

31 March 2006

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Subject: Docket No. 2006D-0017, OC 2005334. Human Subject Protection Information for Institutional Review Boards, Clinical Investigators, and Sponsors: Rescission, Reissuance, and Development of Food and Drug Administration Guidance Documents; Availability.

Quintiles Transnational Corp., a clinical research organization which provides outsourcing services to the pharmaceutical and biotechnology industry, appreciates the opportunity to comment on the above Final Guidance, published in the 03 February 2006 Federal Register (Vol. 71, No.23). The Final Guidance has been reviewed and discussed by representatives of Quintiles Regulatory, Clinical Quality Assurance, and Clinical Operations units. Our comments to this Final Guidance are listed below with details following.

The commendable goal of this Final Guidance intends to improve on the quality, consistency, and need of information to Institutional Review Boards (IRBs), Clinical Investigators, and Sponsors. Generally, Quintiles agrees with much of this Final Guidance, such as the consistent requirements of IRBs, Clinical Investigators, and Sponsors.

In discussions at Quintiles, we identified the list profiled below to be the areas of our primary issues and concerns with this Final Guidance, each of which is discussed in greater detail as follows.

FDA Inspections of Clinical Investigators

1. Types of inspections of clinical investigators
2. Monitor communications and evaluations
3. Medical record history
4. Clinical investigator inspection classifications

FDA Institutional Review Board Inspections

5. IRB Inspection classifications

Waiver of IRB Requirements for Drug and Biological Product Studies

6. IRB waivers for foreign studies

Significant Risk and Nonsignificant Risk Medical Device Studies

7. IRB responsibility in reviewing device studies

Frequently Asked Questions About Medical Devices

1. Types of inspections of clinical investigators

Section III states, "FDA conducts both announced and unannounced inspections of clinical investigator sites." Quintiles recommends that the guidance provide a definition of "for cause" and "directed" inspections. Because this guidance is intended for the clinical investigator, it would be helpful to address the different types of FDA inspections.

2. Monitor communications and evaluations

Section IV states, “the monitor’s communication with the clinical investigator,” as an item that the FDA personnel typically verify. Quintiles recommends that the guidance provide an example of such communication the FDA is referring to as a communication between monitors and investigators. We also recommend that the bullets on monitor’s communications with clinical investigator and the monitor’s evaluations of the progress of the investigation be combined into one bullet point.

3. Medical record history

Section 4 states, “FDA may also examine medical records about the subjects that predate the study...” This guidance is intended to act as an instruction document for clinical investigators and as such, should provide the expectations of the FDA inspectors regarding medical records predating the study. Accordingly, Quintiles recommends this statement be clarified by such words as, “immediately predating”, “recently predating,” or “reasonably predating.”

4. Clinical investigator inspection classifications

Section V. describes the process of closing out the inspection including the issuance of a 483. Quintiles recommends that definitions should be included for Official Action Indicated (OAI), Voluntary Action Indicated (VAI), and No Action Indicated (NAI). Also, it would be helpful if an explanation of the Clinical Investigator Inspection Listing was included in the guidance in order to explain to the clinical investigators that their name, address, date, and outcome of FDA inspection history will be available publicly through the Freedom of Information Act (FOI). An explanation of the NIDPOE process would also be helpful for clinical investigators.

5. IRB inspection classifications

Section V describes the process of closing out the inspection including the issuance of a 483. Quintiles recommends that definitions should be included for Official Action Indicated (OAI), Voluntary Action Indicated (VAI), and No Action Indicated (NAI). Also, it would be helpful if an explanation was included on the publicly available information through FOI on the outcomes of IRB inspections.

6. IRB waivers for foreign studies

Section III describes when the FDA may waive any of the IRB requirements such as when a sponsor wishes to conduct a foreign clinical study under an IND. Quintiles recommends this guidance be clarified to describe whether or not a waiver is necessary if the sponsor is using an IEC in a foreign country. Currently, as written, the guidance suggests that waivers must be used despite the use of IECs in foreign countries. Quintiles suggests the agency clarify this issue, perhaps by a separate paragraph to explain a situation when a sponsor wishes to conduct a foreign clinical study under an IND.

7. IRB responsibility in reviewing device studies

Section V, bullet 1 uses the wording “should have” in reference to IRB SOPs to explain determinations of device risk determination of SR and NSR. Because some FDA 483 findings have included this item deficiency at IRBs, Quintiles suggests the wording “shall have.”

Topics Not Addressed in the Guidance- Suggestions for Inclusion

8. Differences in IRB determinations of SR and NSR

The guidance does not address the situation of one site's IRB determining a study as SR while all the other sites IRBs determination agrees with the Sponsor determination of NSR. It would be helpful to include guidance on this situation as a resource for IRBs.

Quintiles appreciates the opportunity to provide comment to this final guidance. In summary, Quintiles agrees with many aspects of this final guidance and recommends the provision of additional clarity.

Sincerely,

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