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PROTECTING RESEARCH SUBJECTS AND RESEARCHERS

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Using Single IRBs in FDA-Regulated Research (#4)

We continue this month with more of FDA's many proposals to change existing regulations and to add new ones on the protection of human research subjects.

FDA is currently reviewing the many comments it received following its recent major announcement which we covered previously.

We will continue presenting highlights of these proposals as a way of assisting IRBs to prepare for possible future changes to the ways in which they now review research protocols.

We resume our coverage by examining more details on ways that FDA may be planning to change how single IRBs handle the review and monitoring of multisite trials.

In the past, of course, such studies were typically reviewed by several IRBs located at the various involved study sites.

Possible Exceptions to "Single IRB Review"

We begin with FDA's reference to a proposal that we presented in last month's HRR regarding special challenges posed by research with pregnant women at one site, with follow-up research with neonates planned at a separate site.

> "In these instances, utilizing an IRB with obstetrical expertise and a separate, pediatric IRB that has extensive experience in neonatal research may be in the best interest of the two populations of research subjects.
>
> We request comment on whether a single IRB of record would generally be able to supplement its members' knowledge and experience with additional information or expertise to account for these situations, examples of FDA-regulated research in which these circumstances would apply, and any data on the frequency of how often this situation may occur.
>
> FDA is also requesting comment on including an exception for cooperative research with a small number of investigational sites.
>
> SACHRP [the Secretary's Advisory Committee on Human Research Protections] recommended that research involving five or fewer investigational sites should be considered as potentially appropriate for exception to the single IRB review requirement.

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

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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FDA is requesting feedback on whether an exception from single IRB review might be warranted for a multisite study with a small number of sites, what the benefits and burdens are for a multisite study with a small number of sites, and what the appropriate threshold should be for the number of sites involved.

In addition, we request any specific data that can be provided on the relationship between the number of sites and the value of single IRB review" (87 Fed. Reg. 58759, September 28, 2022).

When Single IRB Review Can Be Used Even If Exceptions Apply

"In addition, FDA recognizes that situations may arise in which a federally conducted or supported FDA-regulated clinical investigation would qualify for an exception from single IRB review under this proposed rule but would not qualify for an exception determination issued by a Common Rule Department or Agency pursuant to 45 CFR 46.114(b)(2)(ii) of the revised Common Rule (or vice versa).

Both the revised Common Rule and FDA's proposed rule still permit use of single IRB for review and approval of cooperative research even if an exception applies.

However, we are requesting public comment on any impact that such differences in exceptions from the single IRB review requirement may have on stakeholders, and on possible approaches to avoid or minimize any potential negative effects of such differences for stakeholders, such as whether additional exceptions from the proposed single IRB review requirement should be included or whether providing guidance on the application of FDA's proposed exceptions might help avoid or minimize any differences in exceptions" (supra at pp. 58759-58760).

Are More IRB Exceptions Warranted?

"We also specifically request comment on whether there are unique challenges to use of a single IRB review model for FDA-regulated cooperative research that could not be addressed by FDA's proposed exceptions.

For any challenges identified, we seek comment on whether additional exceptions should be included to address them.

For example, should FDA consider including an exception analogous to the revised Common Rule's exception at 45 CFR 46.114(b)(2)(ii)?

As explained above, we do not believe it is practicable to rely on a broad exemption that would provide for FDA to make case-by-case determinations that use of single IRB review is not appropriate for the particular context as the only means for excepting FDA-regulated cooperative research -- other than research for which more than single IRB review is required by law -- from the proposed new requirement" (supra at p. 58760).

FDA Will Update Single IRB Guidance

"The agency also believes that situations in which use of a single IRB might not be appropriate and in which none of FDA's proposed exceptions apply would be rare.

However, we seek comment on whether including an exception that provides for FDA to determine and document that single IRB review is not appropriate for the particular context, in addition to the exceptions FDA has proposed, could help address any such situations and any negative impacts of differences between FDA's proposed exceptions and exceptions available under the revised Common Rule to a Common Rule Department or Agency supporting or conducting cooperative research.

Lastly, FDA is requesting comment on the proposed exceptions and any other criteria that should be considered when assessing whether an exception to the use of single IRB review might be warranted.

We also encourage the public to provide examples of any additional types of FDA-regulated clinical investigations that they believe should qualify for such an exception.

To help stakeholders comply with these proposed requirements, if finalized, FDA intends to update our guidance on using a centralized IRB review process in multicenter clinical trials" (ibid). © {TBC}