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PROTECTING RESEARCHERS AND RESEARCH SUBJECTS

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FDA's Advice for IRBs on How To Cope With the Coronavirus (#8)

We continue here with a very useful set of recommendations for IRBs on subject protection issues during the COVID pandemic. The relevant FDA guidance is 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."

We resume from where we left off last month with the final few comments from FDA on what to do with submissions of applications for IDE studies. However, we will then devote more attention to the next Q&A from the guidance on particular aspects of human research subject safety in medical device experiments.

"**For IDE studies**, the sponsor should submit a supplement to its existing IDE, with the following information added to the cover letter in the subject line:

CHANGE IN PROTOCOL SUPPLEMENT -- COVID-19 or NOTICE OF IDE CHANGE -- COVID-19, as applicable

TITLE OF PROTOCOL

The submission to the IDE should contain a tracked changes version of the protocol to facilitate review" (guidance, rev. December 4, 2020, p. 11; on the Web at https://www.fda.gov/media/136238/download).

Is Virtual Study Visit Needed for Safety?

"**Q5. Can a sponsor initiate virtual clinical trial visits for monitoring patients without contacting FDA if there is an assessment by the sponsor and investigator that these visits are necessary for the safety of the trial participant and it will not impact data integrity?**

FDA regulations allow for changes to be made to the investigational plan or protocol without prior FDA review or approval, if the change is intended to eliminate an apparent immediate hazard or to protect the life and well-being of trial participants.

Therefore, changes in protocol conduct necessary to immediately assure patient safety, such as conducting telephone or

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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video contact visits for safety monitoring rather than on-site visits, can be immediately implemented with subsequent review by the IRB and notification to FDA.

Since this reflects a protocol deviation (until the amendment is approved), documentation of the required deviations, as described above, would generally be acceptable (i.e., a document that lists each deviation, study reference ID, patient ID, and date).

For example, documenting that all protocol-specified visits will be done by telephone contact rather than on-site visits, and that procedures requiring in-person visits will either not be conducted, or performed by other means (specified, as appropriate).

Since the change to telephone or video contact visits would likely result in some protocol-required procedures not being conducted (e.g., vital signs, blood samples for safety laboratory studies), the sponsor must evaluate the potential impact on patient safety, and consider how to mitigate risks to patients, including the need to discontinue the investigational product" (supra at p. 12).

COVID and Collection of Data

"For IDE studies, sponsors are required to report deviations implemented to address the imminent safety risk to FDA within 5 working days after learning of the deviations.

We recognize that challenges related to the COVID-19 pandemic may make it difficult to meet this timeframe. Sponsors may consolidate implemented deviations when submitting 5-day reports and should update FDA as soon as possible.

Q6. With the rapid changes in clinical trial conduct that may occur due to the COVID-19 public health emergency, including multiple deviations to address patient safety, what is the best way for sponsors and investigators to capture these data?

As noted in the main body of this guidance, it is important to capture *specific* information for individual participants that explains the basis for missing protocol-specified information that includes the relationship to COVID-19 (e.g., from missed study visits or study discontinuations due to COVID-19) ....

If it is not possible to capture this information in the case report form(s), sponsors may develop processes that enable systematic capture of these data across the sites in a manner that enables the appropriate analysis when the data are submitted to FDA ...." (ibid).

When Protocols Need Not Be Amended

"Q7. If patients are currently dispensed investigational product through a pharmacy at the clinical trial site for self-administration at home, can a sponsor switch that to home delivery without amending the protocol?

If there is concern about risk of exposure to COVID-19, home delivery of investigational product that would not raise any new safety risks may be implemented to protect patients from coming to clinical trial sites ....

If the protocol indicates pharmacy dispensing for self-administration at home, and this is changed to direct-to-patient shipments, then a protocol amendment would be required to permit home delivery of investigational product.

If the extent of home delivery is limited to certain participants and not the entire population described in the protocol, documenting the change in the mechanisms of distribution of investigational product administration through protocol deviations may also be acceptable. If the change in the mechanisms of investigational product distribution is then included in a protocol amendment, such a change may be part of a 'cumulative' amendment that includes a number of changes that accrue, rather than [as] an urgent protocol change" (supra at pp. 12-13). © {TBC}