From: Lee, Bonnie on behalf of OC GCP Questions
Sent: Wednesday, April 03, 2002 11:41 AM
To: [purged]
Subject: RE: Informed Consent Questions

Dear [purged], I did not mean to "pick" on your words, because I do think that you have the right idea in mind. I agree that sponsors will be the most informed about safety information and are therefore the best resource for IRBs in terms of trying to understand the various safety issues and risks associated with participating in a clinical trial. We have no magic formula--other than good judgement; and we have no "gold standard" to follow--other than the elements of informed consent contained in 21 CFR 50.25. Hope this helps. My best,

Bonnie

Bonnie M. Lee
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-----Original Message-----
From: [purged]
Sent: Tuesday, April 02, 2002 8:16 PM
To: OC GCP Questions
Cc: [purged]
Subject: Re: Informed Consent Questions

Dear Bonnie:

Thank you so much for your timely and informative response. The Office of GCP is invaluable.

I asked the questions because study sites often ask sponsors to provide a template safety section for the informed consent document, since sponsors presumably know the most about the investigational product's safety profile.

When I made reference to the most common and serious adverse events, I meant to imply all "adverse drug reactions" whether they are common and non-serious or rare and serious. If possible, pharmacovigilance folks try to make a distinction between true adverse drug reactions (i.e., possibly related) and isolated adverse events (i.e., no causal attribution) when it comes to informing about "reasonably foreseeable risks."

As you indicated, the most difficult part of these decisions is determining whether or not there is a "reasonable possibility that the experience may have been caused by the drug." This is particularly difficult for isolated observations, which may meet regulatory serious criteria, but are considered expected disease-related complications or appear to be chance occurrences. In studies of serious and life-threatening conditions, the numbers of such events can be substantial. In this regard, I agree that a "laundry list of every observed AE..., regardless of causal relationship" would not serve the interests of subjects.

I was hoping the FDA had some magic formula to deal with this issue. Like so many things in clinical trials, I suppose good judgment is the best formula.

One last question. Is there a "gold standard" informed consent template (with specific content guidance) that the FDA wishes people would use? If so, would you be so kind as to direct me to it.

Again, thank you for answering my questions.

Kind regards,

[purged]

on 4/2/02 7:27 AM, OC GCP Questions at GCPQuestions@OC.FDA.GOV wrote:

> Dear [purged],
>
> David Lepay asked me to respond to your e-mail (below). It is up to the
> Institutional Review Board (IRB) to determine that a study's informed
> consent form contains the information required by 21 CFR part 50. Most IRBs
> consider both the probability as well as magnitude of harm that may be
> related to use of the test article in considering the risks that are to be
> described to the subjects. Thus, one may have a serious risk, with low
> probability of occurrence, that would need to be described; or a minor risk,
> with a high probability of occurrence, that should also be described; as
> well as those risks in between. Where one can quantify risk, that ought to
> be done; however, in most cases, we recognize that would be difficult.
>
> In terms of causality, we tend to say that "There is a reasonable
> possibility that the experience may have been caused by the drug." Some
> have suggested that it may be more reasonable to ask whether you can rule
> out a connection between the experience and the drug--and if you cannot do
> that scientifically, then causality ought to be considered a possibility.
>
> The greatest challenge, in my mind, is to present the information to the
> subject in a way that is meaningful, balanced, and not misleading. I think
> that a "laundry list of every observed AE..., regardless of causal
> relationship" would not serve the interests of subjects. However to limit
> the information provided to subject to "the most common and serious adverse
> events" would not meet the requirements of the regulations. As I noted
> above, those AEs that are serious, even with a low probability of
> occurrence, must be disclosed.
>
> I hope this is helpful to you. My best,
>
> Bonnie
>
> Bonnie M. Lee
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> -----Original Message-----
> From: [purged]
> Sent: Friday, March 29, 2002 11:22 AM
> To: DLepay@OC.FDA.GOV
> Subject: Informed Consent Questions
>
>
> Dear Dr. Lepay:
>
> I hope all is well with you and your staff.
>
> I am writing to ask a few GCP-related questions that come up often.
>
> My questions have to do with the extent and content of "safety information"
> in the risk section of the informed consent.
>
> In the FDA's IC regulation, what is the intent behind the guidance to
> include "A description of any reasonably foreseeable risks or discomforts to

> the subject" in the informed consent?
>
> I have seen some informed consents with laundry lists of every observed AE
> in a clinical development program, regardless of causal relationship. My
> sense is that this was not the intent of the informed consent regulation.
>
> What guidance can the FDA give to determine what is a reasonable forseeable
> risk during an evolving clinical development program? My guess is that the
> most common and serious adverse events thought to be possibly linked to the
> investigational product based on previous experience and/or cumualtive data
> analyses are the most important to summarize in the IC.
>
> As always, your input is greatly appreciated.
>
> Kind regards,
>
> [purged]