From: Hommel, Carolyn - OC on behalf of OC GCP Questions
Sent: Tuesday, October 26, 2004 12:47 PM
To: **[Redacted]**
Subject: RE: Question about Investigator Brochures submitted for clinical research studies

Dear Ms. **[Redacted]** :

Your e-mail to the GCP Questions account was forwarded to me for a response.

You asked: "Is there any guidance or regulations regarding the IRB's responsibilities for Investigator Brochures (IB)? Does the IRB need to keep on file all versions of the IB submitted for a clinical research study or is it adequate to have access to the IB within the institution (i.e., PI's research files) if needed?"

Answer: FDA's regulations for IRBs, found in 21 CFR 56, are fairly general and do not specifically mention the "Investigator's Brochure" (IB), although they do require the IRB to maintain "...Copies of all research proposals reviewed..." [See 21 CFR 56.115 (a)(1).] Such records must be retained for "at least 3 years after completion of the research and ...shall be accessible for inspection and copying by authorized representatives of the Food and Drug Administration..." [See 21 CFR 56.115(b).]

FDA's official guidance, the ICH E-6 "Good Clinical Practice: Consolidated Guidance," states:

"3.1.2 The IRB/IEC should obtain the following documents: Trial protocol(s)/amendment(s), written informed consent form(s) and consent form updates...***Investigator's Brochure (IB)...*** and any other documents that the IRB/IEC may require to fulfil its responsibilities." [Emphasis added.]

Section 8 (Essential Documents for the Conduct of a Clinical Trial), subsection 8.2.1 recommends that the IB be maintained by the Investigator/Institution and the Sponsor, "[t]o document that relevant and current scientific information about the investigational product has been provided to the investigator."

So, in answer to your questions, because the regulations are not specific, the IRB and institution have some discretion in developing procedures that would specify where copies of the IB and other documents are to be maintained.

You also asked, "What do FDA auditors look for in terms of IBs when doing site visits?"

Answer: All of the procedures that FDA's field investigators use to inspect all of the various establishments under FDA's jurisdiction are found in the Compliance Program Guidance Manual (CPGM), which is posted on the website of FDA's Office of Regulatory Affairs (ORA).

There is a link to the CPGM chapters pertaining to bioresearch monitoring (clinical investigators, IRBs, Sponsors/Monitors/CROs) on FDA's Good Clinical

Practice website (http://www.fda.gov/oc/gcp). [Once at that page, click on "Bioresearch Monitoring Program" at the bottom of the middle column.] Your IRB might find it helpful to review the CPGM pertaining to IRB inspections, as it generally describes the issues that the FDA field investigator would likely raise during any interviews with the IRB staff and also describes the various documents that he/she might wish to review during the inspection.

With respect to your specific question, in describing the procedures that the FDA investigator should use to "determine whether the IRB provides a system for receiving and distributing the material submitted by the clinical investigators," the IRB CPGM chapter (Attachment A, Section C1) suggests that "An acceptable package for initial review would contain the proposed protocol, the consent form, and the investigator's brochure provided by the sponsor. When an investigator's brochure is not available, the protocol should contain an appropriate description of the previous animal and human experience associated with use of the investigational article..."

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: Wednesday, October 13, 2004 1:33 PM
To: gcpquestions@oc.fda.gov
Subject: Question about Investigator Brochures submitted for clinical research studies

Is there any guidance or regulations regarding the IRB's responsibilities for Investigator Brochures (IB)? What do FDA auditors look for in terms of IBs when doing site visits? Does the IRB need to keep on file all versions of the IB submitted for a clinical research study or is it adequate to have access to the IB within the institution (i.e., PI's research files) if needed?
Thank you.
[Redacted]