Implementing Regulation
setting up the rules and procedures for the cooperation of the Member States in safety assessment of clinical trials

DG SANTE
EMA/HMA-CTFG/COM DG SANTE joint training
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Implementing Regulation for safety cooperation in clinical trials

- Art 44.2 of the CTR provides the COM to adopt an implementing act for cooperation in the assessments of annual safety reports (ASR) and suspected and unexpected safety adverse reactions (SUSARs)
- Expected outcomes:
  - Increased efficiency through fair workshare taking into account existing expertise
  - Improvement of safety data for marketing authorization applications
  - Participants' and patients' protection

IR drafting and adoption process

- developed in close collaboration with Member States and EMA support
- joint meetings with CTEG/CTFG
- COM LS: no legal possibility to postpone the start of the coordinated safety assessments.
- COM adoption process started -> toward submission to the Standing Committee on Medicinal Products for Human Use (Art 88, CTR)
- Target date for adoption: Go live of the CTR (31/01/2022)

Scope

- the assessment of information submitted on **suspected unexpected serious adverse reactions** (incl. 3rd country SUSARs) and of information contained in **annual safety reports** regarding active substances in IMPs used in clinical trials the EU;

- **excluded**: mono-national active substances, active substances in investigational medicinal products used as reference products, including as a placebo, or to active substances used in auxiliary medicinal products

- a best practice guidance is under development by CTGF with additional procedural details also on Member State cooperation in the assessment of other safety information → see presentation on the BP guidance

Rules and procedures for the cooperation of Member States

- selection and reselection of safety assessing Member States;
- assessment of information in SUSARs and ASRs
- development of general recommendations for the RMSs and MSCs aimed at addressing safety concerns from the assessments for corrective measures and other actions related to the safety of the active substance;
- involvement of the saMS in the assessment of substantial modifications to the reference safety information;
- cooperation between saMS, RMSs and MSCs in clinical trials using the same active substance.

Key concepts

- **saMS**: the Member State that assesses the information submitted as SUSAR (incl. 3rd country SUSARs) and ASR for clinical trials involving all IMPs with the **same active substance**.
- **Multinational active substance**: an active substance, which is used in IMPs in clinical trial(s) authorised in more than one Member State.
- **Active substance basis**: to reinforce oversight and harmonisation and to avoid redundant assessments by different MSs, a single saMS should assess the safety of all IMPs with the same active substance. This will also provide sufficient context and is in line with ICH E2F that recommends a single safety update report for an active substance.
- **Risk adaptations:** screening frequency, the extent of the assessments and the timelines for reporting based, amongst others, on existing knowledge (e.g. authorized vs. unauthorized).
- **saMS selection:** based on fair workshare or on existing expertise with the given active substance.

Information systems to support the cooperation in safety assessment (Art 11)

- The functionalities developed shall:

(a) searchable listing of active substances in IMPs

(b) recording of the saMS for a given active substance including the names of previous saMSs

(c) searchable listing of different active substances with responsible saMS for multi-national active substances, or in the case of mono-national active substances RMS;

(d) traceable recording and storage of the assessment of SUSARs and ASRs

(e) access to safety reports for all Member States, communication between Member States, and with sponsors;

(f) provide information on when an annual safety report is overdue;

(g) support the screening of SUSARs;

(h) support cooperation between Member States in the assessment of changes to the reference safety information, when required.

Information systems to support the cooperation in safety assessment (Art 11)

- Integrated use of data in the EudraVigilance database, the Clinical Trial Information System and the EU Medicinal Product Dictionary

- Clinical trial documentation will be available as necessary to safety assessing Member States also when they are not a Member State concerned with a specific clinical trial.

- EMA shall, together with the Member States and the Commission develop the information system to support the selection and re-selection procedure of the safety assessing Member State by the end of the transition period of CTR

- Clinical trials using the same active substance shall be identified based on the EU active substance code referred to in Article 81(3) of Regulation (EU) No 536/2014.

EU4Health – sub-action for clinical trials

Coordinated safety assessment in clinical trials: ~ 5 M EUR in the 2021 work program for 3 years

- Expert exchange program (0.5M EUR procurement to reimburse expenses)
- Co-payment for safety assessors, secretariat for administrative support for the coordinated safety assessment, BP guidance for sustainability (4.5M EUR in a joint action)
- Outcome: support **capacity and expertise building** for safety assessments
- Timelines:
  - submission of nominations closed: n=26 EU/EEA MSs

Thank you

European Commission