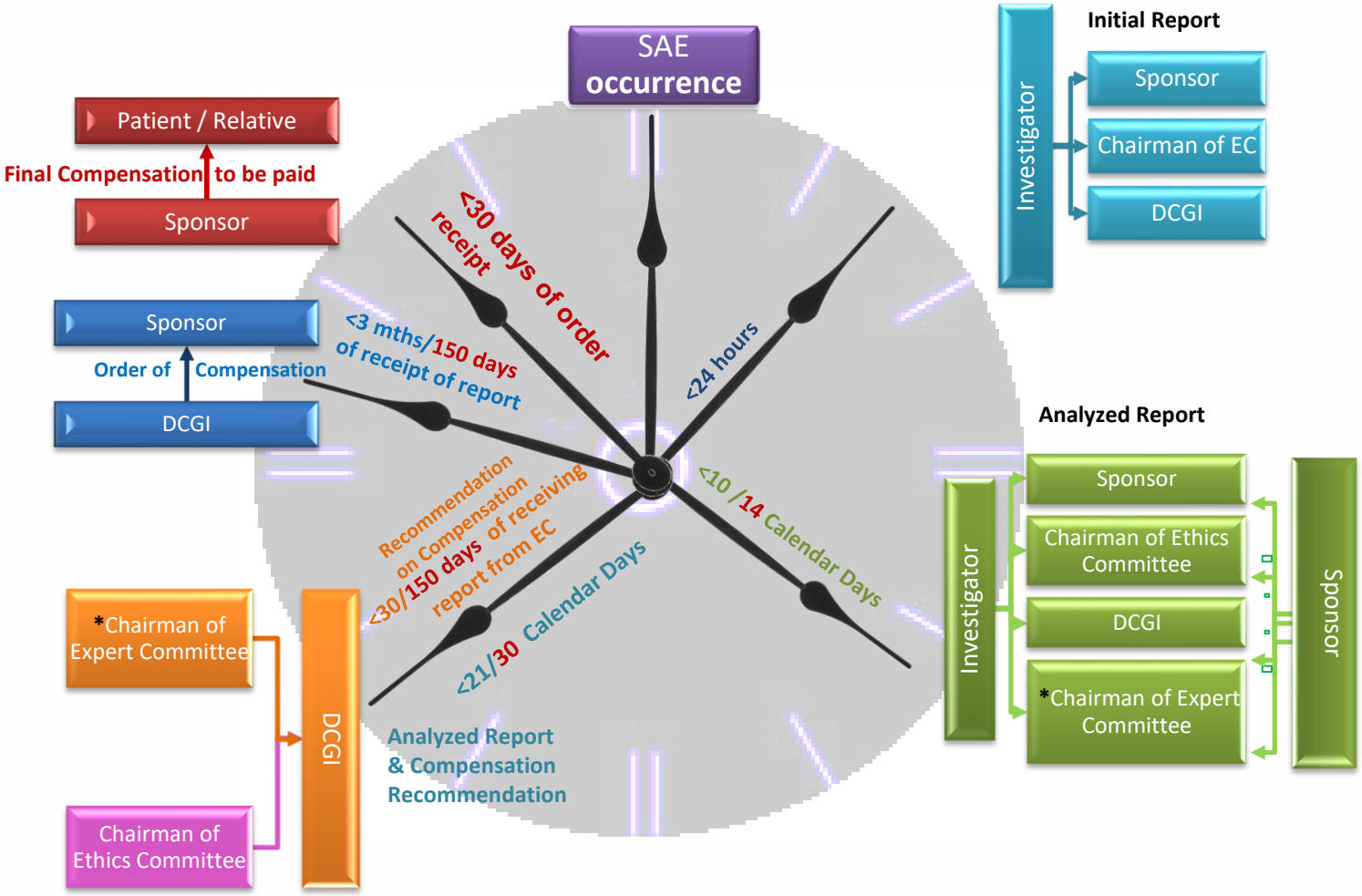
Clinical Trial Initiation and Site Start up

AE Reporting

Module 6 Topic 1_5

New SAE Reporting Process



* In case of Death

Definitions

Adverse Event (AE)

- Any untoward medical occurrence in a patient or clinical trial subject administered a medicinal product and which does not necessarily have a causal relationship with this treatment

- *Comment:* An adverse event can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of an investigational medicinal product, whether or not considered related to the investigational medicinal product.

Definitions

Adverse Reaction (AR)

- Any untoward and unintended responses to an investigational medicinal product **related** to any dose administered
- *Comment:* All adverse events judged by either the reporting investigator or the sponsor as having a reasonable causal relationship to a medicinal product qualify as adverse reactions. The expression “reasonable causal relationship” means to convey in general that there is evidence or argument to suggest a causal relationship.

Definitions

Unexpected Adverse Reaction (UAR)

- An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g. investigator's brochure for an unauthorised investigational product or summary of product characteristics for an authorised product)
- *Comment:* When the outcome of the adverse reaction is not consistent with the applicable product information this adverse reaction should be considered as unexpected.

Definition of Seriousness

Serious Adverse Event (SAE) or Serious Adverse Reaction (SAR) or Suspected Unexpected Serious Adverse Reaction (SUSAR)

Any AE, AR or UAR that at any dose:

- results in death
- is life-threatening*
- requires hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability or incapacity
- consists of a congenital anomaly or birth defect

Definition of Seriousness

- Medical judgement should be exercised in deciding whether an adverse event/ reaction is serious in other situations. Important adverse events/ reactions that are not immediately life-threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, should also be considered serious.

- Life-threatening in the definition of a serious adverse event or serious adverse reaction refers to an event in which the subject was at risk of death at the time of event. It does not refer to an event which hypothetically might have caused death if it were more severe.

Risk Assessment – type of events being collected

- Due to the risk associated with the clinical trial and the nature of the study it was concluded that is it appropriate to reasonable to just collect SAE's

- The proposed safety recording, notification and reporting procedures is detailed in the trial protocol and safety reporting SOP

Assessment

- Assessment of an adverse event covers three main areas:
  - Assessment of Seriousness
  - Assessment of Causality
  - Assessment of Expectedness

Assessment of Seriousness

- *results in death*
- *is life-threatening*
- *requires hospitalization or prolongation of existing hospitalization*
- *results in persistent or significant disability or incapacity*
- *consists of a congenital anomaly or birth defect*

Note: The term "severe" is often used to describe the intensity (clinical severity) of a specific event. This is not the same as "serious," which is a regulatory definition based on patient/event outcome or action criteria. For example, a headache may be severe but not serious while a minor stroke may be serious but not severe.

Assessment of Expectedness

- The evaluation of expectedness is based on knowledge of the adverse reaction and any relevant product information.

- What might we expect to see?
  - very little it is very safe
  - AE's reported have been…..

Adverse Events: Sponsor Responsibilities

- The Regulations require the sponsor to keep detailed records of all adverse events relating to a clinical trial of which they have been notified by investigators in that trial. The sponsor may be required to submit these records to the licensing authorities on request.

- Responsibility for reporting to the relevant competent authorities and to the Ethics committee rests with the Sponsor (or the entity to whom this responsibility has been delegated).

- The agreed responsibilities for each trial should be documented in the protocol and also in the SOPs for the trial.

Expedited Reporting

- The Regulations set time limits for expedited reporting:

Fatal or life threatening SUSARs:

- Not later than **7 calendar days** after the sponsor has information that the case reported fulfils the criteria for a fatal or life-threatening SUSAR, with any follow up information to be reported within a **further 8 calendar days**.

All other SUSARs:

- Not later than **15 calendar days** after the sponsor has information that the case fulfilled the criteria for a SUSAR.

Expedited Reporting

- As well as SUSARs the following safety issues require expedited reporting:

1. Single case reports of an expected serious adverse reaction with an unexpected outcome (e.g.: a fatal outcome)
2. An increase in the rate of occurrence of an expected serious adverse reaction, which is judged to be clinically important
3. Post-study SUSARs that occur after the patient has completed a clinical trial and are notified by the investigator to the sponsor should be reported to the manufacturer indefinitely.