Factory CRO

Verdiepende sessie klinisch onderzoek in de MDR

Perspectief van CRO

Klinische evaluatie en klinische studies

23 mei 2019

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Rijksoverheid

Ministerie van Volksgezondheid, Welzijn en Sport

Major changes MDR

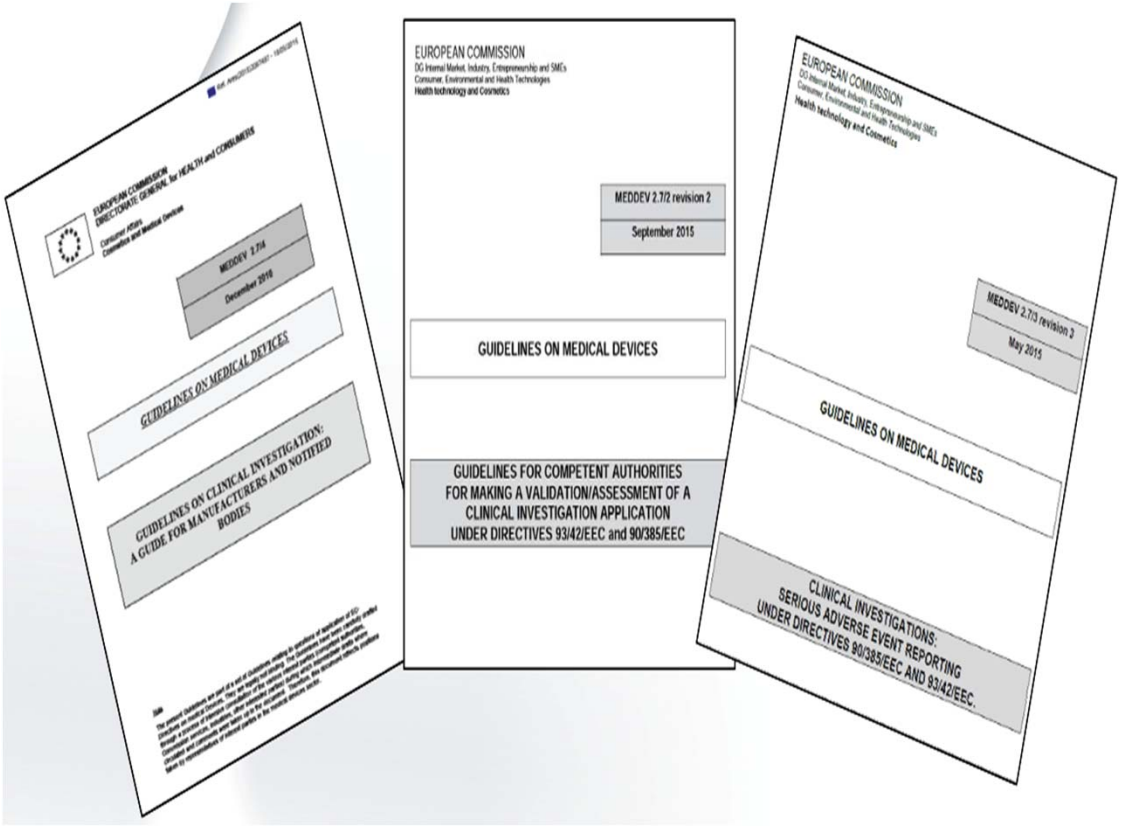
General

- From directive to regulation
- Requirements MEDDEV guidance documents in body text
  - MEDDEV 2.7/1 rev 4, Clinical Evaluation
  - MEDDEV 2.7/4, Guidance on Clinical Investigations
  - MEDDEV 2.7/3, Clinical Investigations - SAE reporting
  - MEDDEV 2.12, Post Market Clinical Follow-up
- Requirements harmonized standards in body text
  - Good Clinical Practice (ISO 14155:2011)

Concerning clinical investigations and clinical evaluation

- Reinforcement of the rules on clinical evidence
- Reassessment of all devices, even when on market (no grandfathering)
- Life cycle approach
- Active approach
- EUDAMED
- Coordinated assessment procedure for clinical investigations

Guidance



INTERNATIONAL STANDARD **ISO 14155**

Second edition
2011-02-01

Clinical investigation of medical devices for human subjects — Good clinical practice

Investigation clinique des dispositifs médicaux pour sujets humains — Bonnes pratiques cliniques

Clinical investigations and Clinical Evaluation

MDR art 61: Demonstration of conformity with GSPR include a clinical evaluation

- Systematic and planned process to continuously generate, collect, analyse and assess clinical data pertaining to a device in order to verify the safety and performance, including clinical benefits, of the device when used as intended by the manufacturer

MDR art 62: Purpose of Clinical Investigations

a) Verify device achieves performance intended by manufacturer
b) Verify device establishes clinical benefits
c) Verify device establishes clinical safety
   - Undesirable side effects
   - Acceptable risks benefit ratio

MDR art 64: Perform clinical investigations for implantables and class III

a) Exempt when on market based on sufficient clinical data

MDR Clinical Investigations

MDR art 62

- Conformity assessment
- No CE Mark
- EC / CA

MDR art 74

- Conformity assessment
- CE Mark
- Within / outside scope of intended purpose
- PMCF investigation
- EC / CA (notification in case not burdensome or extra invasive)

MDR art 82

- IIS (academic)
- EC (no negative vote)

ISO14155:2011 in 1 minute

- Standard - choice
- No certification – audited by third party

- Patient safety
- Data integrity

- Consent patients
- IP accountability / labelling
- Report SAEs
- Ensure training and qualification

- Comply with the CIP

MDR requirements Clinical Investigations

- Many MDR CI requirements similar to AIMDD, MDD, MEDDEV, ISO
  - CI in line with well-established international guidance (such as ISO14155:2011)
- Article 2(49): Introduction of sponsor
  - Investigators initiating IIS responsible for meeting MDR CI requirements
  - IIS valuable source of clinical evidence when sponsor is informed and trained on GCP requirements
- Article 62: Appoint legal representative
  - Sponsors not in EU
  - Responsible for ensuring sponsor obligations
- Annex XV: Appoint independent monitor (independent from site)
- Annex XV: Policy for FU of PD from CIP, prohibition of waivers
- Article 78: Coordinated assessment procedure
  - Single electronic application for multicentre CI in EUDAMED
  - Budget and timeline implications
  - MS to agree < 6 days which MS is coordinating
  - No agreement, proposed MS is coordinating
- Article 80: Report SAE with causal relationship to device, comparator or investigation procedure to MS without delay

CRO observations

< # pivotal CI (CE marking)

- Sense holding pattern until NBs communicate decisions on clinical data collection / clinical strategy
- Other geographies

> PMCF CI

- Demand from NB including strict due dates
- Manufacturers reach out: I need to obtain clinical data for my NB / what kind of data? / clinical data

More sophisticated PMCF

- More site engagement
- Higher expectations regarding data points
- Better databases
- RBM

Manufacturers understand CEP > CER

- However still short term approach, even when CER interval 5Y

Manufacturers understand PMCF plan follows CER

- Still room for improvement
- Not just outline of future CI, data collection
- Alignment of documents, close gaps

CRO observations

Feedback manufacturers: need of clinical expert to review CER

- Request from NB
- MEDDEV 2.7.1 rev 4, Annex VII, section 3.2.4 > NB requirement to have relevant clinical expertise including input from qualified medical practitioner

Conduct SoA literature review starting to become key concept

- Requirement for CEP, CER, CIP, IB under MDR and ISO14155:2019
- No longer background info for CI

For CRO EUDAMED is unclear

- Difficult to prepare manufacturer on database
- Difficult to prepare manufacturer on related procedures

Clinical Evaluation Plan

Purpose

- Procedure future CE for device or family

Device description

- Classification
- Regulatory history
- Intended use
- Indication for use
- Intended users
- Intended clinical benefit
- Warnings precautions
- Clinical harms / risks
- Performance claims
- Safety claims

Equivalent devices

- Justification use of data

Clinical Evaluation Plan

SoA

- Alternative / conservative treatment
- Study end points alternative / conservative treatment
- Performancy and safety in studies alternative / conservative treatment
- Relevant outcome parameters
- Possible risks relevant for your device
- Pro's and con's of possible treatments (clinical benefit / unmet clinical need)

Identification of pertinent data

- Clinical Investigations
- PMCF plans
- PMS data

Analysis of data

- Compliance with GSPR
- Alignment with CER, IFU
- Risk management, residual risks, unanswered questions

Planning and responsibilities