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IRBs Must Receive Reports from Researchers on Risks to Subjects (#1)

A new FDA guidance is designed to assist IRBs and researchers with a certain aspect of safety reporting. We will focus on the section that directly addresses the role of IRBs in this regard.

The remainder of the guidance advises researchers how to report risks and safety concerns in studies to their IRB. We will leave those portions of this guidance for researchers to study on their own.

"The draft guidance provides recommendations to help clinical investigators comply with the safety reporting requirements of investigational new drug application (IND) studies and investigational device exemption (IDE) studies.

The guidance is intended to help clinical investigators of drugs identify safety information that is considered an unanticipated problem involving risks to human subjects or others and that therefore requires prompt reporting to institutional review boards (IRBs) and to help clinical investigators of device identify safety information that meets the requirements for reporting unanticipated adverse device effects (UADEs) to sponsors and IRBs" (86 Fed. Reg. 54208-54210 at p. 54208, September 30).

Waiting for the Final Version …

This new draft guidance is an attempt by the agency to clarify issues raised by the research compliance community about previous guidances on this topic, including one guidance referred to as "the merged 2021 guidance."

"The merged 2021 draft guidance ["Sponsor Responsibilities -- Safety Reporting Requirements and Safety Assessment for IND and Bioavailability/Bioequivalence Studies (June 2021)"] does not, however, include the recommendations for investigator responsibilities that are included in the 2012 final [merged] guidance.

Instead, the recommendations on the safety reporting responsibilities of the investigator are the primary focus of this guidance.

Additionally, this draft guidance incorporates concepts pertaining to investigator re-

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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sponsibilities for adverse event reporting that are described in the guidance for clinical investigators, sponsors, and IRBs entitled "Adverse Event Reporting to IRBs -- Improving Human Subject Protection" (January 2009) (the 2009 procedural final guidance[2]).

[FN #2: Available at https://www.fda.gov/media/72267/download.]

When finalized this guidance will supersede corresponding sections in the 2012 final guidance and the 2009 procedural final guidance. Until that time, however, the 2012 final guidance and the 2009 procedural final guidance continue to represent FDA's current thinking on investigator responsibilities for safety reporting for investigational medical products" (guidance, September, p. 9; on the Web at https://www.fda.gov/media/152530/download).

"Prompt Reporting" to the IRB Is Required

"V. Investigator Reporting to Institutional Review Boards for IND Studies[18]

[FN #18: Guidance provided in this section may be applicable for companies conducting IND-exempt BA/BE studies to comply with §320.31(d)(3).]

Investigators are required to 'promptly report to the IRB … all unanticipated problems involving risk to human subjects or others' (§312.66), including adverse events that represent unanticipated problems, as further described in this section.[19]

[FN #19: We note that IND-exempt BA/BE studies are not subject to the requirements in §312.66. However, they must still be conducted in compliance with the requirements for review by IRBs established in CFR part 56. See §320.31(d)(2).

Section 56.108(b)(1) provides that an IRB will ensure the prompt reporting to the IRB of 'any unanticipated problems involving risk to human subjects or others …' FDA interprets this language in a manner consistent with the interpretation of §312.66 laid out in this guidance.]

Note that the requirements for IND safety reporting under §312.32 do not address safety reporting by investigators to IRBs. The types of unanticipated problems that must be reported to the IRB are discussed in sections A and B below" (ibid).

"Adverse Events" Must Be Included in Reports to IRBs

"A. Adverse Events as Unanticipated Problems That Must Be Reported to the IRB

Investigators are required under §312.66 to report all 'unanticipated problems involving risk to human subjects or others' to the IRB. FDA considers a serious and unexpected adverse event ... to be an unanticipated problem involving risk to human subjects or others that therefore must be reported to the IRB by the investigator.[20]

[FN #20: In general, the occurrence of an SAE is very unusual in a BA/BE study because 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.

For these reasons, FDA considers the occurrence of any SAE in a BA/BE study that is subject to an IND to be an unanticipated problem involving risk to human subjects.

Accordingly, the investigator of a BA/BE study that is subject to an IND must report to the IRB any SAE that occurs in the study (21 CFR 312.66).]

IND safety reports and reports of SAEs from IND-exempt BA/BE studies provide FDA and participating investigators with important information relevant to the safety to human subjects receiving the investigational drug.

IND safety reports provide information on potential serious risks, including unexpected SAEs for which there is a reasonable possibility that the investigational drug caused the events" (supra at pp. 9-10). © {TBC}