Clinical Trial Regulation 536/2014

Coordinated safety assessment under Art 44.2 (COM Implementing Regulation)

Edit Szepessy, DG SANTE

EC-DG SANTE/HMA-CTFG/EMA

joint training - March 9-10, 2021

Background

- CTR Art 44.2 gives the Commission the mandate to adopt implementing acts to set out and modify the rules for Member States on **cooperation for the assessment of safety information** reported in accordance with **Art 42 and 43** in the context of clinical trials.
- The overall aim of the coordinated safety assessment is to introduce **harmonised-standards of safety for clinical trial participants** and future patients and to improve the **quality and robustness of safety data assessment** in clinical trials.
- Target date of adoption of the IR: **end of 2021**, probably with limited support by CTIS at the beginning
- **CTFG guidance to MS** with detailed procedural aspects and with good practice recommendations for safety assessment activities which are not in the scope of the IA

Timelines

- First stable draft (CTFG/CTEG/SANTE B4) – end of January 2021 ✓
- Submitted to SANTE legal colleagues and a wider drafting team (as above + EMA PV + CTFG safety subgroup) – early February, 2021 ✓
- Review by the drafting team – by mid March, 2021 (in progress)
- Draft submitted in parallel to CTEG and CTFG late-March, 2021
- (First) focused joint CTEG/CTFG meeting dedicated to the article-to-article review of the draft IR – mid/late April, 2021

Scope

- IMPs and AxMPs with MA (Article 46 of Regulation* (EC) No 536/2014) and their corresponding active substance used in clinical trials conducted in the Union
  - rules for the cooperation of Member States in the assessment of **SUSARs** (Art 42) and **ASRs** (Art 43)
  - the **selection of safety assessing Member States**;
  - the development and coordinated implementation of **recommendations for corrective measures and/or mitigating actions**;
  - role of the safety assessing Member States in the assessment of **substantial modifications to the RSI**;

* With COM legal service

Safety assessing Member State

- 'Safety assessing Member State': the Member State performing the coordinated assessment of 'SUSARs' and ASRs for trials in the EU using the same active substance as 'investigational medicinal product'

The saMS is selected when the

- (1) first **initial clinical trial application** with a new active substance is submitted in the Clinical trials information system and at least one MSC **authorises** the trial or
- (2) when a **substantial modification to add a new active substance in the EU is authorised** in at least one Member State concerned.
- saMS selection will be based on **fair-workshare and expertise with a given active substance**
- When there is already a saMS for an active substance, preferably the **existing saMS will become the saMS in any new trial with this active substance**, irrespectively whether these have a common or a different sponsor.

Art 3: saMS selection*

saMS selection		
New active substance in the EU – no saMS	Mono-national trial	MSC acts as saMS
	Multi-national trial	Volunteers and/or based on fair work share
Active substance is already in use in the EU - saMS exists	Second trial after first mono-national trial	MSC in first trial saMS with the option to transfer the role to a volunteering MSC (expertise or work-share)
	All other trials	Preferably the existing saMS for this active substance

* CTIS will support coordinated assessment, including saMS selection

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Role and tasks of the saMS

- **SUSAR and ASR assessment** (preparation and submission of assessment reports)
- **request missing or further information from sponsors** for SUSAR/ASR assessments;
- support the assessment of **Substantial Modifications to the RSI**, when it has added value
- ensure that relevant MSC and RMS are **appropriately informed and involved**
- recommend appropriate **corrective measures and/or mitigating actions**
- support their coordinated implementation by MSC/RMS
- assist MSC when requested with any additional safety related matters to the active substance it is responsible for

Art 15. Transitional measures

When a clinical trial, which has been authorised under Directive 2001/20/EC is transitioned to Regulation (EC) No 536/2014 and there is no existing safety assessing Member State for the active substance used in this trial as an investigational medicinal product, a safety assessing Member State shall be assigned to this active substance according to Article 3 of this Regulation (safety assessing Member State selection).

If there is already an existing saMS for this active substance, it will become the saMS for this new trial

Thank you

European Commission