From: OC GCP Questions
To: [redacted]
Subject: RE: Applicability of 45 CAR 46
Date: Thursday, December 18, 2014 4:21:00 PM

Dear [Redacted]-

Thank you for your question. I am not able to provide you an interpretation of the HHS regulations at 45 CFR 46 as OHRP is the group you need to speak to for any clarifications on those regulations. If you would like to get OHRP's perspective, you must separately contact OHRP. You can contact OHRP at:

> Toll-Free Telephone within the United States: (866) 447-4777
> Telephone: (240) 453-6900
> Fax: (240) 453-6909
> E-mail: OHRP@hhs.gov

Based on the limited information provided, I'm not able to give you a definitive response as there are other details about the scenario you describe that would need to be considered. However, I will try to provide you with some thoughts on how you may consider assessing your scenario.

It is not clear from your question whether or not the study you refer to is subject to the regulations at 45 CFR 46 (i.e., HHS-conducted or -supported research). If the study is federally conducted or supported/funded, then you will need to direct any questions about the regulations at 45 CFR 46 to OHRP at the contact information provided above.

You indicate that, as the sponsor, you determined that the study is a clinical investigation that is subject to FDA regulations. Assuming that the proposed study is FDA-regulated, then the regulations at 21 CFR part 56 apply for the IRB.

If the study is FDA-regulated and also federally conducted or supported/funded, then the regulations at 21 CFR part 56 and 45 CFR 46 both apply for the IRB. When both sets of regulations apply to a study, then both sets of regulations must be followed. In situations where the regulations differ, the more stringent regulations apply.

However, for purposes of this response, I will assume the proposed study is FDA-regulated only. If the proposed study is FDA-regulated then the IRB regulations at 21 CFR 56 apply. The FDA regulations at 21 CFR56.105 (see http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=56.105) state:

> Sec. 56.105 Waiver of IRB requirement.
>
> On the application of a sponsor or sponsor-investigator, the Food and Drug Administration may waive any of the requirements contained in these regulations, including the requirements for IRB review, for specific research activities or for classes of research activities, otherwise covered by these regulations.

Just for your information and future reference, FDA does have an Information Sheet Guidance for Sponsors, Clinical Investigators, and IRBs titled, "Waiver of IRB Requirements for Drug and Biological Product Studies" that can be found at http://www.fda.gov/downloads/regulatoryinformation/guidances/ucm126500.pdf. Please note that FDA will not waive the requirement of IRB review for investigations of medical devices conducted under section 520(g) of the Act because IRB review is a statutory requirement for such studies (see 520(g)(3)(A)(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360j(g)(3)(A)(i)).

Your question says that the site had the study waived from IRB review under 45 CFR 46. If the FDA regulations apply to your study, I'm not sure I understand how this was done. I may be missing some details about this scenario that would provide more clarification; however, I suggest you talk to the clinical investigator/site and possibly the IRB to get more information about which regulations the IRB used to review the study. If this study is an FDA-regulated study then IRB review would be required in accordance with 21 CFR part 56.

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

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: Tuesday, December 16, 2014 1:12 PM
To: OC GCP Questions
Subject: Applicability of 45 CAR 46

One of our sites for an IVD study (testing protocol using samples provided from an IRB approved prospective collection study) had our study waived from IRB review based on 45 CAR Part 46. Our assessment as the sponsor is that we are operating under 21 CFR 56, and while there are similarities there are also differences. We feel that an IRB should not be waived unless it meets the criteria delineated in 21 CFR 56, and if such criteria is not met, the IRB shouldn't waive review of our study.

What is the agencies thoughts on this? Can our study be waived under 45 CFR 46 or must we fall under 21 CFR 56?

Many thanks,

[Redacted]