From: OC GCP Questions
To: [redacted]
Cc: [redacted]
Subject: RE: Question re: Devices
Date: Monday, June 08, 2015 6:45:00 PM
Attachments: [redacted]

Dear [redacted] -

Thank you for your question. I consulted some of my device colleagues with your question and they confirmed that FDA requires that the IRB make the Significant Risk/Non-significant Risk (SR/NSR) determination at a convened meeting. I have provided the rationale below. Please don't hesitate to contact me should you need additional information/clarification.

The regulations for applicability of the IDE regulations found at 21 CFR 812.2(b) state the following (see http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.2):

> **Sec. 812.2 Applicability.**
>
> (b) Abbreviated requirements. The following categories of investigations are considered to have approved applications for IDE's, unless FDA has notified a sponsor under 812.20(a) that approval of an application is required:
>
> (1) An investigation of a device other than a significant risk device, if the device is not a banned device and the sponsor:
>
> (i) Labels the device in accordance with 812.5;
>
> (ii) Obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval;
>
> (iii) Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, informed consent under part 50 and documents it, unless documentation is waived by an IRB under 56.109(c).
>
> (iv) Complies with the requirements of 812.46 with respect to monitoring investigations;
>
> (v) Maintains the records required under 812.140(b)(4) and (5) and makes the reports required under 812.150(b)(1) through (3) and (5) through (10);
>
> (vi) Ensures that participating investigators maintain the records required by 812.140(a)(3)(i) and make the reports required under 812.150(a) (1), (2), (5), and (7); and
>
> (vii) Complies with the prohibitions in 812.7 against promotion and other practices.
>
> (2) An investigation of a device other than one subject to paragraph (e) of this section, if the investigation was begun on or before July 16, 1980, and to be completed, and is completed, on or before January 19, 1981.

A clinical investigation of a device to determine safety and effectiveness that is determined to be NSR **is considered to have an approved IDE** and is subject to the abbreviated IDE regulations specified in 812.2(b).

The IRB has responsibility for making the SR/NSR determination when it receives a device study for review. The regulations at 21 CFR 812.66 state the following (see http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.66):

> **Sec. 812.66 Significant risk device determinations.**
>
> If an IRB determines that an investigation, presented for approval under 812.2(b)(1)(ii), involves a significant risk device, it shall so notify the investigator and, where appropriate, the sponsor. A sponsor may not begin the investigation except as provided in 812.30(a).

As stated in the guidance [Redacted] mentioned (*Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors, Significant Risk and Nonsignificant Risk Medical Device Studies* found at http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126418.pdf), IRBs should have standard operating procedures that explain how the IRB makes SR and NSR determinations and that the decision should be documented. FDA considers this determination to be part of the IRB's responsibilities for conducting its initial review of a study (21 CFR 56.108).

In making an SR/NSR decision, the IRB is actually determining if the sponsor's categorization of the study as NSR is accurate (i.e., that the study should not instead be considered SR), therefore a decision could not be made by the IRB under expedited review.

I can appreciate that in reading the guidance [Redacted] referenced that one might interpret the sentence, "*IRBs should make the SR or NSR determination about a study by reviewing relevant information at a convened meeting.*" as being a recommendation vs. a requirement, but this determination is part of the initial review by the IRB, which is done at a convened meeting for all but minimal risk studies that qualify for expedited review. We appreciate the opportunity to clarify FDA's requirements and expectations. This same guidance document also includes a section on page 7 that states (see

http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126418.pdf):

> IRBs should understand distinctions between certain important concepts that are frequently confused …
>
> **B. Difference Between SR/NSR Determinations and Approval Decisions**
>
> IRBs should not confuse their responsibility to review and approve research for conduct at a clinical site with the SR/NSR determination. IRBs make the SR/NSR determination before the IRB conducts its review of the study under Part 56. The judgment about whether a study poses a significant risk or nonsignificant risk is based on the significance of the potential harm that may result from participation in the study, including the use of the device; whereas the IRB's decision to approve a study for implementation is based on the study's risk-benefit assessment.

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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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: Thursday, June 04, 2015 10:44 AM
To: Donnelly, Janet
Cc: [redacted]
Subject: Question re: Devices

Dear Janet:

I hope this finds you well!

[redacted]

Separately, I have a question that I'm hoping you might be able to shed some light on. I recall [Redacted] OHRP [Redacted] that "shoulds" were considered non-enforceable if some other alternative could be supported (as opposed to "musts"). However, I'm not exactly sure how FDA enforces that.

The issue in question is making the SR/NSR determination in a device study.

[Redacted] looked at the following guidance document and stated the following:

http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126418.pdf

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"After review of these guidance documents it was determined that FDA does not require that the determination of whether a device fulfills the requirements for an abbreviated IDE (e.g. a non-significant risk device determination) be made by the convened IRB."

However, this guidance document has the following statement:

> IRBs *should* make the SR or NSR determination about a study by reviewing relevant information at a *convened* meeting [emphasis added]. This information includes the description of the device, reports of prior investigations conducted with the device, the proposed investigational plan, and subject selection criteria. The sponsor should provide the IRB with a risk assessment and the rationale used in making its SR or NSR determination.

Could you provide me some input on this? I understand that this is a guidance document – do you have any other information as to whether this is a requirement by the FDA or only a suggestion?

Any insight you may have to offer on this will be greatly appreciated.

[redacted]