would delineate whether one IRB is fully responsible for review or if review is apportioned between the IRBs, as indicated in this additional excerpt from the central IRB guidance:

When an institution, an institution's IRB, and a central IRB agree to apportion IRB review responsibilities between the two IRBs, each IRB must have written procedures describing how it implements its responsibilities under the agreement (21 CFR 56.108, 56.115(a)(6)).

A DSMB is a data safety monitoring board, sometimes referred to as a data monitoring committee (DMC). FDA requires such a committee for emergency research studies, those conducted under 21 CFR 50.24, for which informed consent is not required before a subject is considered part of the study. FDA may also request that a DMC be formed if the study is or could be of very high risk to subjects and/or the subject population is considered particularly vulnerable. There is a guidance document on the use of DMCs that is available at www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM127073.pdf. The main purpose of a DMC is to monitor data from clinical studies of high risk, to determine if and when the study should be modified or even stopped due to adverse events. Many drug studies are blinded and the DMC has the ability to periodically break the blind to analyze the results. It is also possible for such a committee to stop a study because the findings are so positive that it would not be considered ethical to further delay an application/submission for marketing.

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

have additional questions.

Kind regards,

Doreen M. Kezer, MSN
Senior Health Policy Analyst
Office of Good Clinical Practice
Office of the Commissioner, FDA

From: [redacted]
Sent: Wednesday, August 31, 2016 4:50 PM
To: CDER DRUG INFO; OC GCP Questions
Subject: Ref- Urgent Question about Clinical trial and local IRB mandatory requirement

Dear Madam,

My name is [redacted] I am working as Clinical Research Coordinator in a medical center which is brand new to research. I will be developing research team for various research studies in various disease areas.

I have a Masters Degree In Clinical Research Administration from [redacted] and I have good experience in conducting the clinical trials.

I wanted to give you some background about my questions.

The Medical Center I am working has Local IRB and Steering Review Committee (SRC) . SRC committee review the study and see if the study is feasible in this medical center.

We do have Clinical Research Sops and IRB SOPS (IRB SOP is not so detail when it comes to SAE or protocol deviation reporting- this is because we are planning to keep central IRB as IRB of record). We don't have Data Safety monitoring Board.(DSMB)

As I mentioned above we are planning to make central IRB as IRB of record so all SAE or protocol deviation could be directly reported to Central IRB – central IRB which is used by the sponsor.

I just wanted to confirm following things

- If we are making central IRB as IRB of record then is it ok if we submit protocol deviation and SAE only to central IRB (not to local IRB)?
- And as a local IRB- instead of having detail SOP for protocol deviation and SAE we can just mentioned in our IRB-SOP that we will be making central IRB as IRB of record and all SAE, protocol deviation, quarterly report will be reviewed by central

IRB not by the local IRB - Is that Ok?

- In above case we don't have to have Data safety monitoring board committee (DSMB) – Is that Ok?
- Local IRB will only approve / disapprove initial submission of protocol and its amendment, rest of events related to protocol conduct will be submitted (SAE, protocol deviation, quarterly report) only to central IRB only. Is that fine?
- Do we need to fill out Local IRB detail application for each protocol amendment- I understand local IRB approval is required for every amendment.
- We will follow above steps for each study protocol - research study for which we will referring central IRB as IRB of record.
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Your response will be highly appreciated.

Thanks and Regards

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