From: Hommel, Carolyn - OC on behalf of OC GCP Questions
Sent: Thursday, December 09, 2004 3:55 PM
To: [Redacted]
Cc: CDER DRUGINFO
Subject: What do you think, #1?

Dear Ms. [Redacted]:

Your question to the CDER DRUGINFO e-mail account was forwarded to me for a response. I apologize for the delay in responding to you. You asked who is responsible for disclosing to participants in a clinical trial new information about possibly life threatening adverse events discovered during the course of the trial.

Generally, information about significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation are provided to the subject(s) by means of the informed consent process. It would be unethical and a violation of FDA's regulations to withhold such information from study subjects.

FDA's regulations state, "An investigator shall promptly report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug. If the adverse effect is alarming, the investigator shall report the adverse effect immediately." [See 21 CFR 312.64(b).]

Each investigator is also required to sign a Form FDA-1572 before the study begins; the form includes the investigator's commitment that he/she "will promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects or others, and will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to the human subjects." [See 21 CFR 312.53(c)(1)(vii).]

FDA's informed consent regulations require specific information to be provided to each subject, including
"...(2) a description of any reasonably foreseeable risks or discomforts to the subject..." [See
21 CFR 50.25(a)(2).] Under "Additional elements of informed consent," the regulations state, "When appropriate, one or more of the following elements of information shall also be provided to each subject:...
(5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject." [See 21 CFR 50.25(b)(5).]

Thus, at the very least, FDA would expect (1) the consent forms to be revised to reflect the new information, (2) the revised consent forms to be submitted to the IRB for review and approval prior to use, and (3) study subjects to be re-consented, so that they are given the opportunity to withdraw from the study if they so choose. The IRBs would also be responsible for evaluating the overall risk-benefit ratio of the study in light of the new information and determining if additional steps need to be taken to protect the rights and welfare of the subjects.

FDA's official guidance on the conduct of clinical studies, the ICH E-6 "Good Clinical Practice: Consolidated Guidance," also addresses this issue. Section 4.8.2 states: "The written informed consent form and any other written information to be provided to subjects should be revised whenever important new

information becomes available that may be relevant to the subject's consent. Any revised written informed consent form and written information should receive the IRB/IEC's approval/favorable opinion in advance of use. The subject or the subject's legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the trial. THE COMMUNICATION OF THIS INFORMATION SHOULD BE DOCUMENTED." [Emphasis added.]

All of FDA's regulations and the ICH guidance may be viewed in their entirety on FDA's Good Clinical Practice website: http://www.fda.gov/oc/gcp .

I hope this answers your question.

Sincerely,

Carolyn Hommel
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Good Clinical Practice Program
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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.

-----Original Message-----
From: CDER DRUGINFO
Sent: Friday, November 12, 2004 11:31 AM
To: OC GCP Questions
Subject: FW: DrugInfo Comment Form FDA/CDER Site

-----Original Message-----
From: [Redacted]
Sent: Thursday, November 11, 2004 11:28 PM
To: druginfo@cder.fda.gov
Subject: DrugInfo Comment Form FDA/CDER Site

Name: [Redacted]

E-Mail: [Redacted]

Comments: I am a Pharmacy Student at [Redacted] and I am doing research for a presentation I will be giving to other students. I have studied your website and have come across two federal regulations including 21CFR50.25 and 45CFR46 which are relevant to the information I need, however I am not sure if I'm interpreting these laws correctly.

The information I will be presenting involves Clincial Trials. In short, if a researcher discovers possibly life threatening adverse events during the course of a clinical trial with an investigational drug is it illegal for the researcher to not disclose this new information to the trial participant or is it up to the discretion of the IRB to reveal or not to reveal this information?

Thank you for attending to my question.

[Redacted]