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Safety Reporting Assessment

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Clinical Trial Facilitation and Coordination Group
CTFG

Safety assessment in Clinical Trials

Initial assessment and surveillance of a clinical trial:
positive benefit-risk – ensure patients safety

- Submission for approval:
  Initial CTA, substantial modification, incl. reference safety information (RSI)
- Safety reports:
  - Expedite reporting like SUSAR (anytime, acute),
  - Annual safety report (ASR, cumulative assessment of Adverse Event/ Reaction reported annually)
- Safety relevant notifications : via CTIS submitted per CT
- Safety relevant information other sources
- End of trial : results reported 1 year after

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Safety relevant information

Notifications submitted to CTIS per clinical trial

- Urgent safety measures (Art. 54)
- Temporary halt CT – due to changed benefit risk (B/R) 'safety' (Art. 38)
- Premature end – due to changed B/R 'safety' (Art. 38)
- Unexpected events impact benefit risk (Art. 53)
- Serious breaches : GCP-IWP working on guidances (to sponsor, to MSs) (Art. 52)
- Substantial Modifications : protocol, IB ± RSI, IMPD (Chapter III)
- Restart CT (SM, Art. 38)

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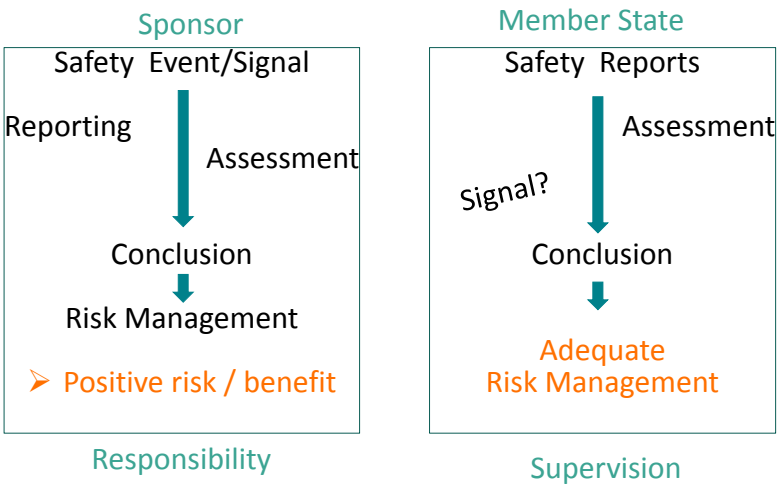
Ensure Participants Safety



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Clinical Trial Regulation 536/2014

Chapter VII Safety Reporting in the context of a Clinical Trial

- Eudravigilance database modules for ASR and SUSAR by EMA (Art. 40)
- Reporting requirements for SUSARs (Art. 42) and ASR (art 43)

- **Article 44** (2):
  MS shall cooperate in assessing the information reported in accordance with Articles 42 (Suspected unexpected serious adverse reaction, SUSAR) and 43 (Annual safety report, ASR)
  COM could by implementing act set up and modify the rules for such cooperation
  - ➢ EU COM gave the task to develop and set up this cooperation to CTFG

  (3) Ethics involved as of member state

Annex III Safety reporting including Reference Safety Information (RSI)
EudraLex Vol 10 QnA, section 7 ‚safety'

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Difference CT applications and Safety supervision

Clinical Trial	Safety
+ *Subst. Modifications, notifications...*	SUSAR, ASR, other
Submission / Assessment	Reporting / Assessment
↓	↓
Portal/Database (CTIS*)	EudraVigilance- Database or CTIS
↓ per CT	↓ per IMP*
↓	↓
Reporting MS / MSCs	Safety assessing MS / MSCs

* CTIS = EU Portal/D database and safety module on ASR, Adhoc Assessment
IMP = Investigational Medicinal Product and same for non-IMP
(the AxMP = Auxilary Medicinal Product) – both mostly on basis of active substance

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IMP - AxMP - Active Substance

IMP
Investigational Medicinal Product = product being tested or as reference
'Test , Comparator or Placebo'
AxMP
Auxiliary medicinal products = product used for needs of the clinical trial, not IMP
'rescue medication, challenge agent, medicinal product to assess endpoint , background treatment'
Active Substance
= active pharmaceutical ingredient of IMP or AxMP

AxMP Safety Reporting, like SUSAR, ASR, changes benefit/risk et cetera
SUSAR reporting required if suspected to be related to AxMP only :
Authorised AxMP as of Pharmacovigilance Regulation (Art 46)
Non-authorised AxMP like IMPs
Both: Take relevant up in annual safety report of IMP

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Principle of Work Share

ONE Safety Assessing Member State ,the **saMS**' responsible for **ONE Active Substance**

The *‚Pharmacovigilance' Expert*
Expert on safety profile of the active substance
Information hub of any safety issue

Basis is tight **communication / exchange of**

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saMS Responsibilities

- Selection after 1st authorisation in EU/EEA
  - Continuity should be given – discussion ongoing
  - Fair work share
- Responsibilities
  - Assessment of ASR
  - Screening and assessment of SUSARs (EU and 3rd country*)
  - Support assessment of RSI (update)
  - Support coordinated assessment of any safety issue with the active substance,
    e.g. notifications or other sources (e.g. IRN, class effects) affecting the active substance/s and more than 1 CT

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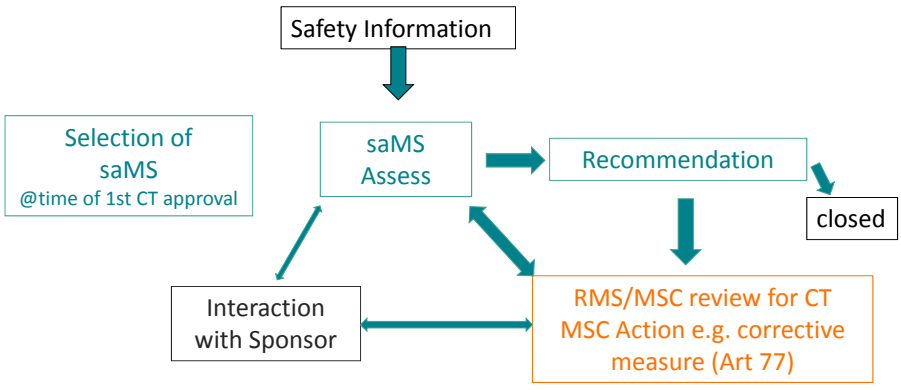
*in discussion

Procedures*



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*Details :
CTFG internal guidance on cooperation in safety assessment
under revision

Procedures and Pilots

ASR worksharing : started with ICH E2F ⇒ Pilot ongoing (CZ)
saMS ⇒ Pilot started, incl. SUSAR cooperation / work share (AT)

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- Exchange on safety issues of active substance relevant to one or more CTs ⟶ serious/urgent/specific issues
- Consolidated common opinion / actions
  e.g. ……'long list exists at CTFG'…..
- Procedure on cooperation safety issue any source fast/regular

➢ **Join the pilots , get trained , get experiences**

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Thank you very much for your attention!

Contact

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