From: Toth-Allen, Jean
Sent: Thursday, May 04, 2006 1:09 PM
To: [purged]
Subject: RE: Help

Dear [purged]:

Thank you for your inquiry concerning subject numbers in clinical studies.

The section of the regulation that speaks to numbers of subjects as an element of the informed consent document, 21 CFR 312.25(b)(6), is actually under the sub-heading "Additional elements of informed consent." As such, this information is not a required element of the consent document but the sponsor, investigator, or IRB may decide that such information is pertinent to the study subjects and so choose to include it. For example, if knowledge about the investigational product is so limited that the approved study were to have only very few initial subjects, this information may be pertinent to an individual's decision to take part in the study. A sponsor, investigator, or IRB may choose to include this information even if it is not so pertinent to an individual's decision to participate, but it is not a required element.

If the number of subjects to be treated at a given site is an actual part of the protocol reviewed and approved by the IRB, then inclusion of additional subjects without concurrence from the IRB would be considered a protocol deviation. (Such exceptions to the protocol also need to be approved by the study sponsor.) If the number of subjects to be treated was a factor in determining whether or not to grant study approval, it would be a relevant concern no matter what study phase was involved.

While more common for device than pharmaceutical studies, sponsors can be limited in total study enrollment by the approval conditions for the IDE/IND. The sponsor may therefore evenly distribute that number among the investigational sites or apportion them according to the size or experience of the sites involved. As the study progresses, some sites may enroll faster than others and a sponsor may choose to redistribute the subject numbers. The reviewing IRB(s) should be informed of this before the additional subjects are enrolled in the study if a total subject number for the site was part of the originally approved study protocol, even if this did not affect the IRB's decision to approve the study.

Hope this information is useful.

If you need further information and/or have additional questions, please submit them once again to the official GCP mailbox, gcpquestions@oc.fda.gov, in lieu of responding to my personal e-mail address.

Sincerely yours,
Jean Toth-Allen, Ph.D.
Good Clinical Practices Program
OSHC, Office of the Commissioner, US FDA

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: [purged]
Sent: Wednesday, April 26, 2006 3:19 PM
To: OC GCP Questions
Cc: [purged]
Subject: Help

Dear Sir/Madam,

As an auditor, I always have an issue with the clinical personnel when they exceed the total number of patients /subjects stated in the protocol.

Can you please give me some guidance as to how to a interpret the 21 CRF part 50- Protection of Human Subjects: Informed consent .(6) The approximate number of subjects involved in the study.

I am aware that this issue is more significant when a study is in phase I, but what about when the phase of the study is phase II or phase III.

My usual reasoning is that when the total number of patients/subjects is more than what was stated in the protocol, this is a protocol violation. The IRB should be notified because there are more patients/subjects exposed to the clinical trials activities/investigational product than what was approved by the

IRB/Ethics committee.

Thank you for your help. I hope to hear from you

Sincerely,

[purged]