QUINTILES

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852
http://www.fda.gov/dockets/ecomments

Subject: Docket No. 2005D-0101: Draft Guidance for Industry on Using a Centralized Institutional Review Board Process in Multicenter Clinical Trials.

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services to the pharmaceutical and biotechnology industry, appreciates the opportunity to comment on the above draft guidance published in the 28 March 2005 Federal Register (FR Doc #05-05977, Vol. 70). The proposed guidance has been reviewed and discussed by representatives of Quintiles Clinical Quality Assurance, Clinical Operations, and Regulatory units. Our comments to this proposed guidance are summarized below with details following.

The commendable goal of this Proposed Guidance is intended to assist sponsors, institutions, institutional review boards (IRBs), and clinical investigators involved in multicenter clinical research in meeting the requirements of 21 CFR part 56 by facilitating the use of a centralized IRB review process and to possibly improve efficiencies in the review process. Additionally, it is noted that the draft guidance describes the roles of the participants in a centralized IRB review process, provides guidance on how a centralized IRB review process should consider the concerns and attitudes of the various research communities, and provides recommendations on documenting various processes, such as agreement between a central IRB and the institution's IRB. Generally, Quintiles agrees with most aspects of the guidance document, such as outlining the roles of the various parties, the need to address local aspects of clinical research, and the need to document the agreement between the IRBs through written procedures. However, we propose that a few aspects be clarified to offer further guidance. Below, we make recommendations that, we believe, would accomplish FDA's admirable purpose and offer efficiencies in the process without compromising human subject protections.

From a Clinical Research Organization perspective, for multicentered trials we have had the opportunity to interact with several centralized IRBs, both large and small, and with multiple institutional IRBs. We agree that multiple reviews by multiple IRBs, in many cases, results in unnecessary duplication of efforts, delays, and increased expenses in the conduct of multicenter clinical trials. In addition, at times it creates confusion from site to site due to inconsistencies and can result in frustrations of involved study personnel. We believe that more reliance on a centralized IRB review process, in appropriate circumstances, has the potential to reduce IRB burdens of duplication of efforts, delays in the conduct of multicenter trials, and reduce overall costs.

In our discussions at Quintiles regarding use of Centralized IRBs and the proposed draft guidance, we note that the areas most concerning to us are already described within the document, namely 1) whether the IRB is competent to understand the local context of the research and suggested methods to accomplish that goal and 2) establishment of written procedures to define the documentation process of the agreement between the centralized IRB and the institution's IRB. However, we offer a recommendation to clarify the written procedures of the institution's IRB regarding apportioning the review of the study.

First, the guidance document notes that the requirement is stated in 21 CFR 56.107(a), that the IRB must be sensitive to community attitudes, have a familiarity with the standards of professional conduct and practice where the research takes place, and knowledge about local laws and regulations applicable to the study. In our experience with some centralized IRBs, this appears to be a consistent deficiency in their processes. We have observed certain centralized IRBs where their only process was to inquire of the clinical investigators via a single line item question on their submission application, and others who actually solicit a name and phone number of a local community advocate. However, even in the last situation, the centralized IRB's process did not require that they actually follow up and contact the local community advocate for input. So, it is our view, that this guidance document will provide a concrete means that centralized IRBs may utilize to implement this requirement of the regulations.

Secondly, our other area of concern is the establishment of written procedures to define the documentation process of the agreement between the centralized IRB and the institution's IRB. The guidance document describes the roles and responsibilities of the various parties via a single model (in Section III). It describes the need for the institution's IRB to develop policies, that the sponsor may facilitate the agreements and communication, that the clinical investigator should adhere to the institution's policies, and that the centralized IRB should review studies in accordance with 21 CFR part 56. However, the one theme consistent in the guidance document describes that the institution's IRB should determine whether they will apportion certain review responsibilities. It is our opinion that if the review process is apportioned so that both the centralized IRB and the institution's IRB are responsible for certain aspects, this does not accomplish the end goal of reducing the duplication of efforts and affording efficiencies.

Recommendations:

Our first recommendation is that: 1) the entire study review should be the responsibility of either the centralized IRB or the institution's IRB. We agree, however, that the centralized IRB should solicit input and advice from the institution's IRB where necessary if local issues need to be considered; and 2) central IRBs should establish written policies that describe their requirement of all or none of the review responsibilities, with the stipulation that they will involve the institution's IRB if they require it or if needed based on the local circumstances.

Additionally, Section V- IRB Records, states "...we recommended that they document the agreement..." between the two IRBs and that all other parties receive copies of the agreement. The initial sentence of the paragraph reiterates the regulatory requirement for IRBs to maintain adequate documentation of their activities. In light of the regulatory requirement, we recommend that the wording of this second sentence be revised to emphasize that documentation of such IRB activities are NOT optional.

Accordingly, we suggest that this second sentence be revised as follows: ". . . they should document that agreement and ensure . . ."

In summary, Quintiles agrees with the content of the draft guidance document regarding use of centralized IRBs for multicentered trials. We believe this document will provide a framework for IRBs to better implement the regulations of 21 CFR part 56, and that it will possibly improve efficiencies in the review process without compromising human subject protections.

Sincerely,

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