ICH Overhauls 22-Year-Old Clinical Studies Guideline

For the first time in 22 years, the International Council on Harmonization (ICH) is almost completely overhauling the guideline ICH E8 – General Considerations for Clinical Studies, the international standard for designing and developing trials.

The major rewrite of the 1997 guideline, which is expected to go into effect in June 2020, would replace the development methodology section of the original document with five new sections that apply the quality-by-design method to trial development:

- Designing quality into clinical studies;
- Drug development planning;
- Design elements for clinical studies;
- Conduct and reporting; and
- Considerations in identifying critical-to-quality factors.

According to the draft, “the quality-by-design approach to clinical research involves focusing on critical-to-quality factors to ensure the protection of study subjects, the generation of reliable and meaningful results, and the management of risks to those factors.”

Critical-to-quality factors, according to Leslie Sam, principal consultant of Wool Consulting Group, “are considered to be critical because if their integrity were undermined by errors of design or conduct, the reliability or ethics of decision-making would also be undermined.”

Designing quality into trials, said Sam in a recent CenterWatch webinar, should begin with identification and prioritization of these factors. Once critical-to-quality factors are determined, it is then the responsibility of the study team to design a protocol that considers impact on risks to subjects and data integrity, and whether risks can be accepted or mitigated, she said.

Trials also should engage patients in study design, the draft says, to provide input on ethical, cultural and regional issues.

Drug development planning does not need to be tied to fixed-time clinical trial phases, the guideline says, but could be driven by other design elements, such as study objective. “Drug development is ideally a logical, step-wise process in which information from small early studies is used to support and plan later, larger and more definitive studies.” The progression should be from human pharmacology studies, to exploratory and confirmatory studies, to post-approval studies.

The draft revision also offers guidance on design elements for trials, including choosing inclusion and exclusion criteria with study objectives in mind, deciding whether the intent of the study is to test or merely observe the effects of a treatment, and identifying methods to reduce or assess bias.

The draft includes three new annexes on types of studies, how E8 fits with other ICH efficacy guidelines, and selected examples of critical-to-quality factors.

The examples in the critical-to-quality annex is a good starting point for designing a study protocol, Sam said, but shouldn’t serve as a checklist.

“That’s not the intention at all. They are intended to be used to facilitate a conversation,” she added. “It’s a great opportunity to bring together the right people to exercise quality culture, so they have a conversation and identify risks to not having those factors.”
At an Oct. 31 FDA public meeting on the revision, critical-to-quality factors was the top concern of industry groups and the public.

“It was interesting how many patient advocacy groups shared their voice on the draft guideline,” said Sam. Generally, the patient groups wanted the guideline to place more importance on patient input, protocols and study designs.

The new guideline is slated to go into effect in June 2020 after it is adopted by the FDA and a number of regulatory agencies in other countries.

Read the draft of ICH E8(R1) here: https://bit.ly/2rb0ZF0.

- By Leslie Ramsey and Colin Stoecker

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