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IRBs and FDA's Advice on How To Cope With Coronavirus (#4)

We continue here with more recent updates for IRBs, researchers, and others on the effects of COVID on certain types of human subjects research. Our focus in this article is on the newly revised guidance from FDA titled "FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency - Guidance for Industry, Investigators, and Institutional Review Boards."

This article adds new information beyond what we've already covered in previous HRRs (e.g., see the May, June, and October 2020 issues).

We resume below where we left off in the October 2020 issue; namely, with the remainder of a key section from the introductory portion of the guidance subtitled **"C. For all trials that are impacted by the COVID-19 public health emergency."**

What Happens When COVID Disrupts Trial?

"Sponsors should describe in appropriate sections of the clinical study report (or in a separate study-specific document):

1. Contingency measures implemented to manage study conduct during disruption of the study as a result of COVID-19 control measures.
2. A listing of all participants affected by the COVID-19 related study disruption by unique trial participant number identifier and by investigational site, and a description of how the individual's participation was altered.
3. Analyses and corresponding discussions that address the impact of implemented contingency measures (e.g., trial participant discontinuation from investigational product and/or study, alternative procedures used to collect critical safety and/or efficacy data) on the safety and efficacy results reported for the study.

Robust efforts by sponsors, investigators, and IRBs/IECs to maintain the safety of trial participants and study data integrity are expected, and such efforts should be documented. As stated above, FDA recognizes that protocol modifications may be required, including unavoidable protocol

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 in brackets [ ] to make the material easier to read, to edit text or formatting, or to add an editorial comment.

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 **{TBC}** in subsequent issues are marked at the end with **{TBC}**.

Also In This Issue

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deviations due to COVID-19 illness and/or COVID-19 control measures.

Efforts to minimize impacts on trial integrity, and to document the reasons for protocol deviations, will be important" (Guidance, rev. December 4, 2020, p. 6 of 35; on the Web at https://www.fda.gov/media/136238/download).

The body of the guidance is relatively brief, but the subsequent Q&A Appendix is extensive and filled with practical tips for researchers and the IRBs that review relevant protocols. The initial Q&A #1 sets the stage for the detailed useful recommendations, as follows.

Monitoring Threats to Safety of Subjects

"Q1. What are some of the key factors that a sponsor should consider when deciding whether to suspend or continue an ongoing study or to initiate a new study during the COVID-19 public health emergency?

A1. Central to any decision should be ensuring that the safety of clinical trial participants can be maintained. Sponsors, in consultation with clinical investigators and Institutional Review Boards (IRBs)/Independent Ethics Committees (IECs), should assess whether the protection of a participant's safety, welfare, and rights is best served by continuing a study participant in the trial as per the protocol or by discontinuing the administration or use of the investigational product or even participation in the trial.

Such decisions will depend on specific circumstances, including the nature of the investigational product, the ability to conduct appropriate safety monitoring, the potential impact on the investigational product supply chain, and the nature of the disease under study in the trial.

As part of this assessment, sponsors should carefully consider the following aspects of clinical trial conduct when deciding how or whether to proceed with a clinical trial:

• Assessing whether the limitations imposed by the COVID-19 public health emergency on protocol implementation pose new safety risks to trial participants, and whether it is feasible to mitigate these risks by amending study processes and/or procedures.

• Assessing the continued availability of the clinical investigator/sub-investigators to provide oversight of the trial and properly assess and manage safety issues that may emerge" (supra at p. 8).

Study Personnel Must Have Enough Supplies to Monitor Subject Safety

"• Assessing whether there will be sufficient clinical trial support staff given the evolving COVID-19 situation and its impact on staff availability. Are there appropriately trained staff that could be available to handle the expected tasks? Is there adequate equipment and materials for clinical trial support staff?

• Assessing whether clinical investigator sites will remain open to trial participants for required in-person assessments or whether the clinical investigator has the ability to provide required in-person assessments at an acceptable alternate location(s), or whether such protocol-specified, in-person assessments can instead be conducted virtually.

• Assessing the continued availability of clinical trial supplies and continued operations of vendors, especially related to supply of the investigational product and/or to clinical trial supplies that are essential to maintaining appropriate safety monitoring or other key trial procedures.

This should include consideration of product stability (shelf life) if the treatment schedule is revised ...." (ibid).