Federal Institute for Drugs and Medical Devices

LÆGEMIDDELSTYRELSEN
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# Day 2, Session 2: Safety Management

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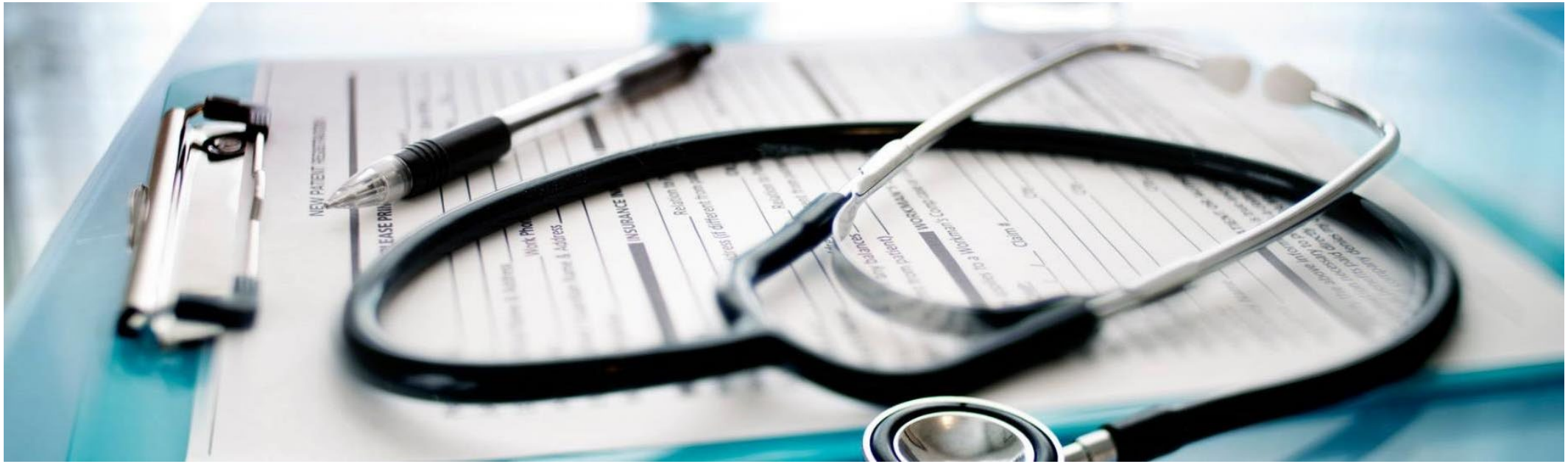

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# Safety Management
## Outline

Relevant changes

- Principles section
- Investigator section
- Sponsor section
- Glossary

# Safety Management
## Principle 1

**REVISED PRINCIPLE 1**

1.1 The rights, safety and well-being of the participants are the most important considerations and should prevail over interests of science and society.

1.2 The **safety of the participants should be reviewed in a timely manner as new safety information becomes available**, which could have an impact on participant safety, their willingness to continue in the trial or the conduct of the trial.

1.3 […]

# Safety Management
## Investigator (1)

**SECTION 2.7 PARTICIPANT MEDICAL CARE AND SAFETY REPORTING (1)**

- New subsection 2.7.2 Safety Reporting includes under
  - (a) a reference to reporting requirements **for unfavourable medical events occurring in participants before investigational product administration** (e.g., during screening) if required by the protocol
  - (b) and explanation for the term "immediate" in relation to SAE reporting by the investigator: "[…] **immediately (after the investigator reasonably becomes aware of the event)** […] ."
  - (c) a reference to the required **causality assessment** in the reports on **serious adverse events** to the sponsor
  - (d) the addition of the **authority as a possible addressee** of requested additional **information on reported deaths** of trial participants, depending on the regulatory requirements

# Safety Management
## Investigator (2)

**SECTION 2.7 PARTICIPANT MEDICAL CARE AND SAFETY REPORTING (2)**

- New subsection 2.12.3

  The investigator should be provided with timely access to data by the sponsor (see section 3.16.1(k)) and be **responsible for the timely review of data, including relevant data from external sources that can have an impact on, for example, participant eligibility, treatment or safety** (e.g., central laboratory data, centrally read imaging data, other institution's records and, if appropriate, electronic patient-reported outcome (ePRO) data). The protocol may provide exceptions for access, for instance, to protect blinding.

# Safety Management
# Sponsor (1)

**SECTION 3.13 Safety Assessment and Reporting (1)**

- New subsection 3.13.1 Sponsor Review of Safety Information
  - Reference to the sponsor responsibilities for **timely review of all relevant safety information**, after **prior aggregation where appropriate**, which may result in updating the protocol, investigator's brochure, informed consent documents and related documents.
  - Statement that the purpose is to **assess whether there is any new data that may affect** the participant's willingness to continue in the trial, impact the conduct of the trial, or alter the approval/favourable opinion of the IRB/IEC and/or regulatory authority(ies), as applicable.
  - Indication that any information of this should be **communicated** to the participants, investigator, IRB/IEC and regulatory authorities, as applicable, **in a timely manner**.

# Safety Management
## Sponsor (2)

**SECTION 3.13 Safety Assessment and Reporting (2)**

- New subsection 3.13.2 Safety Reporting includes under
  - (c) a reference to the required **assessment of "expectedness" of any (S)AEs** on the basis of applicable reference safety information (RSI)
  - (d) a statement that **the reporting of SUSARs to investigator(s)/institutions(s) and to the IRB(s)/IEC(s)** should be undertaken in a manner that reflects the urgency of action required, taking into consideration the evolving knowledge of the safety profile of the product **in accordance with applicable regulatory requirements** and that **in some regions, periodic reporting of line listings** with an overall safety assessment may be appropriate.
  - (e) a clarification that **urgent safety issues** requiring immediate attention or action should be reported to the IRB/IEC and/or regulatory authority(ies) and investigators without undue delay and in accordance with applicable regulatory requirements.

# Safety Management
## Sponsor (3)

**SECTION 3.13 Safety Assessment and Reporting (3)**

- New subsection 3.13.2 Safety Reporting includes under
  - (f) a reference to **alternative arrangements for safety reporting to regulatory authorities, IRBs/IECs and investigators and for reporting by investigators to the sponsor** in line with **ICH E19** *A Selective Approach to Safety Data Collection in Specific Late-Stage Pre-Approval or Post-Approval Clinical Trials.*

- New subsection 3.9.7, stating that the **sponsor may consider establishing an IDMC** to assess the progress of a clinical trial, including the safety data and the efficacy endpoints, at intervals and to recommend to the sponsor whether to continue, modify or stop a trial.

# Safety Management
## Sponsor (4)

**SECTION 3.16 Data and Reords**

- New subsection 3.16.1 Data Handling includes under
  - (k) a reference that the sponsor should **ensure that the investigator has timely access to data** collected in accordance with the protocol during the course of the trial, **including relevant data from external sources (e.g., central laboratory data, centrally read imaging data and, if appropriate, ePRO data)**. This enables the investigators to make decisions (e.g., on eligibility, treatment, continuing participation in the trial and **care for the safety of the individual trial participants.** (see section 2.12.3).

# Safety Management
## Glossary Terms (1)

**Adverse Drug Reaction (ADR)**

Further clarifications regarding the concept of a causal relationship between a medicinal product and an adverse event:

- *The level of certainty about the relatedness of the adverse drug reaction to an investigational product will vary.*
- *If the ADR is suspected to be medicinal product-related with a high level of certainty, it should be included in the reference safety information (RSI) and/or the Investigator's Brochure (IB).*

# Safety Management
## Glossary Terms (2)

**Serious Adverse Event (SAE)**

Extension of definition:

*An **important medical event** that may not be immediately life-threatening or result in death or hospitalisation, that may jeopardise the participant or that may require intervention to prevent serious outcomes (see ICH E2A and E19) should generally be considered as serious.*

# Safety Management
## Glossary Terms (3)

**Suspected Unexpected Serious Adverse Reaction (SUSAR) as new Glossary term**

*An adverse reaction that meets three criteria: suspected, unexpected and serious.*

- *Suspected: There is a reasonable possibility that the drug caused the adverse drug reaction.*
- *Unexpected: An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator's Brochure or alternative documents according to applicable regulatory requirements; see RSI).*
- *Serious: See above for SAE.*

# Thank you very much for your attention!

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