From:	OC GCP Questions
To:	[redacted]
Subject:	Protocol amendment extending duration of multicenter study - questions about sites choosing not to continue beyond origianl protocol period
Date:	Friday, November 21, 2014 11:03:56 AM
Attachments:	image001.png

Good morning –

If a site does not want to continue to participate in the trial for the additional two years, you would need to notify FDA that the site is terminating it involvement in the study. Since the FDA-regulated study and data might be submitted to FDA under an NDA it is best to contact the FDA project manager that is overseeing the IND to obtain specific answers to your questions.

Additionally, if the site does not participate in the extended two years, they would have to notify the reviewing IRB as well. An amendment constitutes a change in the research that must be promptly reported to the IRB for review and approval. The exact nature of the amendment is not clear from the information provided, but changes in research may not be initiated prior to IRB approval, unless the change is necessary to eliminate apparent immediate hazards to human subjects.

If a site drops out of a study FDA must determine poolability of study data across sites and therefore the power of the given study. In assessing the data submitted to support marketing, FDA therefore needs to have complete data to ensure the sponsor performed a proper analysis of study results from all sites

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

Kind regards,

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Office of Good Clinical Practice
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From: [redacted]
Sent: Thursday, November 20, 2014 3:34 PM
To: OC GCP Questions
Subject: Protocol amendment extending duration of multicenter study - questions about sites choosing not to continue beyond origianl protocol period

Situation:

A protocol being conducted at multiple investigational sites was originally intended to provide an *X*-year treatment period. The protocol has been amended to provide for an *(X + 2)* year treatment period. Additional study procedures and efficacy and safety measurements have been added to cover the additional 2 years.

The original protocol was intended to support a marketing application requesting approval for use of the product for *X* years. It is anticipated that the amended protocol will support approval of a supplemental NDA claiming safety and effectiveness of the product for *(X + 2)* years.

Questions:

If a site does not want to continue participation in the trial beyond the *X* years covered in the original protocol:

1. Does the site need to submit the protocol amendment covering the *(X + 2)* year treatment period to their IRB?
2. Can the site operate under the original protocol, ignoring the *(X + 2)* year amendment and all the associated procedures and measurements?
3. Does this situation raise any informed consent issues?
4. Would a subject that terminated at *X* years because the site did not want to extend participation to (*X* + 2) years be considered as having *completed* the study or would the subject be considered as having *discontinued* from the study, eg, due to "Investigator Decision" not to participate in the study beyond the *X* years called for in the original protocol?

Thank you in advance for your response.

[redacted]