From: OC GCP Questions
To: [redacted]
Subject: question regarding protocol waivers
Date: Saturday, January 31, 2015 10:27:42 AM

Good morning --

There is very little discussion of protocol waivers in FDA guidance documents. While I am not aware of any discussion in a guidance document, FDA has addressed protocol waivers in Untitled and Warning Letters following FDA inspections, particularly to sponsors who have been found to give numerous protocol waivers. Since the effect is the same on the poolability of the data as protocol deviations, sponsors should discourage requests for protocol waivers. If many requests are received for a given study, the sponsor needs to reassess the protocol to determine if an amendment is necessary with regard to any requirement CIs find difficult to meet. A meeting with CIs may be necessary to determine if such requirements are too restrictive given the nature of the intended study population or present a major departure from standard medical practice that the CIs do not see as warranted for accruing the desired study endpoints.

Kind regards,

Doreen M. Kezer, MSN
Senior Health Policy Analyst
Office of Good Clinical Practice
Office of the Commissioner, FDA

From: [redacted]
Sent: Friday, January 30, 2015 2:37 PM
To: OC GCP Questions
Subject: RE: question regarding protocol waivers

Thank you for your response. I will check with the RPM with regards to this particular situation. As a general question, would there be situations in which protocol waivers are acceptable? I have heard from some sources that FDA would not allow protocol waivers under any circumstance, although I haven't been able to find anything in the GCP or CFR that would support that conclusion.

Thank you,

[redacted]

From: OC GCP Questions [mailto:gcp.questions@fda.hhs.gov]
Sent: January 30, 2015 1:29 PM
To: [redacted]
Subject: question regarding protocol waivers

Good afternoon –

This is best to ask the sponsor to speak to the regulatory project manager of the IND at FDA for guidance to answer your question. From a GCP standpoint, I cannot specifically answer your question.

Kind regards,

Doreen M. Kezer, MSN
Senior Health Policy Analyst
Office of Good Clinical Practice
Office of the Commissioner, FDA

From: [redacted]
Sent: Friday, January 30, 2015 10:35 AM
To: OC GCP Questions
Subject: question regarding protocol waivers

Hello,

I would like to get some clarification on the FDA's position regarding "pre-approved protocol waivers".

In this specific case, a protocol has a weight restriction in the inclusion/exclusion criteria to exclude patients over a certain weight. This exclusion was added due to a limited supply of investigational product and not for any reason related to patient safety. The sponsor would now like to allow some sites to enroll heavier patients who currently do not qualify based on the weight restriction, by providing site specific, pre-approved protocol waiver for that particular exclusion criteria. Due to the limitation with the supply of investigational product, the sponsor does not want to amend the protocol to allow for heavier patients to be enrolled at all sites, but only at sites where there are a higher percentage of heavier patients.

As per 21 CFR 312.30(b), I do not believe this change would be one that would "significantly affect the safety of subjects, the scope of the investigation, or the scientific quality of the study", thereby requiring a protocol amendment. The pre-approved waiver would be reviewed by the IRB prior to implementation as required by 21 CFR 312.66 and ICH E6 4.5.2.

Would an IRB pre-approved protocol waiver be acceptable in this scenario?

Thank you in advance for your assistance

[redacted]