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The Signal

The Center for Drug Evaluation's (CDE) draft PRO guidance

In the landscape of rapidly growing numbers of pharmaceutical clinical trials in China, the Chinese Center for Drug Evaluation (CDE) recently expanded regulatory guidance with their draft regulation on patient-reported outcomes (PROs) this past September. In doing so, they reinforce the growing importance of capturing the patient perspective in clinical evaluations of new treatments.

My interpretation of the guidance is that it falls broadly in line with other guidance published by other regulatory bodies, such as the FDA's 2009 guidance on patient-reported outcome measures.

The CDE indicates that patient-reported outcome measures (PROMs) should reflect the patient's perception of the drug's efficacy, but they may also measure aspects of safety, quality-of-life, or primary and secondary endpoints.

The draft guidance covers aspects of development and adaptation of PROMs in addition to the process of their translation and cultural adaptation for use in the Chinese population. The described processes are consistent with industry standard approaches in these topics. Like other regulatory bodies, the CDE expects the choice of PROMs to be justified in the research plan, and measurement comparability evidence provided for PROMs migrated from a different format. Interestingly enough, the use of computerized adaptive testing and item libraries is mentioned along with the importance of providing comprehensive supporting information related to the conceptual framework and PROM validity.

The importance of understanding interpretability by being able to identify a minimally clinically important difference (MCID) in group means for PROM endpoints is also stated. However, the CDE does not explicitly mention the use of individual responder definitions.

The CDE argues the importance of mitigating missing data. The CME expects researchers to define rules to indicate the degree of missing data that would be associated with the inability to derive a reliable outcome measure for each PROM. They do not direct statisticians to any one method of dealing with missing data in the statistical analysis, but do suggest there are occasions where it may be acceptable to impute missing values based on the data collected on other related scales. Where possible, they encourage researchers to continue to collect PROM data after early withdrawal from medication.

In the draft guidance, they describe ePRO solutions as typically being of two types: interactive voice response (IVR) systems and screen-based solutions that require a smartphone, tablet, or computer. They list advantages associated with electronic collection, including accuracy, completeness, real-time data access, compliance to completion times (and prevention of entries outside suitable completion windows), privacy, and efficiency. They also express that certain populations, such as the elderly, young, or those with dexterity issues, may find it difficult to operate the devices associated with electronic PROM data collection.

In common with the recent EMA draft guidance on computerized systems, the CDE underlines the importance of the investigator's responsibility for eSource data as well as the responsibility of sites to confirm source records are accurate. They stress that systems should ensure data security through access control and prohibit untraceable modification or deletion of the data, and provide a full audit trail.

Overall, this helpful guidance echoes the guidance provided by other regulatory bodies, such as FDA and EMA. The development of guidance by China's CME demonstrates the increasing importance they attach to patient-reported outcomes in clinical drug development.

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