

Adverse Event Reporting to IRBs FDA Guidance

In January of 2009, the FDA provided Guidance to Clinical Investigators, Sponsors and IRBs regarding Adverse Event Reporting to IRBs. The guidance provides recommendations to assist sponsors and investigators differentiate between those adverse events that must be reported to an IRB and those that are not. The guidance also makes suggestions about how to efficiently communicate adverse event information to IRBs.

The term adverse event (AE) will represent the following terms provided in the FDA regulations: adverse effect, adverse experience and unanticipated problem.

According to the Guidance, “an AE observed during the conduct of a study should be considered an unanticipated problem involving risk to human subjects, and reported to the IRB, *only* if it were unexpected, serious and would have implications of the conduct of the study.” “...an aggregate analysis of other occurrences of the same (or similar) event may reveal that the event rate is higher in the drug group compared to the control arm. In this case, the AE would be considered an unanticipated problem.” Although AEs which are listed in the investigator’s brochure may not be considered unexpected, there are exceptions when the incidents in which the specificity or severity of the event does not coincide with the information provided in the investigator’s brochure, or that it has been observed that the occurrence for a serious, expected AE in the clinical trial represents an increase in the expected rate of occurrence.

Single or multiple occurrences of the following uncommon events which are also strongly associated with drug exposure, such as angiodema, agranulocytosis, anaphylaxis, hepatic injury or Stevens Johnson syndrome must be reported to the IRB.

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“Adverse Event Reporting to IRBs” continued Reporting to the IRB

In multicenter studies, the investigator must rely on the Sponsor to provide information about AEs that occur at other investigative sites. The regulations state that it is the responsibility of the investigator to provide these reports to the IRB. “If the investigator knows that the sponsor has reported the unanticipated problem directly to the IRB, because the investigator, sponsor and IRB made an explicit agreement for the sponsor to report directly to the IRB, and because the investigator was copied on the report from the sponsor to the IRB, the FDA intends to exercise its enforcement discretion and would not expect the investigator to provide the IRB with a duplicate copy of the report received from the sponsor.

Declaration of Helsinki Update

IRBs have relied on the Declaration of Helsinki to provide guidance for ethical review of research since 1964. The US FDA rejected the 2000 and subsequent revisions (recognizing only the third revision of 1989) and announced in 2006 that it would eliminate all references to the Declaration. On April 28, 2006 a final rule was issued that non-IND foreign clinical studies be conducted in accordance with GCP (Good Clinical Practice) rather than the 1989 Declaration effective October 2008.

For more information about reporting AEs to IRBs, or for a copy of the final rule on the Declaration of Helsinki, please visit the FDA website or contact Christina Billias at Harrison IRB for a copy of the publications. She can be reached at 740-845-0814 or by email at cbillias@harrisonirb.com.