Clinical trial Initiation and site start up

AE Reporting

Module 6 Topic 1_5

Adverse Event Reporting

Introduction

- Why determine SAFETY???
- Safety monitoring in clinical studies
  - General
  - Specific
- General safety goals
- To detect and characterize common ADR
- To determine tolerability in subjects
- To identify risk factors for particular ADR

Glossary

- Adverse Event (AE)
- Adverse Drug Reaction (ADR)
- Serious Adverse Event (SAE)
- Suspected Unexpected Serious Adverse Reaction (SUSAR)

Classification of ADRs

- Rawlins and Thompson classification
  - Type A
  - Type B

- Based on Intensity of ADR
  - Mild
  - Moderate
  - Severe

Relationship between Adverse Reaction and Drug

- Definite
- Probable
- Possible
- Unknown
- Not related

Relationship of an AE to Trial Drug

- 6 basic points to be considered :
  - Previous experience with the medicine
  - Alternative reasons for AE
  - Timing between administration and AE
  - Medicine levels and evidence
  - De-challenge
  - Re-challenge

Safety Data Reporting

- Appendix-11 as per Schedule Y
- Expedited Adverse Drug Reaction Reports
- Periodic Safety Update Reports (PSUR)
- FDA 3500 for Voluntary reporting
- FDA 3500A for Mandatory reporting

ICH E2A

- Generally involves reporting of events previously “unobserved” or “undocumented”
- All ADRs that are both serious and unexpected are reported
- Causality assessment is required
- Others

Rule 122 DAB

- In the case of an injury occurring to the clinical trial subject, he or she shall be given free medical management as long as required

- In case the injury occurring to the trial subject is related to the clinical trial, such subject shall also be entitled for financial compensation over and above any expenses incurred on the medical management of the subject

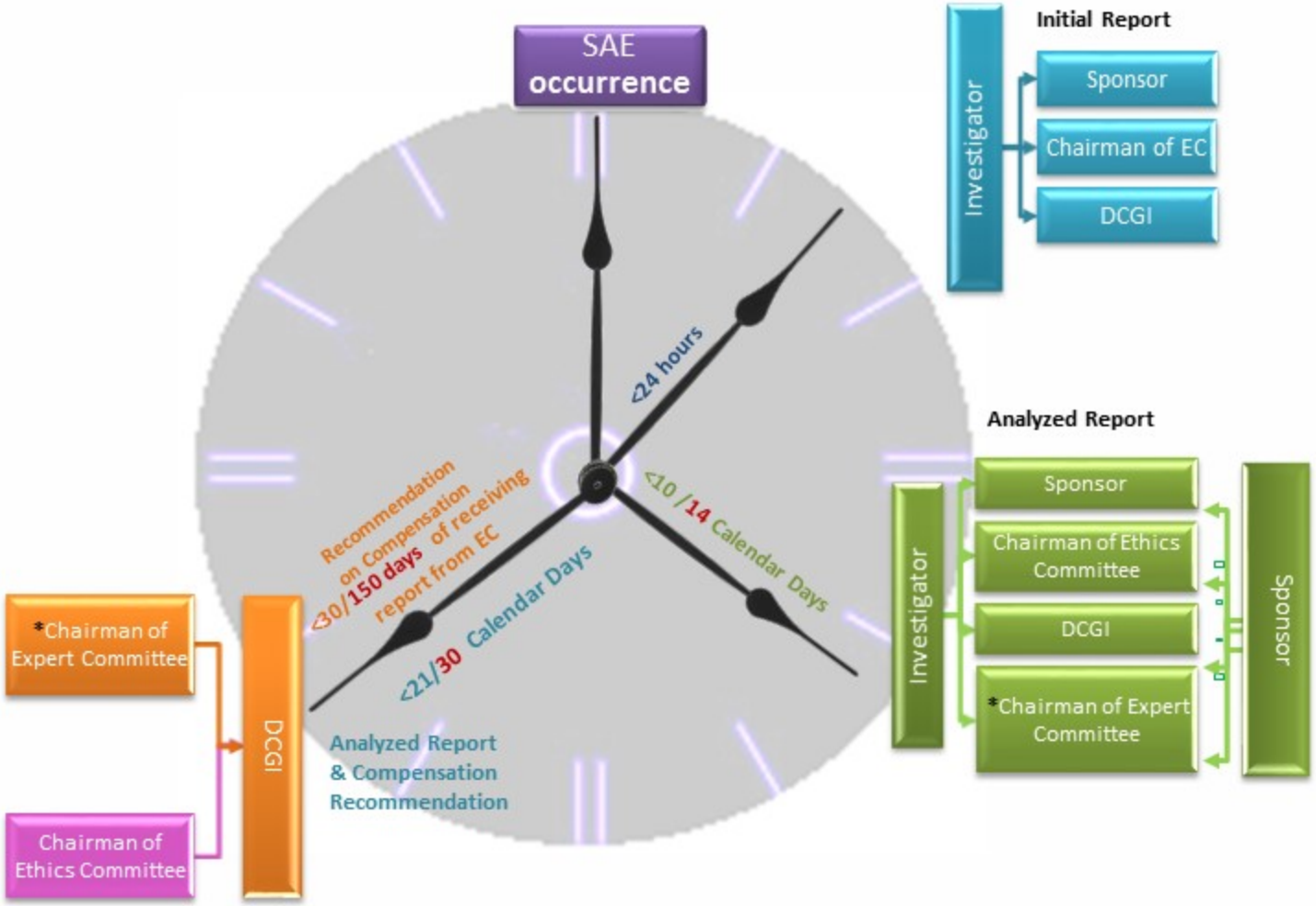
New SAE Reporting Process

New SAE Reporting Process

New SAE Reporting Process

* In case of Death

New SAE Reporting Process



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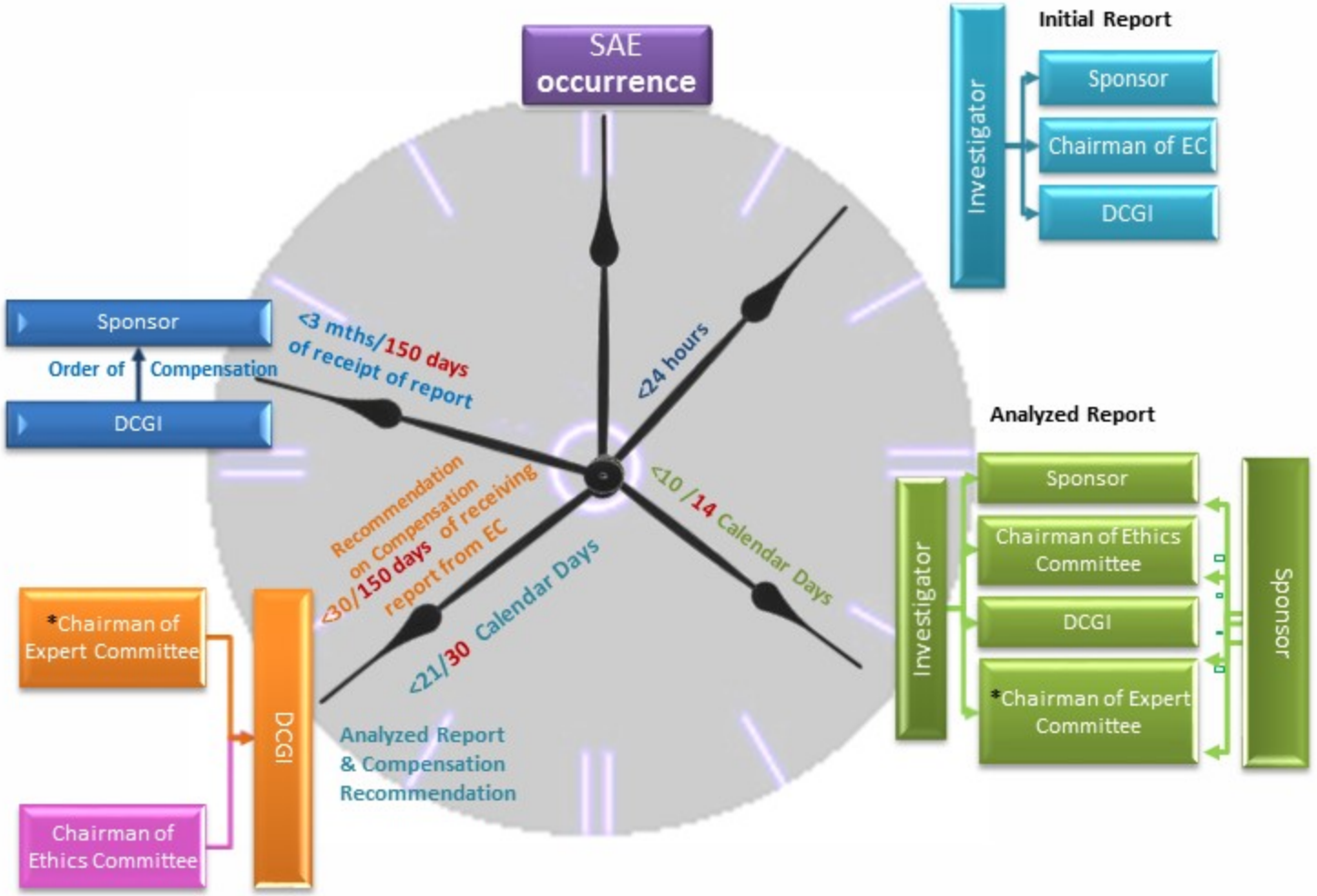
New SAE Reporting Process



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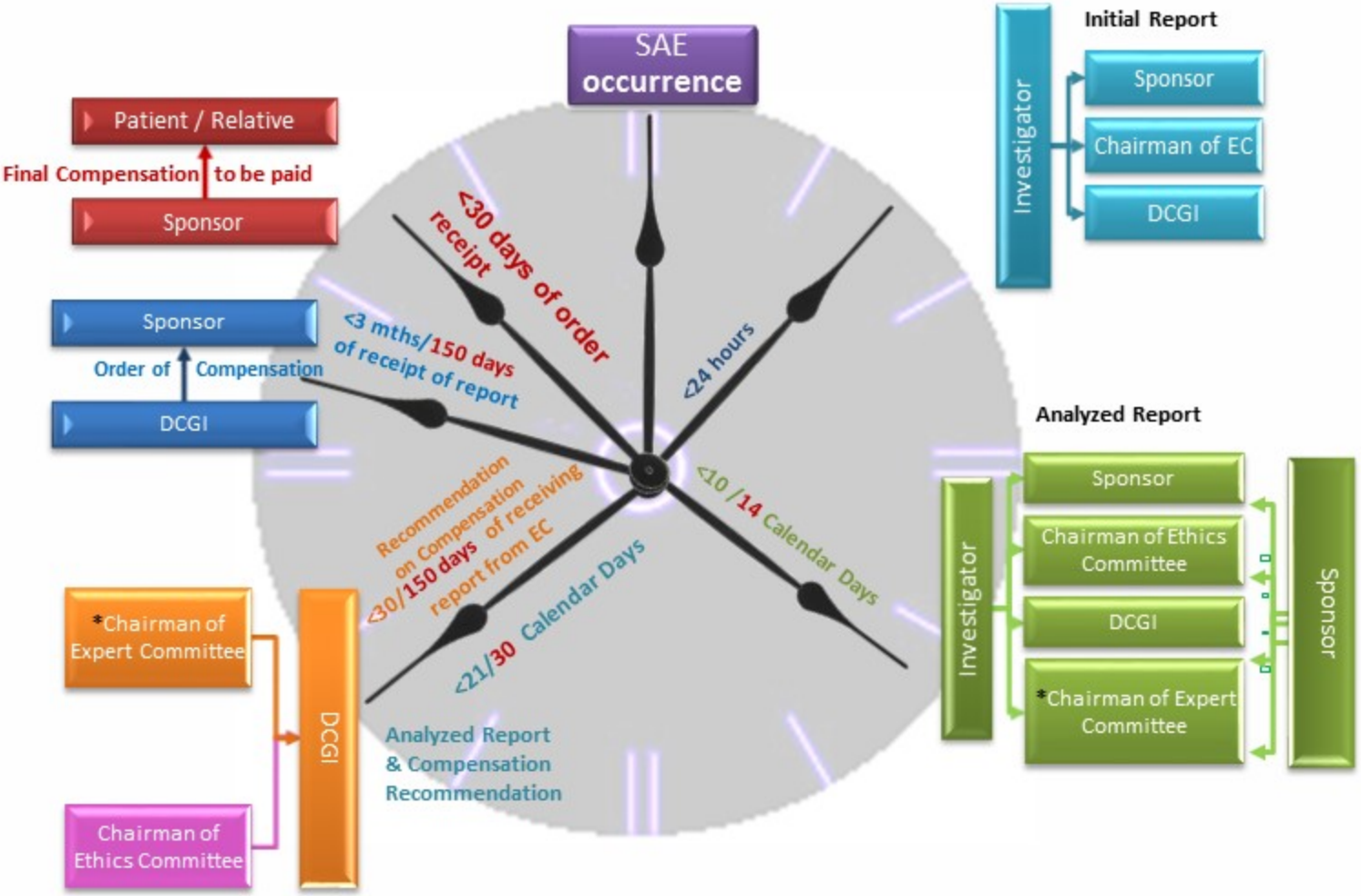

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Fatal SAE

- In the case of clinical trial related death of the subject, his/her nominee(s) would be entitled for financial compensation will be over and above any expenses incurred on the medical management of such subject

- The expenses on medical management and financial compensation in the case of clinical trial injury or death of the trial subject shall be borne by the sponsor of the clinical trial

Related SAE

- Adverse effects due to concomitant medication excluding standard care, necessitated as part of approved protocol
- For injury to a child in-utero because of the participation of parent in clinical trial
- Any clinical trial procedures involved in the study

Undertaking

- The Sponsor, whether a pharmaceutical company or an institution shall give an undertaking along with the application for clinical trial permission to the Licensing Authority defined in clause (b) of Rule 21, to provide compensation in the case of clinical trial related injury or death for which subjects are entitled to compensation

Failure to Pay

- In case the Sponsor fails to provide medical management for the injury and / or financial compensation to the trial subject/nominee for clinical trial related injury/death the Licensing Authority may after giving an opportunity to show cause, suspend or cancel the clinical trial and/ or restrict Sponsor including his representative(s) to conduct any further clinical trials in the country or take any other action deemed fit under the rules

Timelines

- PI to EC & Sponsor: 24 hours
- EC to DCGI: 30 days
- DCGI to sponsor: 4 months
- Sponsor to subject: 30 days

References

- http://eclinical.mednetstudy.com/blog/investigator-meetings-an-important-contributor-to-team-engagement
- https://www.iqvia.com/-/media/library/media-coverage/key-to-successfull-start-up-2020pharma.pdf
- https://www.nidcr.nih.gov/sites/default/files/2017-12/guideline-study-startup-em-studies.docx