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# Safety Reporting

Reporting of Adverse Events and Serious  
Adverse Events in Clinical Trials for Investigator  
Site Staff

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# Presentation Topics

1. Definitions
2. Legal Framework
3. General Expectations
4. AE Reporting: Expectations and Common Inspection Findings
5. SAE Reporting: Expectations and Common Inspection Findings
6. Sponsor Responsibilities



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# References

- Note for Guidance on Good Clinical Practice: Consolidated Guideline (ICH Topic E6, Step 5, CPMP/ICH/135/95)
- European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations, 2004 to 2009 (SI No.190 of 2004, as amended)
- Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001
- EudraLex - Volume 10, Clinical Trial Guidelines



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# Definitions (Ref: SI No.190 of 2004)

- **Adverse Event:** Any untoward medical occurrence in a subject to whom a medicinal product has been administered, including occurrences that do not necessarily have a causal relationship with treatment
- **Adverse Reaction:** Any untoward and unintended response in a subject to an investigational medicinal product which is related to any dose administered to that subject



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## Definitions (Ref: SI No.190 of 2004)

- **Serious Adverse Event/Serious Adverse Reaction:** Any adverse event or adverse reaction that, at any dose,
  - a) Results in death,
  - b) Is life-threatening
  - c) Requires hospitalisation or prolonged hospitalisation
  - d) Results in persistent or significant disability or incapacity
  - e) Consists of a congenital anomaly or birth defect



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## Definitions (Ref: SI No.190 of 2004)

- **Unexpected Adverse Reaction:** In respect of an investigational Medicinal Product, an adverse reaction, the nature or severity of which is not consistent with the information about that medicinal product as set out
  - a) In the case of a product which is the subject of a marketing authorisation, in the summary of product characteristics for that product
  - b) In the case of any other investigational medicinal product, in the Investigators brochure relating to the particular clinical trial.



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# Legal Framework

## ICH GCP 4.11

- Immediate reporting of SAE to the Sponsor
  - Immediate = within 24 hours
- Report AE and laboratory abnormalities in accordance with protocol requirements
  - If no instruction in protocol regarding lab abnormalities → report as AE if clinically significant

*SI No. 190 of 2004: Regulation 29*



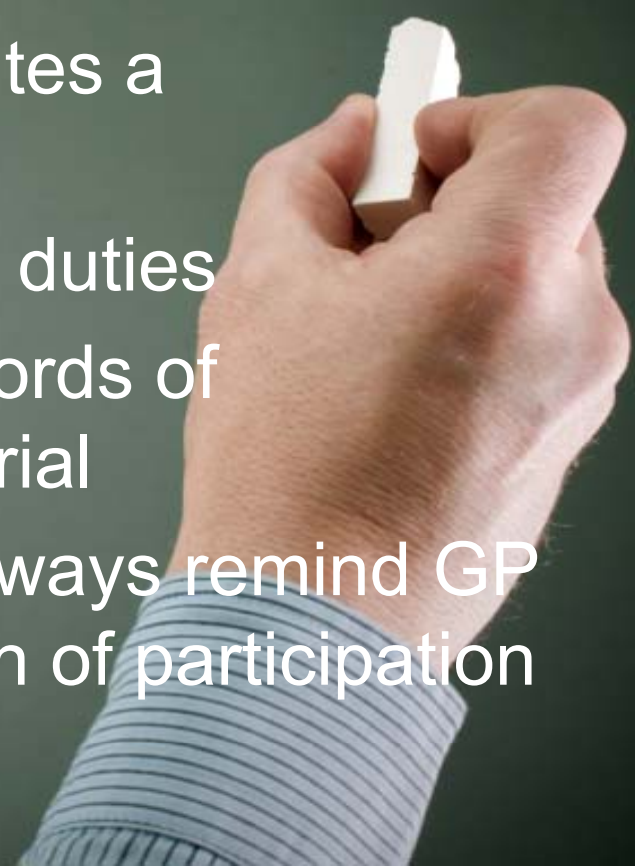
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# General Expectations

- Adequate training of staff in safety reporting requirements
  - Understand what constitutes a Serious Adverse Event
  - Appropriate delegation of duties
  - Reference in medical records of participation in a clinical trial
  - Encourage Subjects to always remind GP or other treating Physician of participation in a clinical trial
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# Expectations for Adverse Event Reporting



- As required by the protocol
- Complete and accurate source documentation
- Assessment of event documented in real time



Include: Mild, Moderate, Severe  
and/or Grade 1, 2, 3, 4, 5

- Investigator assessment of causality



Relationship to trial medication:  
Probable, Possible or Unrelated

- Documentation of treatment (if any)



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# Expectations for Adverse Event Reporting



- Seriousness Assessment of each event
- Adequate review of medical records for events
- Accurate and timely completion of event in CRF
- Concomitant Medication → Corresponding AE



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# Remember

SI No. 190 of 2004, Schedule 1, Part 2:

The medical care given to, and the medical decisions made on behalf of, subjects shall be the responsibility of an appropriately qualified registered medical practitioner

*Note: "Registered Medical Practitioner" means a person registered in the register established under the Medical Practitioners Act 1978*

# Common Deficiencies



- Unreported AE
- AE not recorded in CRF in timely manner
- No assessment/documentated Investigator assessment of AE
- Inadequate source documentation
- Poor quality CRF data
- Concomitant Medication ➡ No corresponding AE
- Laboratory abnormalities not reported (where required)



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# Use of Worksheets



- Mainly Oncology trials
- Worksheets used by Research Nurses to record events (eg. common chemo toxicities)
- Physicians documenting events in medical records
- Duplicate recording of events  
    → inconsistencies between both
- Which is source ?



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# Reminder

**Serious Adverse Event/Serious Adverse Reaction:** Any adverse event or adverse reaction that, at any dose:

- ✓ Results in death,
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# Expectations for SAE Reporting



- Minimum criteria for initial SAE Report:
  - Identifiable subject
  - Identifiable reporter
  - Event description
  - Product
- Report within 24 hours: Verbally/Written
  - If verbal, then immediate follow-up in writing
- Investigator assessment of causality/relationship
- Investigator sign-off of event
- Adequate Follow-up



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# Common Deficiencies



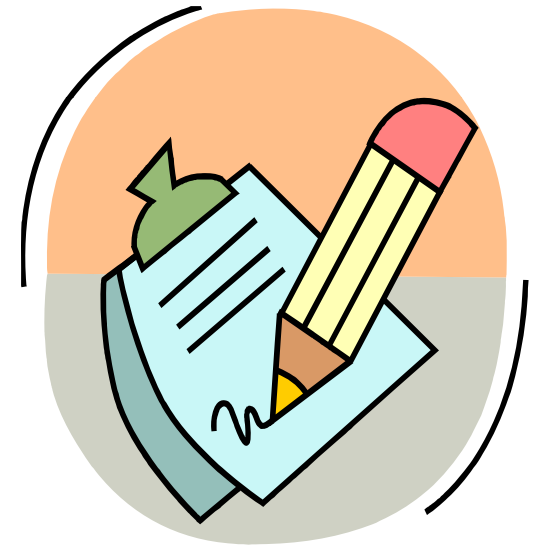
- Unreported SAE
- Late reporting of SAE
- Poor quality reports
- Inadequate/Inaccurate source records
- No Investigator assessment of causality
- Inadequate Follow-up



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# Expectations for Follow-up

- Monitor event until resolution
- Provide follow-up information to Sponsor as soon as it becomes available, e.g.
  - Discharge records
  - Laboratory reports/Other reports
  - Autopsy reports for deaths
- Don't wait for Sponsor requests for FU
- Clear and accurate data
- Answer all queries from Sponsor in timely manner



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# Sponsor Responsibilities

- Expectedness assessment → recognised adverse effect of the medication or is it unexpected
  - SPC
  - Investigator Brochure
- Onward SUSAR reporting to Competent Authorities
- Continuous evaluation of safety data:
  - Facilitate identification of new safety concerns
  - Establish safety profiles of medicinal substances
  - Ensure timely and appropriate regulatory action
  - Support prompt communication of any safety concerns as necessary



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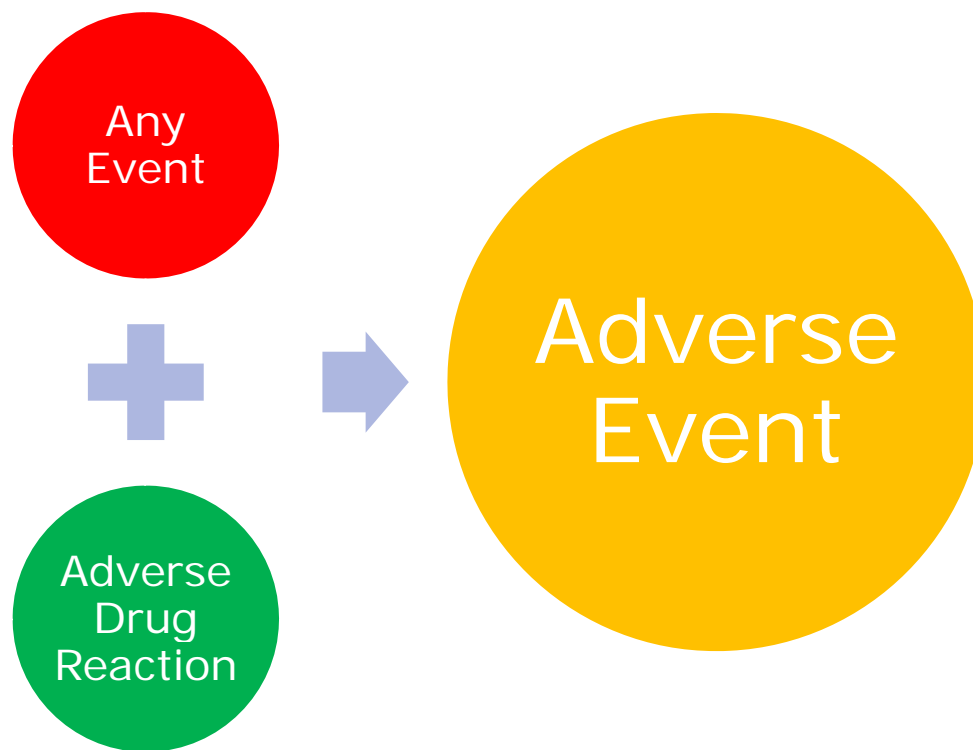
# Summary

- Timely reporting of SAE and AE
- Adequate & accurate source records
- Clear & accurate reports
- Investigator assessment of causality
- Adequate Follow-up



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# Adverse Events



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Thank You

NO THANKS



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# Abbreviations

AE	Adverse Event
ADR	Adverse Drug Reaction
AR	Adverse Reaction
CRF	Case Report Form
SAE	Serious Adverse Event
SUSAR	Suspected Unexpected Serious Adverse Reaction



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