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Guidance for Clinical Investigators,

Contains Nonbinding Recommendations

Guidance for Clinical Investigators, Sponsors, and IRBs[1] Adverse Event Reporting to IRBs — Improving Human Subject Protection

The major exceptions to the general rule that an isolated event is not informative are serious AEs that are uncommon and strongly associated with drug exposure, such as angioedema, agranulocytosis, anaphylaxis, hepatic injury, or Stevens Johnson syndrome. In most cases, a single, unexpected occurrence of this type of event would be considered an unanticipated problem involving risk to human subjects and, thus, must be reported to the IRB. Similarly, one or a small number of serious events that are not commonly associated with drug exposure, but are otherwise uncommon in the study population (e.g., tendon rupture, progressive multifocal leukoencephalopathy)

unanticipated problem involving risk to human subjects. We recommend that a discussion