An ISO 141552020 Primer — Good Clinical Practice For Medical Device Trials

Article · February 2021

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Guest Column | February 2, 2021

An ISO 14155:2020 Primer — Good Clinical Practice For Medical Device Trials

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The International Organization for Standardization (ISO) recently released *ISO 14155:2020, Clinical investigation of medical devices for human subjects — Good clinical practice,*[1] a standard developed to guide clinical research professionals during the design, conduct, recording, and reporting of clinical trials related to the safety and effectiveness of medical devices. For post-market clinical trials, it should be followed as much as it is relevant to the particular clinical trial or according to regional requirements. The standard outlines requirements to:

- Protect of the rights, safety, and well-being of human subjects,
- Ensure the conduct and the credibility of the results of the clinical trial,
- Define the responsibilities of the sponsor and the investigator, and
- Assist sponsors, investigators, ethics committees/IRBs, regulatory authorities, or other applicable personnel involved in the medical device clinical trial.

Designing and conducting a clinical trial should be done with good clinical practice (GCP) and quality in mind to ensure the reliability of trial results as well as to follow requirements of regulatory authorities. Organizations usually understand the necessity of following ICH E6(R2) to ensure GCP; however, there is frequently a gap in training internal teams, contractors, CROs, and sites on ISO 14155:2020 GCP for medical devices. Following the standard is a key part of building globally recognized GCP into the full life cycle of the medical device clinical trial and can complement the current GCP training.

Changes In ISO 14155:2020 Version

The new version of the ISO 14155:2020 standard better aligns with the European Medical Device Regulation (EU MDR 2017/745), the ICH E6(R2) guideline on Good Clinical Practice, and FDA guidance documents, with a focus on medical devices. These updates allow the standard to remain relevant and maintain acceptance by the global medical device industry. The main focus of the updates is on increasing safety and data reliability. For example, a new section adds GCP principles in alignment with ICH E6(R2) and the Declaration of Helsinki.

Additionally, it interplays with ISO 14971:2019 *Medical devices — Application of risk management to medical devices*.[2] A newly added Annex H maps the two standards and explains the applicability of ISO 14971 to clinical trials. ISO 14971 is similar to risk based quality management (RBQM) as described in the European Medicines Agency's (EMA's) *Reflection Paper* on *Risk Based Quality Management in Clinical Trials*, but with a focus on medical devices. The new ISO 14155 standard establishes a need for developing a risk management plan throughout the product life cycle and incorporating it into the clinical investigation plan (CIP) (protocol) before the study begins. Previously, the focus of the 2011 version of ISO 14155 was on identifying risk of failures rather than proactive measures. ISO 14155:2020 also interweaves the need for effective root cause analysis (RCA) and corrective and preventive actions (CAPAs) for significant noncompliance as well as for device deficiencies throughout the conduct of clinical trials. This is a big step in realization that effective risk management is one of the most integral parts of a successful clinical investigation.

Another update to the new standard allows for additional risk-based monitoring and is more in line with ICH E6(R2)[3] section 5 and FDA guidance for risk-based monitoring (*Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring*[4]) and draft guidance (*A Risk-Based Approach to Monitoring of Clinical Investigations Questions and Answers*[5]). The risk assessment completed during RBQM informs the risk-based monitoring plan chosen and supports the rationale. On-site monitoring is still preferred, but centralized monitoring can be used to complement, or in some exceptional circumstances, be used along with other procedures to complete the requirement for monitoring. This is a softening of the more rigid requirements of the previous version of the ISO 14155 standard.

ISO 14155:2020 When Is It Enforceable?

ISO standards help ensure global consistency in a variety of areas and industries, including clinical trials. Although the standards are voluntary, some regulatory authorities or companies require an ISO standard to be followed. If an ISO standard is listed in the protocol as a requirement, documented training and compliance on the standard is needed, not just on the protocol. In these instances, the ISO standard would be enforceable. In the United States, ISO standards are not required by the regulatory authorities but may be enforceable at the protocol level. U.S. regulatory authorities want evidence of training and compliance where applicable.

Other Considerations

Because medical device trials can be very costly in the U.S., they are frequently conducted in other countries. Data collected in foreign nations that follow ISO 14155:2020 are recognized by the FDA as clarified in the guidance *Acceptance of Clinical Data to Support Medical Device Applications and Submissions Frequently Asked Questions*.[6] A final rule that updated 21 CFR Part 814 in February 2018 allows data collected in the EU to be used in the submission of an investigational device exemption (IDE) application, a premarket notification (510(k)) submission, a request for De Novo classification, a premarket approval (PMA) application, a humanitarian device exemption (HDE) application, or a product development protocol (PDP) application.

In addition to following this standard, stakeholders need to be aware of any other country or regional requirements for the conduct of medical device clinical trials, such as the EU MDR 2017/745, now expected to go into effect in May 2021. For medical device clinical trials conducted in the EU under MDR, notified bodies will only accept clinical data to obtain or renew CE certification that was collected while following ISO 14155:2020. To proactively plan for the potential of EU-based clinical trials and to ensure data are accepted by regulatory authorities, it is important to build the requirements of the standard into organizational procedures and every stage of medical device development. For clinical trials, this needs to happen before protocol development.

Conclusion

The ISO 14155:2020 standard is a welcome change for the medical device industry. The updates modernize the standard in line with current regulatory requirements or guidelines and other changes in the industry. For example, it includes considerations for Software as a Medical Device, highly relevant for the ever-changing landscape of electronic devices being utilized in clinical trials and increasingly in study participants' homes. This may include wearable devices that can transmit electronic data to the clinical site or handheld devices that can assist with the consent process. Modern medical devices range the gamut in complexity. The new standard is more relevant to requirements for medical devices being developed today while being mindful of subject safety and data integrity.

References:

1. International Organization for Standardization ISO 14155:2020 *Clinical investigation of medical devices for human subjects — Good clinical practice,* 2020.
2. ISO 14971:2019 *Medical devices — Application of risk management to medical device,* 2019.
3. ICH E6(R2) *Guideline for Good Clinical Practice*, November 2016.
4. FDA Guidance on *Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring*, August 2013.
5. FDA Draft Guidance on *A Risk-Based Approach to Monitoring of Clinical Investigations Questions and Answers*, March 2019.
6. FDA Guidance on *Acceptance of Clinical Data to Support Medical Device Applications and Submissions Frequently Asked Questions,* February 2018.

About The Authors:


Sandra "SAM" Sather, MS, BSN, CCRC, CCRA, is an industry-leading consultant whose mission is to promote clinical quality systems for sponsors/CROs and investigators/research institutions. She has over 35 years of clinical experience, with a BS in nursing and an MS in education with a specialization in training and performance improvement. Sather is the VP of Clinical Pathways, a consulting firm with clients in the medical device and pharmaceutical industries located in the Research Triangle Park area in North Carolina. She is dual certified by the Association for Clinical Research Professionals (ACRP) for over 15 years (CCRA and CCRC) and a current ACRP Fellow, which is awarded to individuals who have made substantial contributions to the Association and the industry at large. Learn more at www.clinicalpathwaysresearch.com.


As the operations director at Clinical Pathways, Jennifer Lawyer's focus is on implementing processes to improve quality and on-time delivery for eLearning development and project management. As an eLearning project manager, she ensures the day-to-day processes run efficiently and products are high-quality and completed on time. Prior to joining Clinical Pathways, Lawyer worked as a clinical research professional and a private duty nurse. She holds a BS in psychology, an AS degree in nursing, and two clinical trials research associate certificates (core competencies and advanced topics). She is a member of the Association of Clinical Research Professionals (ACRP) and is working on her professional certification.