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What are the best practices for handling changes to ePRO data?

The recent draft guidance on "computerised systems and electronic data in clinical trials" published by EMA[1] provides useful perspective on the topic of making changes to eCOA data reported by the patient. The draft guidance states:

"It is not acceptable that data clarification procedures introduced by the sponsor or vendor whether or not described in the protocol do not allow for changes in trial participant data when justified e.g. if the trial participant realises that data has not been entered correctly."

This is very much in line with FDA's position on ePRO data. They state, in their 2009 PRO guidance[2], that:

"Sponsors should avoid:

- Source document control by the sponsor exclusively
- Clinical investigator inability to maintain and confirm electronic PRO data accuracy."

Source data must be accurate, and by implication, this means that a procedure should be in place in case a patient reports to the Investigator that they have made a mistake in entering their data.

While trial participants may not to the ability to make changes to their ePRO data themselves, regulatory guidance and ICH GCP principles indicate that processes need to be in place to enable data changes when necessary, such as when the Investigator is using a data change request (DCR) process.

But when do data changes enhance data reliability and when do they undermine it?

Certainly, if a patient realizes that they have misinterpreted a response scale, then it would not be an illogical view to consider that timely changes to the data might improve its reliability. However, requesting changes much later on from the point of data entry may cast doubt on the reliability of the new values entered. After all, is it possible to accurately recall discrete aspects of health status from many weeks ago?

Sensible approaches need to be considered to ensure adherence to the regulatory position on control and responsibility of source data, while maintaining the integrity and reliability of

the ePRO data. Many sponsors, vendors, and sites are developing working processes to deal with this.

Some important considerations in developing these processes include:

1. **Defining the risk profile of the specific data that is requested to be changed.**
   Low-risk data may include metadata, such as patient identifiers. Higher risk data may be the clinical outcomes data values themselves, especially if they are associated with clinical endpoint calculations.

2. **Determining the process for DCR review.**
   A working practice for how low risk and higher risk data changes should be handled by the vendor should be agreed upon. This working practice might differentiate based on the risk profile of the data. For example, low-risk data changes may be executed directly by the vendor upon request of the investigator. However, a working practice may define that the ePRO vendor should alert the Sponsor of the DCR when the data in question represents a higher risk category. This gives the Sponsor the opportunity to discuss data changes needed with the Investigator and vendor. Such a discussion would be conducted, not with an aim of controlling the data, but in an effort to understand the request. This would ensure data integrity and reliability is maintained, not to mention guaranteeing sufficient documentation can be produced to support the change.

3. **Maintaining an audit trail of data changed by DCR processes.**
   Audit trail records will need to be created and be sufficient to support data changes made by the vendor in response to a DCR.

4. **Working practice documentation.**
   A provided document should define the process for DCR review to Investigators ahead of study participation.

Ultimately, of course, the decision belongs to the site, and this must be respected. But a thoughtful process helps mitigate the risk of undermining data integrity and assure regulatory compliance.

In reality, the quantity of data change requests we see is unlikely to affect the interpretation of the results of ePRO data analysis. However, establishing appropriate processes that enable sites to fulfil their responsibility for these source records, in addition to maintaining data integrity and reliability are essential for regulatory acceptance.

References

1. EMA (2021). Draft guideline on computerised systems and electronic data in clinical trials. https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/draft-guideline-computerised-systems-electronic-data-clinical-trials_en.pdf
2. FDA (2009). Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-reported-outcome-measures-use-medical-product-development-support-labeling-claims

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