



# Directive 2001/20/EC Reporting of Suspected Unexpected Serious Adverse Reactions (SUSARs)

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# Current IMB Requirements

- Control of Clinical Trials Act 1987 and 1990
- Irish Medicines Board Act, 1995
- Note for Guidance of Good Clinical Practice (ICH E6).
- Clinical Safety Data Management-  
Definitions and Standards for Expedited  
Reporting (ICH E2A).



# Clinical Trial Directive Requirements

Article 2 - Definitions

Article 16- Notification of Adverse Events

Article 17- Notification of Serious Adverse  
Reactions

Article 18 – Guidance concerning reports



# Article 16 – Notification of Adverse Events

## Investigator Responsibilities:

- Immediate reporting of all SAEs to the sponsor followed by detailed written reports.
- Identify trial subjects by unique code numbers



# Article 16 – Notification of Adverse Events (contd.)

## Investigator Responsibilities (contd):

- Notification of laboratory abnormalities and/or adverse events critical to safety evaluation, according to requirements
- Provide additional information related to reported deaths to the sponsor and Ethics Committee as required.



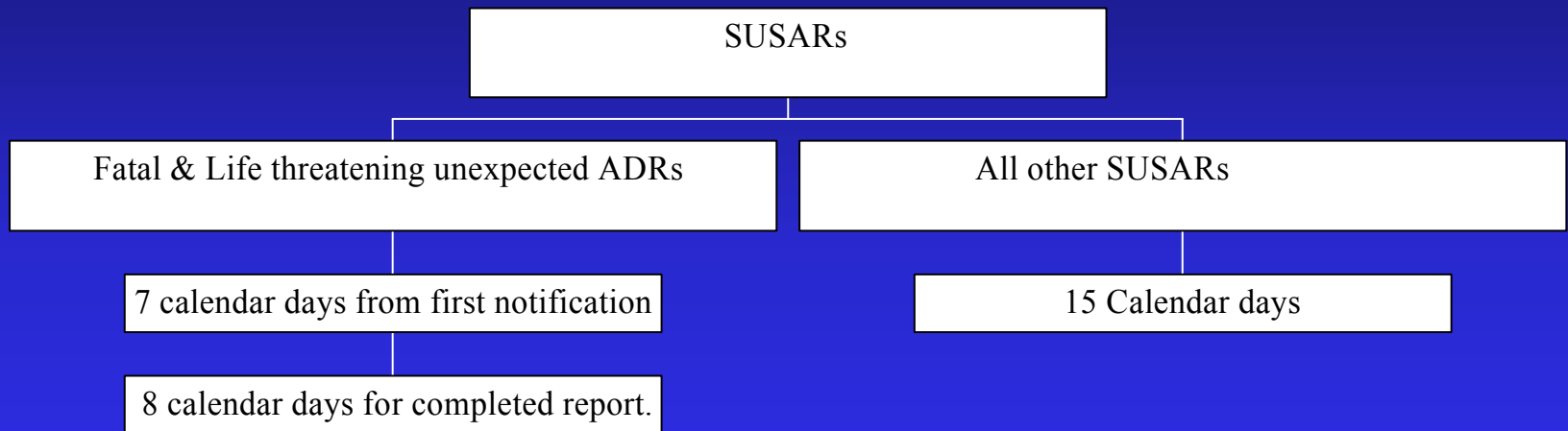
# Article 16 – Notification of Adverse Events (contd.)

## Sponsor Responsibilities

- Must keep detailed records of all adverse events reported.
- Sponsor should submit these records to the competent authorities, if requested.



# Article 17: Notification of Serious Adverse Reactions



**Reporting to competent authorities and Ethics Committees.**

**Provision of safety information to investigators.**



# Clinical Trial Directive Requirements

## Article 18 – Guidance concerning reports

Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use (April 2003).



# Minimum Reporting Criteria

- A suspected investigational medicinal product
- An identifiable subject
- An adverse event assessed as serious & unexpected, & for which there is a reasonable suspected causal relationship
- An identifiable reporting source



# Minimum Reporting Criteria (contd.)

When available & applicable

- A unique CT identification, if applicable (EUDRACT number or in case of non-EU trials the sponsors trial protocol code number).
- A unique case identification



## Other safety issues that may require expedited reporting

- Single case reports of an expected serious adverse reaction with an unexpected outcome (e.g.. Fatal outcome)
- An increase in the rate of occurrence of an expected serious ADR, which is judged to be clinically important
- Post-study SUSARs that occur after the patient has completed a clinical trial & are reported to the sponsor by the investigator



# Other safety issues that may require expedited reporting (contd.)

**A new event likely to affect the safety of subjects**

- a SAE which could be associated with the trial procedures and which could modify the conduct of the trial**
- a significant hazard to the subject population such as lack of efficacy of an IMP used for the treatment of a life threatening disease**
- a major safety finding from a newly completed animal study such as carcinogenicity**



# Managing “Blinded” Cases

- Break “Blind” for cases meeting criteria for expedited reporting
  - only for specific patient
  - preferably by sponsor
- Fatal/Serious outcomes as primary efficacy endpoints, liaise with competent authorities on reporting arrangements.



# Annual Reports

Once a year throughout the clinical trial the sponsor shall provide the Member States in whose territory the clinical trial is being conducted and the EC with a line-listing of all suspected serious adverse reactions which have occurred over this period and a report of the subjects safety.



# Time Frame for Annual Reports

- The annual report should be submitted within 60 days of the birthday of the first authorisation date by any MS of a clinical trial on that IMP.



# Content of Annual Reports

- Report on the subjects safety in the concerned clinical trial
- A line listing of all suspected SARs and SUSARs
- Summary tabulation of suspected SARs



# Annual Reports

**The sponsor should include a total (global) analysis of the actual safety profile of the tested IMP, based on the experience of all clinical trials performed by the sponsor and all available data.**



# Summary

- **Annual Safety reports must be submitted yearly.**
- **Makes explicit GCP requirements for sponsors, investigators and competent authorities.**
- **In keeping with existing GCP & ICH E2A requirements for definitions and timeframes.**