MessageFrom: Hommel, Carolyn - OC on behalf of OC GCP Questions
Sent: Wednesday, January 19, 2005 11:59 AM
To: [purged]
Subject: RE: Can you help?

Dear Dr. [purged]:

I apologize for the delay in responding to the second question in your November 20, 2004 e-mail: "The same IRB judged a trial of an SR device to be minimal risk. Do you know of circumstances in which this might be appropriate?" I have pasted into this e-mail, a section from FDA's Information Sheets that discusses "significant risk" device studies:

Significant Risk and Nonsignificant Risk Medical Device Studies
The Investigational Device Exemption (IDE) regulations [21 CFR part 812] describe two types of device studies, "significant risk" (SR) and "nonsignificant risk" (NSR). An SR device study is defined [21 CFR 812.3(m)] as a study of a device that presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject. An NSR device investigation is one that does not meet the definition for a significant risk study. NSR device studies, however, should not be confused with the concept of "minimal risk," a term utilized in the Institutional Review Board (IRB) regulations [21 CFR part 56] to identify certain studies that may be approved through an "expedited review" procedure. For both SR and NSR device studies, IRB approval prior to conducting clinical trials and continuing review by the IRB are required. In addition, informed consent must be obtained for either type of study [21 CFR part 50].
Distinguishing Between SR and NSR Device Studies
The effect of the SR/NSR decision is very important to research sponsors and investigators. SR device studies are governed by the IDE regulations [21 CFR part 812]. NSR device studies have fewer regulatory controls than SR studies and are governed by the abbreviated requirements [21 CFR 812.2(b)]. The major differences are in the approval process and in the record keeping and reporting requirements. The SR/NSR decision is also important to FDA because the IRB serves, in a sense, as the Agency's surrogate with respect to review and approval of NSR studies. FDA is usually not apprised of the existence of approved NSR studies because sponsors and IRBs are not required to report NSR device study approvals to FDA. If an investigator or a sponsor proposes the

initiation of a claimed NSR investigation to an IRB, and if the IRB agrees that the device study is NSR and approves the study, the investigation may begin at that institution immediately, without submission of an IDE application to FDA.

If an IRB believes that a device study is SR, the investigation may not begin until both the IRB and FDA approve the investigation. To help in the determination of the risk status of the device, IRBs should review information such as reports of prior investigations conducted with the device, the proposed investigational plan, a description of subject selection criteria, and monitoring procedures. The sponsor should provide the IRB with a risk assessment and the rationale used in making its risk determination [21 CFR 812.150(b)(10)].

Given this information, it is difficult to understand how the IRB came to the determination that a significant risk device study could be minimal risk.

It is possible that the IRB may be confused about the definition of "minimal risk", and perhaps believes that the patient population who would receive the device is so ill that adding the risk of the investigational device was minimal risk for that very specific ill patient population. However, the definition of minimal risk in the IRB regulation means that the probability and magnitude of harm of discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

If you would like to provide more information about the specific IRB and study involved, I can forward it to our Center for Devices and Radiological Health for further evaluation and follow-up.

I hope this is helpful.

Sincerely,

Carolyn Hommel
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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: [purged]
Sent: Tuesday, November 30, 2004 11:48 AM
To: DLepay@oc.fda.gov
Subject: Can you help?

Dear David,
I was wondering if you'd be willing to give me an opinion on a couple of issues that have arisen from one of our reviews:
1. Are there circumstances in which research use of an approved prescription drug might appropriately be judged to be minimal risk? The case I'm concerned about is an IRB that judged a comparison of 2 triple therapies for HIV to be minimal risk, apparently using the rationale that they were FDA approved drugs.
2. The same IRB judged a trial of an SR device to be minimal risk. Do you know of circumstances in which this might be appropriate?
Thanks!
[purged]