CONSORTIUM OF INDEPENDENT REVIEW BOARDS

CIRB CIRB

Statement of the Consortium of Independent Review Boards (CIRB)
Presented by John Isidor, CIRB President
FDA Public Hearing on Reporting of Adverse Events to IRBs
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The Consortium of Independent Review Boards is pleased to provide comments on the issues raised in the Food and Drug Administration's notice concerning the reporting of adverse events to IRBs. The Organization appreciates the Agency's recognition of the problems associated with the current system and this important initiative to improve the process. CIRB is a consortium of independent IRBs located in the United States and Canada. The membership has a central mission of promoting the protection and rights of human research subjects, while providing an understanding of how independent IRBs support this goal. Approximately 40% of clinical research in the United States is conducted in non-academic settings and independent IRBs review a majority of this research. Thus, as an organization of IRBs, CIRB has a significant interest in this matter. FDA has asked for comments on the IRB's role in reviewing adverse event reports, perceived limitations under the current system, and recommendations to enhance the IRB's role. CIRB provides the following comments.

I. THE IRB's ROLE IN THE REVIEW OF ADVERSE DRUG OR DEVICE EVENT REPORTS

The IRB's primary regulatory responsibility in the clinical research arena is to assure the protection of the rights and welfare of human subjects participating in clinical research through the review of proposed research and the continuing review of approved research. The review of reports of adverse drug and device reactions associated with IRB-approved clinical trials is a component associated with two of the IRB's regulatory functions associated with continuing review. To be beneficial, the IRB's review of the reports must be used first, to assess the ongoing risk/benefit ratio of the study; and second, to assess the need to inform participants of significant new findings that might affect their continued participation in the research.

II. LIMITATIONS UNDER THE CURRENT SYSTEM

Regrettably, due to the inherent limitations associated with the current system of adverse event reporting, the expansion of large multi-site studies, and the differences in FDA definitions associated with reportable events, IRBs often lack access to critical study information that would allow for a more meaningful review of reported events. Usually,

IRBs randomly receive reports about isolated single events. In connection with drug studies, IRBs usually cannot tell from these reports whether the adverse event involves a participant on placebo, study drug, or comparator. Additionally, the IRB generally has no knowledge regarding the participant's underlying medical or medication history. With multi-site studies, except at the time of continuing review, IRBs do not know at any given time how many sites or participants are enrolled in a study, or how many participants have experienced a similar adverse event. They lack important data available to the study sponsor that track events across multiple studies, including earlier studies, studies conducted overseas, and studies conducted under the oversight of different local and central IRBs. As a result, IRBs are hampered in their ability to assess the significance of adverse events in the overall study with respect to human subject risk.

III. RECOMMENDATIONS

With these limitations in mind, CIRB believes that several steps can be taken to enhance the current system of reporting adverse events to IRBs.

1. Definitions in FDA drug, device, and IRB regulations should be clarified and harmonized to require investigators subject to the IRB's jurisdiction to promptly report to the IRB complete information about adverse events at their sites that are serious, unexpected, and related to the study product. Such reporting is essential to assure that the IRB has up-to-date information on the status of the study at the individual site where the event occurred.

2. Sponsor periodic reports to the IRB of protocol-level aggregated safety data in a summarized form would significantly enhance the IRB's ability to perform its human subject protection function as it relates to the review of adverse events. The frequency of sponsor reports should be consistent with the degree of study risk. CIRB believes the level of report detail should be consistent either with the level of safety information detail contained in the sponsor's Annual Report, or with that called for in the CIOMS Working Group VI proposal on reporting drug safety data from clinical trials.

   CIRB does not believe that IRB receipt of additional critical information from the investigator in connection with individual adverse event reports would result in an efficient use of IRB resources in the protection of human subjects. If such information is not analyzed by the sponsor first, and then provided to the IRB in the form of aggregated reports, IRBs would be required to devote massive resources, in the form of manpower and infrastructure, to the analysis of such data, possibly to the detriment of other critical IRB functions. Moreover, such detailed IRB review of adverse event information would present an unnecessary redundancy given that sponsors already have systems in place, either internally or externally through data safety management boards (DSMBs), to

adequately evaluate the significance of individual adverse event reports with respect to the safety of human subjects.

3. When DSMBs are associated with a research study, a summary of the findings of each DSMB meeting, including the DSMB conclusions, should be sent to the IRB without modification.

CIRB believes that implementation of these three proposals will improve the IRB's ability to conduct meaningful review of adverse event information, placing it in a better position to determine the need to take action, whether it be to require changes to the informed consent, the protocol, or the approval status of the study. CIRB's written comments will provide additional detail concerning these recommendations. On behalf of the organization, I thank FDA for the opportunity to present CIRB's collective comments on this critical issue.