

The CTFG perspectives on safety assessment

Elke Stahl



Clinical Trial Directive: Safety in Clinical Trials

- Sponsor is responsible for monitoring safety continuously and to protect clinical trial participants and public health
- National competent authorities (NCA) and Ethics Committees (EC) have to supervise the sponsor in monitoring of safety
- Sponsor has to collect and submit safety data of investigational medicinal products (IMP) in clinical trials (CT)
 - SUSAR*
 - ASR (DSUR)**
- NCAs and EC to assess safety data received

* Suspected Unexpected Serious Adverse Reaction

** Annual Safety Report (Development Safety Update Report, ICH E2F)

Clinical Trial Directive Safety related Guidances

New Version:

- CT1 guidance „CT“ (2010/C 82/01)
- Q&A Version 6.0
- Substantial amendment form

In review:

- CT3 guidance „Advers reaction reports“ (ENTR/CT3)
- CT4 guidance „SUSAR, EV-CTM*“ (ENTR/CT4)

Facilitation of safety monitoring in CT

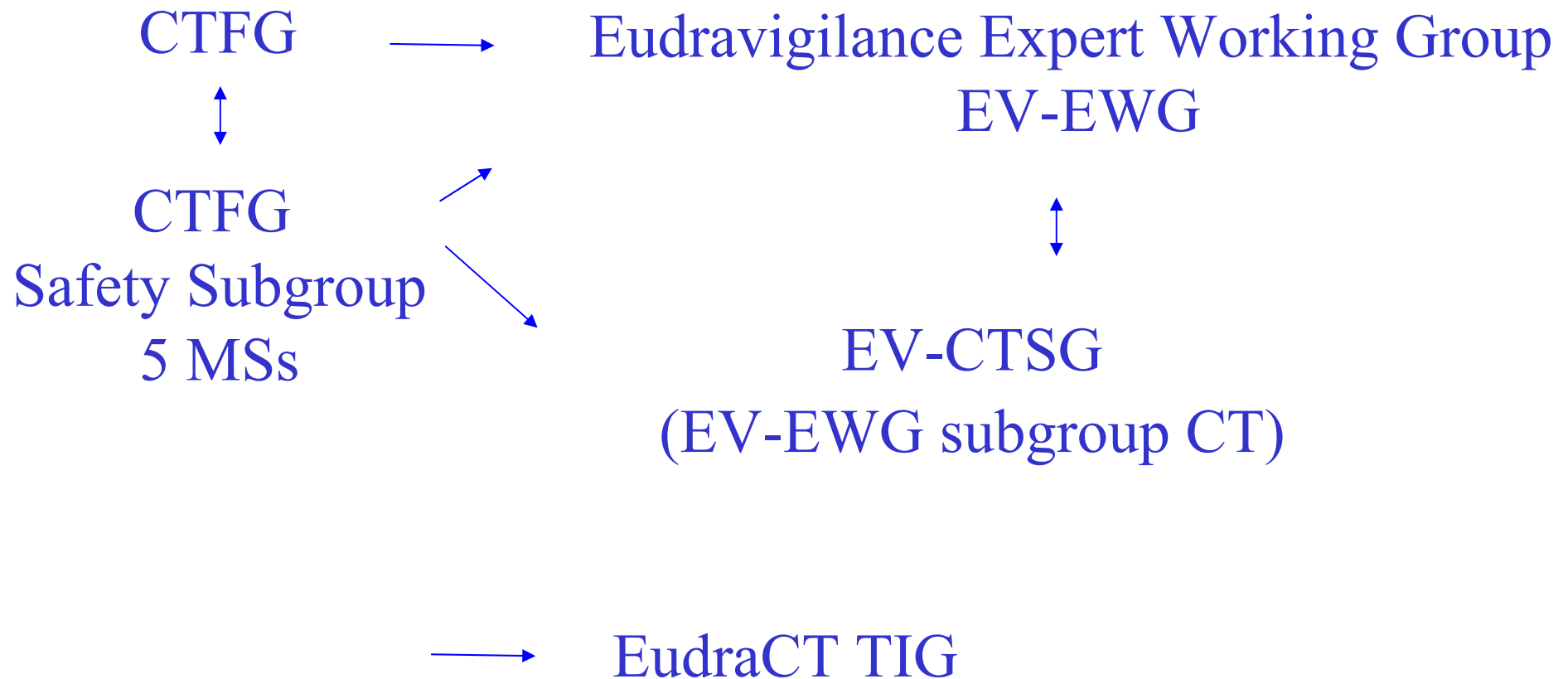
General Objective

- Harmonisation within Member States (MS) – in principle
 - NCA
 - Interaction NCA and EC on national base
 - EC in various legal frameworks
- Work-sharing
- Simplify processes for NCA and Sponsors

CTFG Action Plan 2010+ Safety

- Building a Safety Network
- Harmonisation
- Work-sharing of MSs
- Assist European Commission in
 - EU legislation
 - Improving related guidances
 - Support common interpretation
e.g. with Q&A documents

CTFG Organization and Cooperation Safety



SUSAR - Status

- Sponsor has to notify concerned NCA and EC*
- NCA has to transfer SUSAR to EV-CTM*
- CT1 suggest submitting via EudraVigilance - Clinical Trial Modul (EV-CTM)
 - during transition phase in parallel (NCA and EV-CTM)

* Directive Article 17

SUSAR - Status

- Thousands of IMPs in active CTs in multiple MSs
- Overreporting of SUSAR due to lack of qualified assessment (→ causality and relatedness)
- Different decisions/reactions on SUSARs reported to MSs
- Non-commercial Sponsors often by hardcopy
- Only limited usage of EV-CTM till now

SUSAR goals of CTFG

Network of safety assessors:

- Exchange of information, communication
- Harmonisation of assessment and reaction
- Coordination of decisions

- Work-sharing of SUSAR assessment in alignment with national responsibilities
- Information system for MS (NCA and EC)
- EV-CTM use as the *one* database for SUSAR in all MS in future

EV-CTM goals

- Electronic input by sponsor to EV-CTM only
→ subsequently forwarded to concerned MS
- Access of MSs to all data
- EV-database functionalities sufficient to support responsibility of MS to ensure safety in CT and public health

EV-CTM Functional Requirements

- Ensure quality of data in EV-CTM by
 - Business rules on reporting
 - Training for sponsors and NCA (EC?)
- Specifications for a functioning database (EV-CTM, EV-DAS*, EV-MPD**, EudraCT) defined by user (NCA - via CTFG) to fit essential needs
- Validation of proper function prior to acceptance by all MSs and use as the only database in Europe

EV-CTM Specifications

- Basic „core“ functions
 - Standard queries and reports to retrieve information
 - Alert system for high priority and regular SUSAR
 - Interaction EV and EudraCT, e.g. IMP + EudraCT
 - Input of IMP via dictionary (EV-MPD) from 1st trial, name tracking
- Extended functions
 - Signal detection and warning system
 - E.g. meta-queries, meta-reports

SUSAR - in progress

So far:

- Network of safety assessors
 - Exchange of information
 - Start of harmonization
- Specify needs for EV-CTM
- ...

ASR / DSUR - Status

- IMP in active trial in MS: Sponsor has to submit ASR each year to all MS concerned
- ASR will be replaced by DSUR: Fall 2010, with 1 year transition phase
- Resources consuming

ASR / DSUR goal

- One DSUR per IMP (API) per year
- Work-sharing in assessment
- Alerting concerned MSs
- Coordination of decisions

- Tracking system e.g. by DIBD*
- One repository database for ASR/DSUR and assessment

ASR / DSUR

- Review and finalise concept paper on procedures of DSUR assessment
- Start pilot work-sharing phase
- Adapt process
- Publication of refined guidance
- Implement work-sharing

ASR / DSUR – Issues Procedure

- Workflow: timelines, resources
- Selection of DSUR
 - risk based priority approach
- Simplified DSUR for IMPs with MA
- Harmonisation of content of assessment report „template“

ASR / DSUR - Issues

- Coordinator
- IT support – single repository, tracking
- DIBD – by sponsor (in EudraCT ?)

Safety in CT

- SUSAR and ASR/DSUR are crucial for signal detection and protection of safety of CT participants
- MSs networking for harmonisation and work-sharing
- Support one database as common source in MSs

THANKS !