II. LIST OF TOPICS

This chapter mainly concerns the FDA's Warning Letters that are issued to a Sponsor during clinical trials on human subjects. As such, this chapter does not much concern letters that are issued relating to issues that arise during the marketing or manufacture of drugs that have already received FDA-approval. The topics in this chapter include:

- Authority of FDA inspectors to monitor clinical trials;
- Relation between FDA's Form 483 notices and FDA's Warning Letters;
- How a Sponsor should respond to a Warning Letter;
- Institutional Review Board (IRB);
- Data Monitoring Committee (DMC);
- Consent Forms;
- Protocol violations;
- Drug accountability and record keeping.

These particular topics are related to each other. For example, the most frequent issues of complaint include the IRB's failure to approve consent forms, and the IRB's failure to comply with the FDA's requirements for record keeping.

III. WARNING LETTER DESCRIBING AUTHORITY OF FDA INSPECTORS

As a starting point, the following Warning Letter establishes part of the FDA's regulatory authority, namely, the authority to acquire the investigator's records. Warning Letters are issued as a result of records obtained during the FDA's inspection of the Sponsor's workplace. Thus, it should be taken for granted that the Sponsor actually allows FDA inspectors to enter the workplace and see the records. But on rare occasions, inspection is denied by the Sponsor.

The cited Warning Letter stated that (5), "[b]etween May 24 and June 8, 2005, Ms Barbara Breithaupt, representing the Food and Drug Administration (FDA), met with you to review your conduct of the following clinical study of the investigational drug ... for which you served as the sponsor and clinical investigator." The letter went on to state that the investigator had refused to allow the inspector to see the records and, as a result, the inspector issued a Form 483 notice to the investigator.

The Warning Letter complained that, "[y]ou failed to permit an authorized officer of FDA to have access to, copy, or verify records or reports related to the conduct of the study noted above ... Ms Breithaupt made multiple attempts over a two week period from May 24, 2005 to June 7, 2005, to obtain access to your study records for the above-referenced study, for purposes of copying and verifying those records. Despite Ms Breithaupt's repeated and persistent efforts to obtain access to your study records, you failed to provide access to any of the records that would have been responsive to the inspection request" (6).

The letter listed reasons for the FDA's routine procedure for acquiring records from companies throughout the United States. The FDA's list of reasons was that, "[a]bsent access to source records, FDA is unable to verify any aspect of your study, including, but not limited to, whether adequate informed consent

[5]Warning Letter No. 07-HFD-45-0601 (June 22, 2007) from Gary Della'Zanna of Division of Scientific Investigations, Office of Compliance, CDER, U.S. Food and Drug Administration.

[6]Warning Letter No. 07-HFD-45-0601 (June 22, 2007) from Gary Della'Zanna of Division of Scientific Investigations, Office of Compliance, CDER, U.S. Food and Drug Administration.