From: Hommel, Carolyn - OC on behalf of OC GCP Questions
Sent: Monday, December 06, 2004 2:53 PM
To: [Redacted]
Subject: RE: Question re: Sponsor's Access to Consent Forms

Dear Ms. [Redacted]:

Your question about sponsor access to informed consent documents was forwarded to me, and I apologize for the delay in responding to you.

There are no regulations that explicitly say a sponsor or the sponsor's monitors must be granted access to subjects' informed consent documents and medical records. However, this expectation is clearly implicit in the regulations (CFR) and in our GCP guidance. In my opinion, the regulatory basis to support a sponsor's access to subjects' executed informed consent document and patient medical records would rest most heavily on the regulatory obligation of the sponsor to ensure adequate monitoring under 312.50 and 312.56 (for drug studies) and 812.40 and 812.46 (for medical device studies). You mentioned that you work for a medical device company, so I will try to gear my response to the device regulations.

21 CFR 812.40 states, "Sponsors are responsible for...ensuring proper monitoring of the investigation..." and 21 CFR 812.46(a) states:

> "(a) A sponsor who discovers that an investigator is not complying with the signed agreement, the investigational plan, the requirements of this part or other applicable FDA regulations, or any conditions of approval imposed by the reviewing IRB or FDA shall promptly either secure compliance, or discontinue shipments of the device to the investigator and terminate the investigator's participation in the investigation..."

In order to do this, a sponsor would have to determine whether the investigator is complying with the record keeping requirements in part 812, specifically 812.140(a)(3), which states:

> "(a) Investigator records. A participating investigator shall maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation...
>
> "(3) Records of each subject's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes. Such records shall include: (i) Documents evidencing informed consent...The case history for each individual shall document that informed consent was obtained prior to participation in the study..."

The sponsor would necessarily need to verify that case histories---including the informed consent documents--are being maintained. Adequate monitoring would

therefore necessarily include direct access to each subject's informed consent document(s) and medical information pertinent to the investigation.

FDA's Information Sheet Guidance, "Sponsor-Investigator-IRB Interrelationship," also addresses this issue:

> "Sponsor Access to Medical Records
> "The IRB is responsible for ensuring that informed consent documents include the extent to which the confidentiality of medical records will be maintained [21 CFR 50.25(a)(5)]. FDA requires sponsors (or research monitors hired by them) to monitor the accuracy of the data submitted to FDA in accordance with regulatory requirements. These data are generally in the possession of the clinical investigator. Each subject must be advised during the informed consent process of the extent to which confidentiality of records identifying the subject will be maintained and of the possibility that the FDA may inspect the records. While FDA access to medical records is a regulatory requirement, subject names are not usually requested by FDA unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual cases studied or actual results obtained. The consent document should list all other entities (e.g., the sponsor) who will have access to records identifying the subject. The extent to which confidentiality will be maintained may affect a subject's decision to participate in a clinical investigation. "

This interpretation of what is required for adequate monitoring by the sponsor is further supported by the ICH E-6 Good Clinical Practice: Consolidated Guideline; E-6 makes it quite clear that regulators, sponsors, IRBs, monitors etc. should have direct access to subjects' records. I must point out that while the principles and practices in ICH guidance can be applied (generally) to any clinical investigation, ICH was developed by the Expert Working Group of the International Conference on Harmonisation of Technical Requirements for Registration of *Pharmaceuticals* for Human Use. I am not aware of any similar guidance on good clinical practice that is specific to medical device studies. In any case, the following sections of E-6 that pertain to monitoring and record keeping practices may be of interest to you:

"6.10 Direct Access to Source Data/Documents

> "The sponsor should ensure that it is specified in the protocol or other written agreement that the investigator(s)/institution(s) will permit trial-related monitoring, audits, IRB/IEC review, and regulatory inspection(s) by providing direct access to source data/documents."

Direct access is defined as:

> **"1.21 Direct Access**: Permission to examine, analyze, verify, and reproduce any records and reports that are important to evaluation of a

clinical trial. Any party (e.g., domestic and foreign regulatory authorities, sponsors, monitors, and auditors) with direct access should take all reasonable precautions within the constraints of the applicable regulatory requirement(s) to maintain the confidentiality of subjects' identities and sponsor's proprietary information."

Source Data and Source Documents are defined as follows:

> **"1.51 Source Data**: All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies).
>
> **"1.52 Source Documents**: Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial)."

In other words, sponsors are responsible for monitoring each investigation and thus may need to review subjects' records. The informed consent document should describe who will have access to study records (including subjects' medical files) so that subjects are aware that sponsors, monitors, or regulators may be reviewing them.

I would also like to clarify a point that you raised in your e-mail: Section 8.2.7 of the ICH E-6 guidance recommends that the "Dated, documented approval/favorable opinion of the IRB/IEC of ...Informed consent form(s)" be maintained by both the Investigator/Institution and the sponsor. By contrast, Section 8.3.12 recommends that "***Signed informed consent forms***" [Emphasis added] be maintained in the files of the clinical investigator.

In conclusion, even though the regulations themselves don't explicitly state that a sponsor shall have access to subject informed consent documents and medical records, this expectation is implicit in the regulatory requirements for adequate monitoring and is further suggested in FDA's Information Sheet Guidance and the ICH GCP. All of the documents mentioned above may be viewed in their entirety on FDA's Good Clinical Practice website: http://www.fda.gov/oc/gcp .

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: Thursday, November 18, 2004 2:51 PM
To: gcpquestions@oc.fda.gov
Subject: Question re: Sponsor's Access to Consent Forms

Dear Sir or Madam,

I work for [Redacted] and we often sponsor mulitsite clinical trials. We are working with one hospital who will not allow us (the study's sponsor) to have copies of their subjects' executed consent forms. They've indicated that providing us with this information violates the hospital's patient privacy policy.

As I understand the ICH GCP Guideline, both sponsors and investigators are required to maintain copies of the consent forms, as part of the record keeping process. In addition, I was recently in [Redacted] for a GCP audit and the missing consent forms from this site were 'problematic' - to say the least.

Can you provide me with any additional information that I can use to convince this hospital that their policy prevents us from carrying out our obligations and requirements, as a study sponsor?

Thank you for your help. Any suggestions that you have will be most appreciated!

[Redacted]