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PROTECTING RESEARCHERS AND RESEARCH SUBJECTS

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IRBs Must Receive Reports from Researchers on Risks to Subjects (#2)

With this article, we conclude our presentation of the major highlights of a recent draft FDA guidance that specifically addresses IRB issues and related researcher responsibilities.

Resuming where we left off last month, we finish the guidance's recommendations regarding the reporting of "serious adverse events" (SAEs) by researchers to their IRBs.

"Reports of SAEs from IND-exempt [Investigational New Drug application-exempt] BA/BE [Bioavailability/Bioequivalence] studies provide information on SAEs that occur in those studies, all of which are important to consider for human subject protection reasons because the occurrence of SAEs in BA/BE studies is unusual: the number of subjects enrolled is small, the subjects are usually healthy volunteers, and drug exposure is typically brief, but often at the highest available dosage" (guidance, September, p. 10; on the Web at https://www.fda.gov/media/152530/download).

Safety of Human Subjects Is Paramount

"Reviewing IND safety reports and reports of SAEs from IND-exempt BA/BE studies is essential for protecting the safety of human subjects because each report represents important safety information regarding the investigational drug.

FDA considers the review of these reports critical to fulfilling the investigator's responsibility under §312.60 (21 CFR 312.60) to protect the safety of subjects under their care.

For these reasons, investigators must review all IND safety reports and reports of safety information from IND-exempt BA/BE studies received (see §312.60). In addition, investigators must submit these reports to the IRB because the reports describe important safety information representing unanticipated problems involving risks to human subjects or others (§312.66).

Many study protocols specify that the sponsor will submit IND safety reports to the IRB on the investigator's behalf. In these

NOTE #1: Quoted materials in this newsletter appear exactly as originally published in source documents, including any misspellings, grammatical errors, missing words, etc. However, we will on occasion insert words or edit text/formating in brackets [ ] to make the material easier to read, or to add an underline emphasis.

NOTE #2: Emphases are added to articles by HRR by underlining or adding ***bold/italics*** to selected text, unless stated otherwise.

NOTE #3: Articles **T**o **B**e **C**ontinued in subsequent issues are marked at the end of the article with **{TBC}**.

Also In This Issue

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situations, where the investigator receives confirmation that the report has been sent to the IRB (e.g., the investigator is copied on the report sent to the IRB by the sponsor), FDA would not expect an investigator to provide the IRB with a duplicate copy of the report.[22]

[FN #22: Note that such an agreement should be documented.]" (ibid).

Other Problems That Must Be Reported to IRBs

"**B. Other Unanticipated Problems Requiring Reporting to the IRB**

Some events not meeting the criteria for reporting in an IND safety report or as a BA/BE study premarket SAE would still be considered unanticipated problems involving risk to human subjects or others and, under §312.66, would require reporting to the IRB by the investigator.

Such events may occur at the subject, site, and/or study level. Some possible examples may include reports of medication errors (such as receipt of wrong dose or contaminated study medication), breach of privacy/confidentiality (such as disclosure of personally identifiable information), untimely destruction of study records, and other scenarios.

The investigator must report any unanticipated problems involving risk to human subjects or others. This requirement applies regardless of whether the unanticipated problems related to the study drug or related to study procedures.

Such unanticipated problems may include serious unexpected adverse events that occur prior to test article administration or during a washout period or that are attributable to a screening procedure (e.g., renal failure after receipt of an imaging contrast agent).

Finally, the IRB's written procedures or institutional policy may require the investigator to submit to the IRB other unanticipated problems in addition to those that qualify for reporting under §312.66.

The investigator should be familiar with and adhere to the IRB's written procedures for reporting unanticipated problems involving risks to human subjects or others to the IRB (see 21 CFR 56.108(b)(1)).

Also, as part of their clinical trial monitoring responsibility, we understand that sponsors generally require that investigators report such unanticipated problems to the sponsors as well" (ibid).

Device Problems Must Be Reported to IRBs Too

"**VI. Investigator Reporting to Sponsors and Institutional Review Boards for IDE** [Investigational Device Exemption] **Studies**

The IDE regulations require investigators to report UADEs [Unanticipated Adverse Device Effects] to both sponsors and IRBs.

Similar to the handling of SAEs described previously for IND studies, FDA believes that the sponsor is generally better positioned than the individual investigator to assess UADEs, given that the sponsor has access to UADE reports from multiple study sites and multiple studies and is able to aggregate and analyze these reports.

Therefore, UADE reports are critical to the process, and the IDE regulations require not only timely reporting for investigators, but also timely evaluation by sponsors, as follows:

- For device studies, investigators are required to submit a report of a UADE to the sponsor and the reviewing IRB as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect (§812.150(a)(1)).
- Sponsors must immediately conduct an evaluation of a UADE and must report the results of the evaluation to FDA, all reviewing IRBs, and all participating investigators within 10 working days after the sponsor first receives notice of the effect (§§812.46(b) and 812.150(b)(1))" (supra at p. 11). ©