QUORUM
REVIEW INC.
An Institutional Review Board

April 21, 2005

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

Re: Comments on FDA's Request for General Information: Reporting of Adverse Events to Institutional Review Boards (Docket No. 2005N-0038)

Greetings:

Quorum Review, Inc. is pleased to provide comments on the issues raised in the Food and Drug Administration's ("FDA") notice concerning the reporting of adverse events to institutional review boards ("IRB").[1] Quorum is an independent IRB located in Seattle, Washington. Quorum reviews research that is governed by the FDA regulations and primarily provides oversight for sites that are not affiliated with an institution.

Quorum is a member of the Consortium of Independent Review Boards ("CIRB") and fully supports the comments submitted by CIRB on this same date. Quorum submits these comments to emphasize the need for FDA attention to the role of IRBs in adverse event reporting.

Quorum first asks the FDA to confirm that under the current regulations the role of an IRB with respect to individual adverse event reports is to review only those reports that describe "unanticipated problems involving risks to human subjects or others" ("unanticipated problems").[2] Reports of unanticipated problems assist an IRB in determining whether the risk/benefit ratio of a study continues to be acceptable, whether appropriate informed consent has been provided to study participants and whether the study should otherwise be allowed to continue without modification under 21 CFR 56.111. The only adverse events reports that are germane to these determinations are those that can be characterized as "unanticipated problems" pursuant to 21 C.F.R. § 108(b). If an adverse events report describes a problem that was anticipated at the time of initial review, then the IRB already should have considered its impact when assessing the risk/benefit ratio of the study and the completeness of the risks set forth in the consent form. If an adverse events report describes a problem that does not pose a risk to participants or others, then the IRB does not need to reconsider the risk/benefit ratio, modify the consent form or otherwise reconsider the conduct of the study.

[1] 70 Fed. Reg. 6693 (February 8, 2005).
[2] 21 C.F.R. § 56.108(b); 21 C.F.R. § 312.66.

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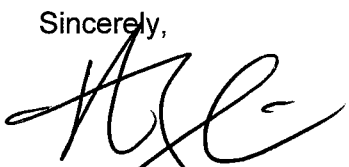
We also ask the FDA to confirm that the IRB's role is to ensure that appropriate reports are made – and not to generate the reports itself. In other words, it is not the role of an IRB to review all adverse event reports generated in a study and attempt to detect unanticipated problems from such data. IRBs do not have access to unblinded data, current enrollment figures, raw data generated by related studies or other meaningful data necessary for a competent analysis of the data; therefore, any attempts by an IRB to monitor adverse event raw data will be inherently unreliable. This is true regardless of the number of sites involved in the study. Even when an IRB has oversight of a study with only one site, the IRB does not have access to unblinded or other meaningful data.

Quorum acknowledges that there are some who believe that an independent body should monitor the safety data generated by a study as a "doublecheck" to the study sponsor and regulatory agencies. To the extent this is true, the solution is not to expect IRBs to analyze adverse event raw data. Instead, this role should be imposed on those who have access to meaningful data and the expertise to analyze it.

For now, in many studies a data safety monitoring board or data monitoring committee (collectively, "DMC") is used to provide independent safety data monitoring. Quorum encourages the FDA to finalize its draft guidance relating to DMCs[3] and to establish that summary reports for all DMC meetings should be submitted to all IRBs with oversight of pertinent sites. Currently the draft guidance does not require or even recommend that DMC reports be sent to IRBs.[4] DMCs serve a valuable function by assessing aggregated adverse events and other data generated in studies, and the DMC's assessment of these data would help IRBs perform their regulatory obligations. Please note that this request is for IRB access to DMC reports that summarize the DMC's assessment of reported safety data and that have not been modified by the sponsor or investigator. IRBs are not seeking access to the raw data reviewed or assessed by the DMC.

Quorum thanks the FDA for the opportunity to comment on this crucial matter. Please do not hesitate to contact us if you have any questions.

Sincerely,



Mark Mynhier
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[3] "Guidance for Clinical Trial Sponsors On the Establishment and Operation of Clinical Trial Data Monitoring Committees" (November 2001), available at http://www.fda.gov/cber/gdlns/clindatmon.htm
[4] *Id.* at Section 4.4.3.2, p. 17.