From: OC GCP Questions
To: [redacted]
Subject: ICF requirement regarding alternative therapy
Date: Monday, January 26, 2015 12:57:34 PM

Good afternoon–

What the sponsor sites as guidance language is correct. And I can only speak to FDA-regulated studies and consent requirements. It appears your study is under OHRP regulations and a FWA.

One of FDA's basic required elements of informed consent under 21 CFR 50.25(a) is as follows:

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject. [21 CFR 50.25(a)(4)]

FDA's Guide to Informed Consent (http://www.fda.gov/RegulatoryInformation/Guidances/ucm126431.htm) states the following on this requirement:

To enable a rational choice about participating in the research study, subjects should be aware of the full range of options available to them. Consent documents should briefly explain any pertinent alternatives to entering the study including, when appropriate, the alternative of supportive care with no additional disease-directed therapy. While this should be more than just a list of alternatives, a full risk/benefit explanation of alternatives may not be appropriate to include in the written document. The person(s) obtaining the subjects' consent, however, should be able to discuss available alternatives and answer questions that the subject may raise about them. As with other required elements, the consent document should contain sufficient information to ensure an informed decision.

There is a new *draft* guidance on informed consent that is still open to the public for comment and at this time should not be used for implementation. However, it might give you a few more ideas on alternative language. Please see the link below. Again it addresses FDA-regulated clinical trials only. Section "4. Alternative Procedures or Treatments" starts in the middle of page 9 and extends to page 10.

http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM405006.pdf

However, the guidance notes that alternative approaches to informed consent may be used if the applicable statutory and regulatory requirements are satisfied and alternative approaches may be discussed with FDA staff (presumably the review division or the project manager of the IND) if the study is FDA-regulated and under IND.

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

and does not bind or otherwise obligate or commit the agency to the views expressed.

From: [redacted]
Sent: Monday, January 26, 2015 11:04 AM
To: OC GCP Questions
Subject: ICF requirement regarding alternative therapy

Hello,

We are a Canadian site and we have been struggling with one of our sponsors regarding language in our informed consent text for "Alternative Treatments". The sponsor is a US cooperative group and the trial is under an active FWA. The sponsor had approached the OHRP previously about this issue and, upon receipt of the OHRP response , informed our REB that they were required to include at least the general language suggested in the sponsor (an NCI CIRB-approved) sample consent form to meet the requirement for providing patients with information about possible alternative treatments.

Our REB's require text is provided below for your reference:
What other choices do I have if I do not take part in this study?
"If you do not wish to take part in this study, your doctor will discuss your treatment options with you."

The sponosr's sample text is provided below for your reference:

What other choices do I have if I do not take part in this study?
Your other choices may include:
- Getting treatment or care for your cancer without being in this study
- Taking part in another study
- Getting no treatment

Talk to your study doctor about your choices before you decide if you will take part in this study.

Our REB provided the following response:
"As you know, official FDA Guidance has a disclaimer, stating that Guidance documents are meant to provide assistance to industry and health care professionals on how to comply with governing statutes and regulations. Guidance documents are administrative instruments not having force of law and, as such, allow for flexibility in approach. In practice, we know regulatory authorities and sponsors/ monitors/auditors seem to make no such distinction, which remains however essential. The main requirement is for participants to be informed that treatment is available even if they choose not to participate in a given clinical trial. Our REB does not allow detailed description of alternative treatments, on the basis that treatments options are specific to each participant, depending on their own particular clinical state. The actual wording in the [redacted] template is meant to avoid giving inaccurate information to participants, as one or many of the treatments listed may not be an option in their case. It is the PI' responsibility to personalize this information, according to each participant's needs and situation."

Therefore, the sponsor's wording was not accepted and the REB asked that its standard ICF text (i.e., "If you do not wish to take part in this study, your doctor will discuss your treatment options with you.") be used.

Given the argument provided by our REB, would you consider our REB's alternative statement acceptable (the single sentence just above in red) to meet the requirement under the federal regulations?

I appreciate your assistance with this request and look forward to your response.

[redacted]