MessageFrom: Beers Block, Patricia
Sent: Wednesday, December 13, 2006 1:35 PM
To: [purged]
Subject: RE: forms for clinical trials

Dear [purged],

There are volumes of information that have been written that are responsive to your questions. . I'll try to briefly address each of the issues about which you request Information, but I strongly suggest you look at our web page, especially the "Educational Materials" and "Guidance" links for more detail. For starters, you may want to look through FDA's Information Sheet guidances and the various guidance documents that have issued on some of the topics about which you request information (I'll get into some of these later in my message).

I'll address each of your topics in the order you provided them in your inquiry:

1) The Forms FDA 1571 and 1572 can be found at http://www.fda.gov/opacom/morechoices/fdaforms/default.html. When you link to this site, you will find blank forms as well as instructions on how to the complete these forms. This should be a good start for you to get the sense for the information that's needed in these forms, and their purpose.

2) The FDA-482 is issued by field investigators prior to starting an inspection of a regulated facility. Here is an example of this form: http://www.fda.gov/ora/inspect_ref/iom/exhibits/5-1.pdf As you can see, the form contains specific regulatory references/statutes that allow FDA to inspect facilities.

3) In answer to your question about emergency research, under FDA regulations, there are two instances when research may be conducted without prior consent from the subject. The first, found at 21 CFR 50.23 (a)-(c) concerns the use of an investigational product on a subject without the benefit of prior consent. This regulation reads as follows:

> "Sec. 50.23 Exception from general requirements.
>
> (a) The obtaining of informed consent shall be deemed feasible unless, before use of the test article (except as provided in paragraph (b) of this section), both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing

all of the following:
(1) The human subject is confronted by a life-threatening situation necessitating the use of the test article.
(2) Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.
(3) Time is not sufficient to obtain consent from the subject's legal representative.
(4) There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.
(b) If immediate use of the test article is, in the investigator's opinion, required to preserve the life of the subject, and time is not sufficient to obtain the independent determination required in paragraph (a) of this section in advance of using the test article, the determinations of the clinical investigator shall be made and, within 5 working days after the use of the article, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.
(c) The documentation required in paragraph (a) or (b) of this section shall be submitted to the IRB within 5 working days after the use of the test article."

FDA's guidance on this specific regulation, found in the Information Sheet entitled " (see http://www.fda.gov/oc/ohrt/irbs/drugsbiologics.html#emergency), notes the following:

"Exception From Informed Consent Requirement
Even for an emergency use, the investigator is required to obtain informed consent of the subject or the subject's legally authorized representative unless both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following [21 CFR 50.23(a)]:
(1) The subject is confronted by a life-threatening situation necessitating the use of the test article.
(2) Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject.
(3) Time is not sufficient to obtain consent from the subject's legal representative.
(4) No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.
If, in the investigator's opinion, immediate use of the test article is

required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the clinical investigator should make the determination and, within 5 working days after the use of the article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. The investigator must notify the IRB within 5 working days after the use of the test article [21 CFR 50.23(c)]. "

The second type of emergency research occurs when a sponsor intends to conduct emergency research throughout the trial and has complied with the regulatory requirements set out in 21 CFR 50.24. A draft guidance recently issued on the this situation; you can find this draft guidance at
http://www.fda.gov/OHRMS/DOCKETS/98fr/06d-0331-gdl0001.pdfare
I've copied the introduction section of this guidance for your ready reference:

"This guidance applies to research studies involving FDA regulated products (drugs, biological
products, and medical devices) . The information provided in this guidance is intended to assist
sponsors, clinical investigators, and Institutional Review Boards (IRBs) in (1) the development
and conduct of research in emergency settings when an exception from the informed consent
requirements is requested under Title 21, Code of Federal Regulations, Section 50.24 (21 CFR
50.24) and (2) understanding their responsibilities for communicating with, and submitting
information to, FDA.

The regulations in 21 CFR 50 .24, and the conforming amendments contained in 21 CFR Parts
56, 312, 314, 601, 812, and 814 provide an exception from the requirement to obtain informed
consent from each subject, or the subject's legally authorized representative, prior to enrollment
in a clinical investigation. The exception applies to emergency research for which, among other
things, (1) an Investigational New Drug Application (IND) or Investigational Device Exemption
(IDE)2 is required, (2) that involves human subjects who have a life-threatening medical
condition (for which available treatments are unproven or unsatisfactory), (3)

that involves
subjects who, because of their condition (e.g., unconsciousness) cannot give
informed consent,
and (4) where, to be effective, the intervention must be administered before
informed consent
from the subjects' legally authorized representative is feasible. Studies
involving an exception
from the informed consent requirements may proceed only after a sponsor has
received prior
written authorization from FDA, and the IRB has found and documented that
specific conditions
have been met.

The regulations for emergency research contain specific human subject
protection requirements
that are in addition to those found in other sections of 21 CFR Parts SO, and
21 CFR 56, 312 and
812. Among these requirements are the need for consultation with
representatives of the
community(ies) in which the research will take place and from which the
subjects will be drawn,
public disclosure of information before the start of the study and following
its completion, a
commitment by the investigator to make efforts to contact a family member to
determine
whether the family member objects to the subject's participation, and
establishment of.an
independent Data Monitoring Committee (DMC). These additional requirements are
necessary
because the emergency research permitted under 21 CFR 50.24 involves a
particularly
vulnerable population : persons with life-threatening conditions who can
neither give informed
consent nor actively refuse enrollment . This lack of autonomy creates a
special need for FDA,
sponsors, IRBs, and clinical investigators to work closely together to protect
the interests of this
vulnerable population of subjects . At the same time, FDA needs to consider
the unmet medical
needs of such subjects and the potential for them to benefit from new
therapies for such
conditions ."

4) The FDA regulations found at 21 CFR 50.50-56, collectively known as "Subpart D- Additional Safeguards for Children in Clinical Investigations", describe additional regulatory requirements that must be considered/addressed when using children as research subjects.

I hope this information is helpful to you.

Sincerely,

Patricia M. Beers Block
Good Clinical Practice Program (HF-34)
Office of the Commissioner/ FDA
Telephone: 301-827-3340
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: Monday, December 04, 2006 11:39 PM
To: OC GCP Questions
Subject: forms for clinical trials

Sub : Clarifications regarding forms required for application for clinical trials

Dear Sir / Madam,
I am engaged in education related to clinical trials. I am interested to receive some details regarding the various forms and requirements related to the following forms of FDA.

1. Form FDA 1571
2. Form FDA 1572
3. Form FDA 482

I also would like to receive information regarding :-
a) use of Investigational new drug in an emergency situation
b) Informed consent for children

Please send relevant information on these matters at your convenience,

Thanking you,

[purged]