NVFG Medical Devices | Annet Muetstege

ISO 14155: 2020 | WHAT TO WATCH OUT FOR?

Medical Devices: a diverse sector

Over 500.000 products (10.000 generic groups) + IVDs !

Clinical trials with medical devices D. Bouchez

ISO 14155: 2020

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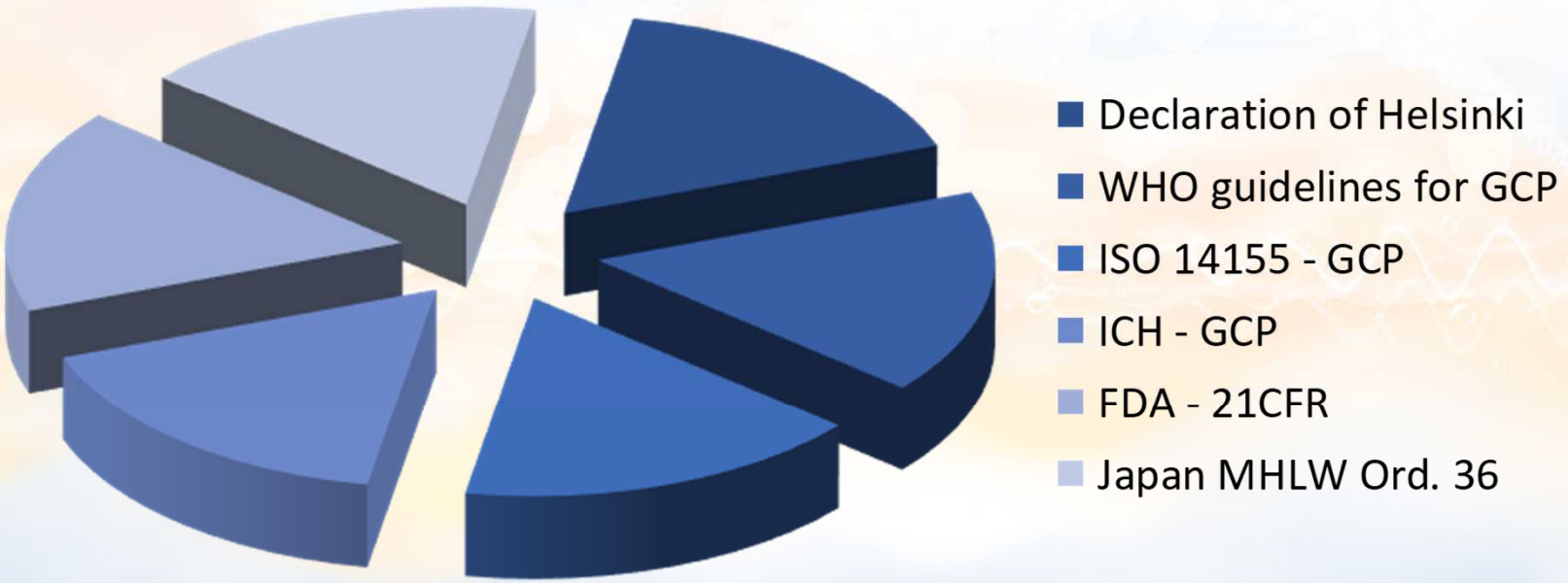
- Apart from definitions & scope own wording used

ISO 14155: 2020 – What changed?

- **Scope:** Includes clinical trials with medical devices already on the market
- Monitoring: New section on risk-based monitoring
- Safety: Updates in terms and definitions, and event escalation
- Risk Management: Updates on risk management activities throughout the full clinical trial cycle

GCP – ISO 14155



ISO 14155 - Objective

- protect the rights, safety and well-being of human subjects,
- ensure the scientific conduct of the clinical investigation and the credibility of the clinical investigation results,
- define the responsibilities of the sponsor and principal investigator, and
- assist sponsors, investigators, ethics committees, regulatory authorities and other bodies involved in the ***conformity assessment*** of medical devices.

Note 1 Users of this document need to consider whether other standards and/or national requirements also apply to the investigational device(s) under consideration or the clinical investigation. ***If differences in requirements exist, the most stringent apply.***

https://www.iso.org/obp/ui/#iso:std:iso:14155:ed-3:v1:en

ISO 14155: 2020 - Scope

- GCP for the design, conduct, recording and reporting of *pre-market clinical investigations* carried out in human subjects to *assess* the *clinical* performance or *effectiveness* and safety of medical devices

- principles also apply to
  - *post-market clinical investigations* and should be followed as far as relevant, considering the nature of the clinical investigation and the requirements of national regulations
  - *software as a medical device for demonstration of the analytical and scientific validity, and clinical performance*

- *not applicable for in vitro diagnostic medical devices*

Effectiveness

Achievement of a clinically significant intended result in a defined portion of the target population when the investigational medical device (3.29) is used within its intended uses and according to its instructions for use, the investigator's brochure (3.31) and the CIP (3.9), as determined by documented scientific evidence

ICH-GCP Rev 2 - Scope

- This guideline should be followed when generating clinical trial data that are intended to be submitted to regulatory authorities.
- The principles established in this guideline may also be applied to other clinical investigations that may have an impact on the safety and well-being of human subjects.

Scope similar

Poll

A pre-market study evaluating the wound healing rate & patient satisfaction of a new band aid has to comply with ISO 14155:2020.

1. True
2. False
3. Depends on study objective

ISO 14155 - Monitoring

The act of overseeing the progress of a clinical investigation to ensure that it is conducted, recorded, and reported in accordance with the CIP, written procedures, this document, and the applicable regulatory requirements

- Centralized monitoring

  Note 1 to entry: Centralized monitoring is a remote evaluation of accumulated data and compliance to provide additional monitoring capabilities that can complement or reduce the extent and frequency of on-site monitoring.

*ISO 14155: 2020

ISO 14155 – Monitoring plan

- Monitoring plan
  - Risk assessment basis for the extent and nature of monitoring for a clinical study
  - In general, on-site monitoring throughout the clinical investigation to be done with centralized monitoring in addition
  - The extent of on-site monitoring versus centralized data review shall be based on complexity of the clinical study and the degree of deviation from normal clinical practice
  - In exceptional circumstances centralized monitoring in conjunction with procedures such as investigator's documented training, meetings, etc is considered acceptable
- Feasible?

ICH-GCP - RBM

" The sponsor should develop a systematic, prioritized, risk-based approach to monitoring clinical trials."

"The sponsor may choose on-site monitoring, a combination of on-site and centralized monitoring, or, where justified, centralized monitoring."

Monitoring same

ISO 14155 - AE definitions
Serious Adverse Event

Adverse event (3.2) that led to any of the following

a) death,

b) serious deterioration in the health of the subject (3.50), ***users, or other persons*** *as defined by one or more of the following:*

1) a life-threatening illness or injury, or

2) a permanent impairment of a body structure or a body function *including chronic diseases*, or

3) in-patient or prolonged hospitalization, or

4) medical or surgical intervention to prevent life-threatening illness or injury, or permanent impairment to a body structure or a body function,

c) foetal distress, foetal death, a congenital abnormality, or birth defect *including physical or mental impairment*

ISO 14155 - AE definitions
Device deficiency

Inadequacy of a medical device (3.34) with respect to its identity, quality, durability, reliability, *usability*, safety or performance

Note 1 to entry: Device deficiencies include malfunctions (3.33), use errors (3.53), and inadequacy ***in the information supplied by the manufacturer including labelling.***

Note 2 to entry: This definition includes device deficiencies related to the investigational medical device (3.29) or the comparator (3.12).

Complaints!

ISO 14155 - AE definitions
Serious health threat

Signal from any adverse event or device deficiency (3.19) that indicates an imminent risk of death or a serious deterioration in the health in subjects (3.50), users or other persons, and that requires prompt remedial action for other subjects, users or other persons

Note 1 to entry: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.

Poll

During a COVID-19 post-market study comparing different PPE's a nurse detects a small tear in his glove after having supported a study patient. He is tested for COVID-19 and the test returns negative. This concerns a reportable event.

1. Yes
2. No
3. Depends on study objective

ISO 14155 – Event escalation

Almost entire new section (7.4)

- *Adverse Events*
  - Timely documentation of all AE's
  - AE's of users or other persons may be documented separate
- *Device deficiencies*
  - Timely documentation of all device deficiencies/ possible CAPA's
  - Device deficiencies of the **comparator**
  - Device deficiencies that **could have led** to SADE
- *Riskmgmt for unacceptable risks*
  - **Any** person identifying information that could impact people's safety, must inform the PI and sponsor
  - Risk assessment - ISO 14971
  - Study suspension
  - Corrective actions
  - Study termination

ISO 14155 - Risk management

- General
  - Risk to be weighted against possible benefit
  - Risk assessment throughout the study
- Investigational device
  - (Residual) risks to be disclosed in the protocol, IFU, and ICF
  - Based on risk assessment outcome, sponsor to decide on the extent of **device training**
- Clinical study process
  - Risk management principles to be applied
  - sponsor to assess risks associated with the study to ensure the ethical and scientific conduct
  - Risk control measures to be weighed for the clinical quality management system and the clinical study conduct

ICH-GCP – Risk management

5.0.2. Risk identification

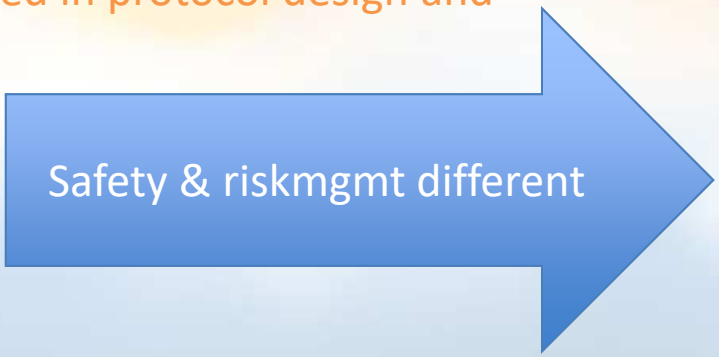
The sponsor should identify risks to critical trial processes and data. Risks should be considered at both the system level (e.g., standard operating procedures, computerized systems, personnel) and clinical trial level (e.g., trial design, data collection, informed consent process).

5.0.3. Risk evaluation

The sponsor should evaluate the identified risks, against existing risk controls

5.0.4. Risk control

The sponsor should decide which risks to reduce and/or which risks to accept. Risk reduction activities may be incorporated in protocol design and implementation, monitoring plans, etc.



Conclusion

- ISO 14155 developed along with the latest developments
  - Guarding patient safety
  - Risk management
- GCPs are becoming more alike
  - Principles
  - Remote & RBM
- Important differences remain
  - Adverse event reporting
  - Risk management/ product training

Questions?

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