From: OC GCP Questions
To: [redacted]
Subject: RE: Question Need to Re-consent Subjects Participating in an Investigational Study
Date: Wednesday, April 16, 2014 12:31:00 PM

Dear [Redacted]-

Thank you for your question. Have you consulted your IRB(s) with your question? As you know, the IRB is responsible for approving any changes to the informed consent form (ICF), determining what the revised ICF includes, and advising whether subjects need to sign the revised ICF (e.g., all current subjects and new subjects, or just new subjects).

As you noted, the FDA regulations regarding the additional elements of informed consent at 21 CFR 50.25(b)(6) require, when appropriate, that the approximate number of subjects involved in the study be provided to each subject in the ICF. Also, the additional element at 21 CFR 50.25(b)(5) requires, when appropriate, that the ICF include a statement that significant new finding developed during the course of the research which may relate to the subject's willingness to continue to participation will be provided to the subject.

FDA has guidance titled, "Institutional Review Boards Frequently Asked Questions - Information Sheet" found at http://www.fda.gov/RegulatoryInformation/Guidances/ucm126420.htm. FAQ #45 states:

> **45. When should study subjects be informed of changes to the study?**
>
> Protocol amendments must receive IRB review and approval before they are implemented, unless an immediate change is necessary to eliminate an apparent hazard to the subjects (21 CFR 56.108(a)(4)). Those subjects who are presently enrolled and actively participating in the study should be informed of the change if it might relate to the subjects' willingness to continue their participation in the study (21 CFR 50.25(b)(5)). FDA does not require reconsenting of subjects that have completed their active participation in the study, or of subjects who are still actively participating when the change will not affect their participation, for example when the change will be implemented only for subsequently enrolled subjects.

You may wish to discuss your question with your IRB(s) as they will be familiar with the nature of the change to the ICF, the reason(s) for the change, and may determine whether a revised ICF should be issued and signed by subjects, or whether an addendum to the ICF may suffice to summarize the changes to the study.

Lastly, we are aware that sometimes sponsors may have their own requirements and may instruct sites to have all subjects sign revised ICFs regardless of the nature of the change(s); however that does not seem to be the case in your scenario.

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: Friday, April 11, 2014 11:09 AM
To: OC GCP Questions
Subject: Question Need to Re-consent Subjects Participating in an Investigational Study

Good morning,

I am writing on behalf of my client, who is conducting a significant risk, investigational device study in the United States under an approved IDE application. This client recently submitted and obtained FDA approval for a protocol amendment to increase the sample size of clinical trial by approximately 20%. There were no safety issues observed that prompted the increase in the sample and the subjects in the study undergo the same procedures and evaluations. The risks and benefits to the participating subjects remain the same.

Our clinical sites are in the process of obtaining IRB approval for the amended protocol and a new consent form will be issued which identifies the increased number of subjects participating in the clinical trial. (All of our sites include the additional element of informed consent (50.25(b) of identifying the "approximate number of subjects involved in the study.") Our clinical sites have asked whether this change in the protocol should necessitate re-consenting subjects who have signed the previous, IRB approved version of the informed consent document, which included the smaller study sample size. Again, the increase in protocol sample size was not due to any safety issue.

My client was slightly surprised by this question because the protocol change was not due to any new information regarding risks and benefits, nor has the protocol changed any specific-specific evaluations or procedures.

I am writing to request the following:

1. Identification of any guidance issued by FDA for either sponsors or IRBs regarding when subjects need to be re-consented during an investigational clinical trial (in this case an investigational device clinical trial).
2. Any guidance that you may be able to provide about whether your office believes an increase in sample size not due to a safety reason should necessitate re-consenting previously enrolled and consented subjects.

Thank you for taking the time to respond to inquiry. I am looking forward to hearing back from you.

Sincerely,

[Redacted]