

# Designing the Future Conditions for Clinical Research in Europe

**Conclusions from the Pharmacovigilance Workshop  
February 8, 2010**

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- **Representatives:**

- EMA
- CA
- EC
- Commercial sponsors
- Investigators/ non-commercial sponsors
- Patient
- CRO

- **Content:**

- Issues
- Proposals

- **Introduction: CTD 2001/20/EC**
- **Current issues**
- **Proposals**
- **Conclusion**

## **Art. 16: Provisions of investigators regarding the reporting of SAEs related to CTs.**

- ◆ Investigator reports all SAEs immediately to the sponsor.
- ◆ Sponsor keeps detailed records of all AEs which are reported to him by the investigators.

## **Art. 17: Provisions of sponsors regarding recording the notification of SUSARs.**

- ◆ Events considered related to IMP
- ◆ SUSAR reports to be entered electronically into EVCTM
- ◆ Agency to provide NCAs with access to the data in EVCTM.

## **Art. 17: Sponsor records and reports on an expedited basis to NCAs and EC all relevant information about SUSARs.**

- ◆ Fatal and life threatening SUSARs: 7 days for initial + 8 days for relevant follow-up
- ◆ All other SUSARs: maximum of 15 days
- ◆ **Sponsors and MS** to continuously monitor safety to protect clinical trial participants and public health;

## **Art. 17: sponsor provides MSs and EC once a year**

- ◆ A listing of all Serious Adverse Reactions (SARs),
- ◆ A report of the subjects' safety (ASR).

## **Art. 18: Detailed guidance**

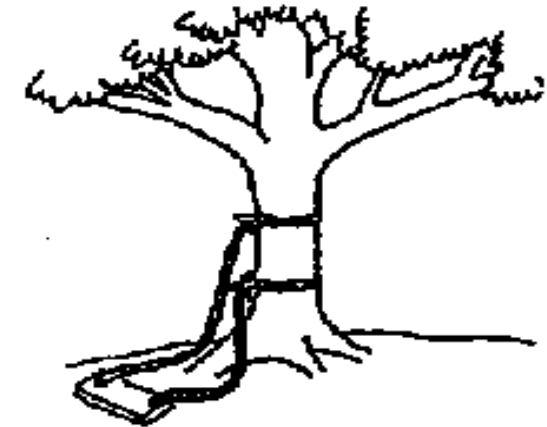
- Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use (ENTR/CT 3)
- Detailed guidance on the European database of Suspected Serious Adverse Reactions - EudraVigilance Clinical Trial Module (ENTR/CT 4)
- Q&As to adverse reactions reporting in clinical trials (Chapter II and V of Volume 10).



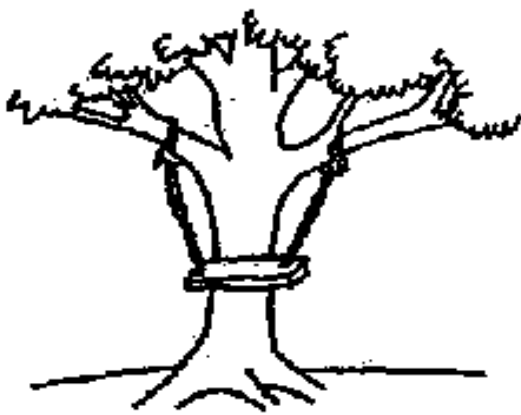
As proposed by the project sponsor.



As specified in the project request.



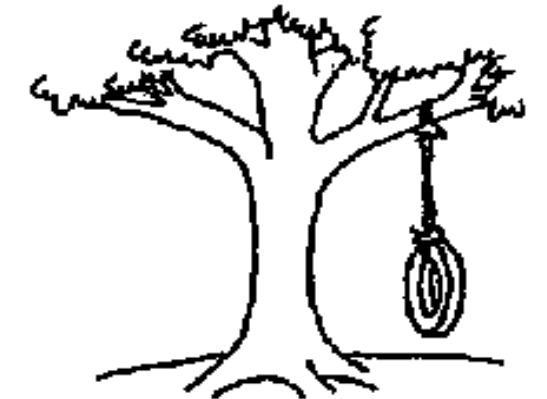
As designed by the senior analyst.



As produced by the programmers.



As installed at the user's site.



What the user wanted.

- The **lack of harmonised implementation** across the MS
- Rules for reporting of SUSARs are **different or not clear**
  - With impact on sponsors (over-reporting, unnecessary burden)
  - And on Eudravigilance (data quality)
- The communication of SUSARs to ethics committees is **variable and excessive**
- Safety info sent to investigators is not streamlined

## General issues for sponsors

- Some sponsors are **not able to fulfill legal requirements**
- Roles of National CAs and ECs **not clear/ overlapping**
- **Increased administrative burden**
- **Fear for legal consequences** of under-reporting

## Specific issues of non-commercial sponsors & investigators

- **Multi-modality** studies (CTD or not)
- Intercontinental trials (**European sponsorship**)
- Difficult access to **drug information**
- Poor knowledge of **electronic reporting**
- Special **trained** staff needed
- **MedDRA** versus CTCAE
- Increased amount of **queries**
- Increased **administrative burden**
- Lack of **resources**

- **Too many** « SUSARs » declared / not only SUSARs
- **EVCTM**
  - Poor Quality
  - Content: NCAs do not receive automatically the information they need to ensure their responsibilities
  - Public benefit of this db not yet demonstrated
- The content of the ASR is **not harmonized**
- **ASR** not part of EVCTM
- Lack of **resources**

- **Info from sponsors varies**
  - ◆ SUSARs from their site
  - ◆ SUSARs from all CTs from all over the world
  - ◆ Non SUSARs
- **ECs cannot handle current masses of information**
  - ◆ Lack of resources
  - ◆ No access to EVCTM
- **Safety signal detection from ECs practice is very rare (only in phase I trials)**
  - ◆ Safety cannot be screened based on single case reports
- **Not all EC have dedicated, educated, accredited or even lay people in their team**



## Goal of proposals

- **Simplified and harmonized reporting requirements and formats in all member states**
- **Avoid duplication of reporting and multiple assessment efforts**
- **Clearer responsibilities for CA vs EC concerning safety assessments**
- **The electronic population of EudraVigilance should be optimized and appropriate analysis tools should be available**
- **Ensure continuation of academic research**

# Simplified and harmonized reporting requirements and formats

- **SUSARs**
  - **Only reporting to EVCTM**, not to separate member states
    - ◆ Reporting timelines
    - ◆ Set of business rules
  - **No individual SUSAR reporting to EC and investigators**
- **ASR**
  - Define a **harmonized content** of the ASR
  - Take into account commercial (by drug) and non-commercial sponsor (by trial)

- **SUSARs**

- **Centralization**: single entry point: EVCTM,
- No need to send to all MS
- No need to send to all ECs (except for phase I)
- NCA still need to receive the info quickly
- Automatic transmission of the data to NCA's

- **ASR**

- **Work-sharing** of CA on assessment of ASRs
- **One repository** for ASR, e.g. EVCTM
- EC receive line listings, ASR or executive summary (of DSUR)

# Clearer responsibilities for CA vs EC concerning safety assessments

## Avoid multiple assessment:

- Clearly define the scopes of NCAs and ECs
- Better use of available resources
- Work-sharing safety data assessment by NCAs
- Central review by CA (cfr. VHP)
- Appropriate tools to perform efficient signal detection are necessary
- Risk based approach?
- NCA can still suspend or prohibit a CT where appropriate

## Role of EC?

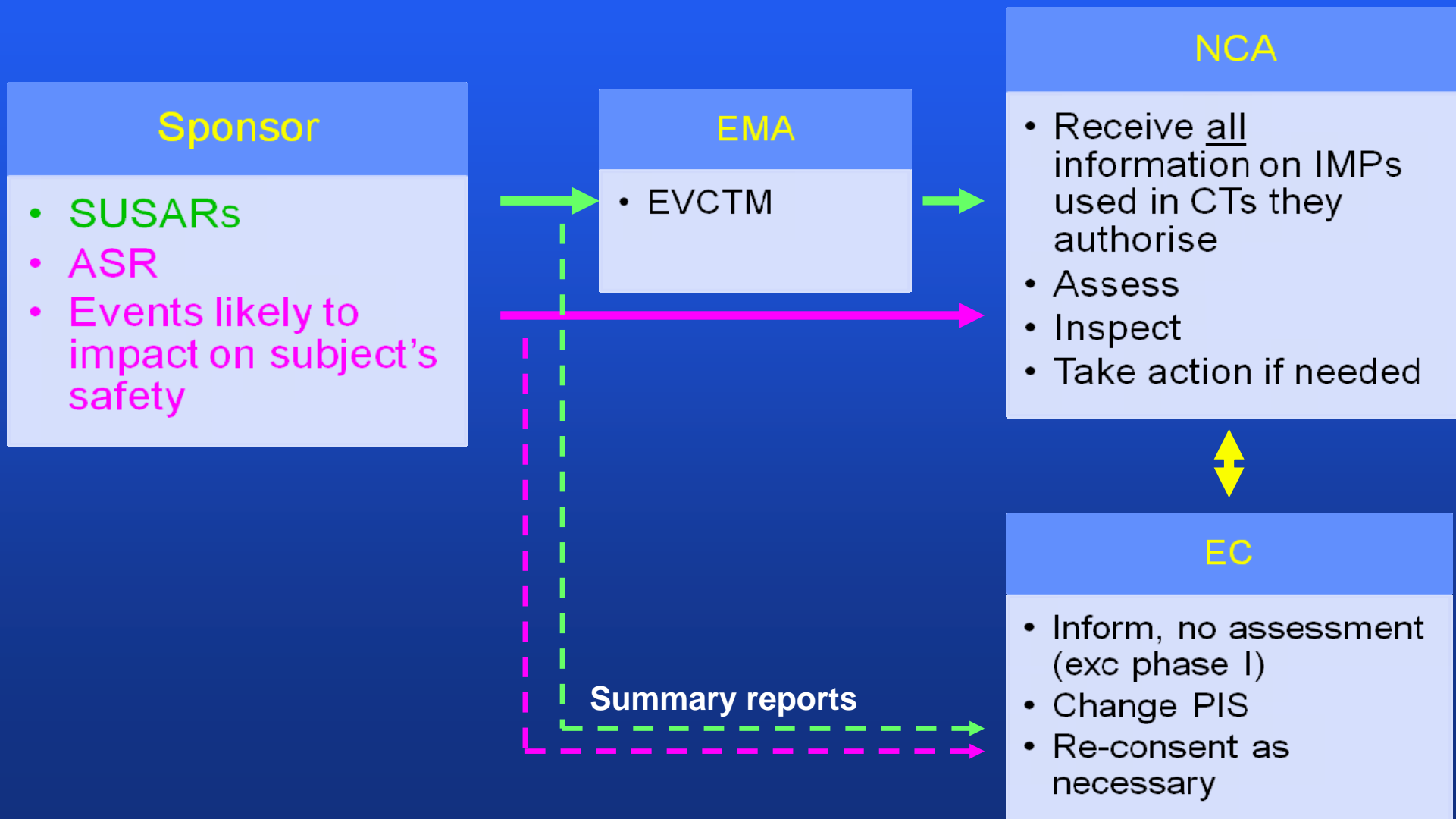
- EC needs to be informed, not assess all data
- If role of EC is changing, is there still a need for EC to have direct access to EVCTM?
- Check influence on PIS and decide whether re-consent is necessary

- Make SUSAR reporting to EVCTM **mandatory**
- Ensure good quality of the data entered
- **Link** Eudract with EVCTM
- **Automatic transmission** by EVCTM to NCAs of all info to ensure their responsibilities
- **More support** for non-commercial sponsors: Allow to report via CA
- **Optimalisation** of use EVDAS

## Ensure continuation of academic research

- **More education** necessary
- More info in **protocols**
- **Better use of resources** to help academics, e.g. trial offices (UK, NL), training by NCA (FR) result in increased/improved reporting
- **CA allow** non-commercial sponsors to report on paper
- **DSMB** should play a more active role in safety review but qualified people necessary

# Proposal for simplified process



- All parties agree **that further clarification of responsibilities** of different partners in the safety assessment is needed. This includes **changes**, but also **sharing** of current responsibilities.
- The data quality and use **of EVCTM** plays a major role in accomodating these aims.
- The ultimate goal is to **reduce/ better use resources** by **improving the communication** and ensuring the **patients' safety** in a clinical trial