From: Hommel, Carolyn - OC on behalf of OC GCP Questions
Sent: Tuesday, January 04, 2005 8:12 AM
To: [Redacted]
Subject: RE: Question regarding GCP studies and waivers
Dear [Redacted]:

Your questions related to a Treatment IND/Expanded Access Study were forwarded to me for a response. I have pasted your questions into this e-mail to make the responses clearer.

Question 1. "We are going to conduct a study that is really sort of a Treatment IND/Expanded access study and would like to know if we can minimize the collection of ICH Essential Documents that we routinely collect in studies. If we do this "in the spirit of GCP" and stipulate in the protocol exactly what documents both we the Sponsor and the Investigator will be required to maintain, is that permissible?"

Answer: As far as I know, the IND regulations' requirements for documentation of clinical studies do not differentiate among various types of INDs. Therefore if it's appropriate to make some accommodation in the types of records that are needed, this should be coordinated with FDA's review division staff as they review the study protocol.

Question 2: "Also, if we get an FDA waiver for IRB approval, how do we do the informed consent without IRB approval (we thought only an IRB could waive the consent process)?

Answer: Your message seems a little confused. First of all, even if FDA waives the requirement for IRB review of a study, that does not mean that the requirements for informed consent are also being waived. FDA regulations contain three exceptions to informed consent:

1) 21 CFR 50.23 (a), (b), and (c) pertain to an immediate life-threatening situation (i.e., emergency use of an investigational article is required to save the life of an individual).
2) 21 CFR 50.23(d) covers an exception related to members of the military in connection with their participation in a particular military operation.
3) 21 CFR 50.24 covers *planned* research studies of treatments intended to be used in emergency settings.

Under FDA regulations, IRBs may not, as you suggest, "waive the consent process"; rather, the IRB may waive the requirement for ***documentation*** of informed consent in two instances: 1) "minimal risk" studies, or 2) if the subject is participating in a study that meets the requirements of 21 CFR 50.24. [See 21 CFR 56.109(c).]

For all other studies involving FDA regulated research, obtaining informed consent from study subjects "shall be deemed feasible". [21 CFR 50.23(a)],

and informed consent must be obtained prior to subjects' participation in the research.

I have pasted the following excerpt from FDA's Information Sheets, "Guidance for Institutional Review Boards and Clinical Investigators," as it appears to be pertinent to your questions:

Waiver of IRB Requirements for Drug and Biologics Studies

In accordance with 21 CFR 56.105, FDA may waive any of the requirements contained in the Institutional Review Board (IRB) regulations [21 CFR part 56] if requested by the sponsor or sponsor-investigator. A waiver can be granted for specific research activities or for classes of research activities otherwise covered by the IRB regulations. ***Note that the waiver provision does not apply to the informed consent requirements [21 CFR part 50]. An institution may still require IRB review on the local level even if a waiver from FDA is granted.*** **[Emphasis added.]**

FDA uses the waiver provision only where it would be in the best interest of the subjects and where alternative mechanisms for assuring the protection of the subjects are adequate. Circumstances which FDA will consider for a waiver include "treatment INDs," i.e., the use of an investigational drug or biologic primarily for the treatment of a subject with a serious or immediately life-threatening disease for whom comparable or satisfactory alternate therapy is unavailable. [See 21 CFR 312.34.] The waiver provision is not needed for an emergency use because the regulations contain a provision for exemption from prospective IRB review in an emergency, provided that such use is reported to the IRB within 5 working days [21 CFR 56.104(c)].

FDA will handle waiver requests expeditiously. A request for waiver should contain the following information:

> (1) The specific requirement or requirements in the IRB regulations for which a waiver is requested.
> (2) The specific research activity for which the waiver will be applied and why this is a special situation.
> (3) Why a waiver would be in the interest of subjects.
> (4) What alternate mechanism(s) for assuring the protection of human subjects is available and would be utilized.
> (5) A copy of the proposed consent document.

The sponsor or sponsor-investigator should submit a request for a waiver associated with an IND to the Review Division in the Center for Drug Evaluation and Research (CDER) or to the Review Division in the Center for Biologic Evaluation and Research (CBER) responsible for reviewing the

IND. **[Emphasis added.]** If the identity of the responsible Review Division is unknown, the waiver request may be sent to:

For DRUG PRODUCTS:
Drug Information Branch (HFD-211)
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857
(301) 827- 4573

For a BIOLOGICAL BLOOD product, contact:
Office of Blood Research and Review (HFM-300)
Center for Biologic Evaluation and Research
Food and Drug Administration
1401 Rockville Pike
Rockville, Maryland 20852
301-827-3518

For a BIOLOGICAL VACCINE product, contact:
Office of Vaccines Research and Review (HFM-400)
Food and Drug Administration
8800 Rockville Pike
Bethesda, Maryland 20892-0001
301-827-0648

For a BIOLOGICAL THERAPEUTIC product, contact:
Office of Therapeutics Research and Review (HFM-500)
Food and Drug Administration
1451 Rockville Pike
Rockville, Maryland 20852-1420
301-594-2860

Question 3: "Whom do the subjects contact regarding subject/rights/welfare, as is typically the IRB? Beyond getting a central IRB approval (not our current plan) in lieu of a local one, how does the consent get approved?"

Answer: The following excerpt from FDA's information sheets addresses this issue:

<u>TREATMENT IND</u>

The treatment IND [21 CFR 312.34 and 312.35] is a mechanism for providing eligible subjects with investigational drugs for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. A treatment IND may be granted after sufficient data have been collected to show

that the drug "may be effective" and does not have unreasonable risks. Because data related to safety and side effects are collected, treatment INDs also serve to expand the body of knowledge about the drug.

There are four requirements that must be met before a treatment IND can be issued: 1) the drug is intended to treat a serious or immediately life-threatening disease; 2) there is no satisfactory alternative treatment available; 3) the drug is already under investigation, or trials have been completed; and 4) the trial sponsor is actively pursuing marketing approval.

Treatment IND studies require prospective IRB review and informed consent. A sponsor may apply for a waiver of local IRB review under a treatment IND if it can be shown to be in the best interest of the subjects, ***and if a satisfactory alternate mechanism for assuring the protection of human subjects is available, e.g., review by a central IRB.*** **[Emphasis added.]** Such a waiver does not apply to the informed consent requirement. ***An IRB may still opt to review a study even if FDA has granted a waiver.*** **[Emphasis added.]**

You may read the information sheets in their entirety on FDA's Good Clinical Practice website: http://www.fda.gov/oc/gcp; once at the site, click on "Guidances and Information Sheets" in the middle column.

I hope this is helpful.

Sincerely,

Carolyn Hommel
Consumer Safety Officer
Good Clinical Practice Program
Office of Science and Health Coordination
Office of the Commissioner
U.S. Food and Drug Administration (HF-34)
5600 Fishers Lane, Room 9C24
Rockville, MD 20857

Phone: 301/827-3340
Fax: 301/827-1169

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: [Redacted]
Sent: Tuesday, December 07, 2004 11:08 AM

To: gcpquestions@oc.fda.gov
Subject: Question regarding GCP studies and waivers

Dear FDA GCP Staff,
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I greatly appreciate any assistance you can provide.

Best regards,
[Redacted]