DSM

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Definition of a DSMB

'An independent data monitoring committee that may be established by the sponsor to assess at intervals the progress of a clinical trial, the safety data, and as the critical efficacy endpoints, and to recommend to the sponsor whether to continue, modify, or stop a trial'

ICH GCP E6 (1.25)

The purpose of DSMB

To provide independent advice to the sponsor on the development of the study and ongoing scientific and ethical validity of the study

The Need for a DSMB

- Randomized control (double blinded) trials specifically focused on clinical efficacy and safety of new intervention
- Studies where *interim analyses* of safety and efficacy are essential to ensure the safety of trial participants.
- Early phases of novel intervention with very limited information on clinical safety

The place of a DSMB

- DSMB constituted and functioning under the authority of the sponsor
- A DSMB is an independent advisory body responsible for assessment of data during the conduct of the study in a manner that contributes to the ongoing scientific and ethical integrity of the study.

The Role of a DSMB

- To review, evaluate and provide advice, at regular intervals, on (usually un-blinded) data collected during study with regard to clinical safety and efficacy outcomes

Constituting a DSMB

- When required by nature of a study
- When requested by the IEC

Sponsor should establish a DSMB to ensure the broadest possible coverage of protection for potential research participants, and to ensure the integrity and validity of the scientific result that is obtained

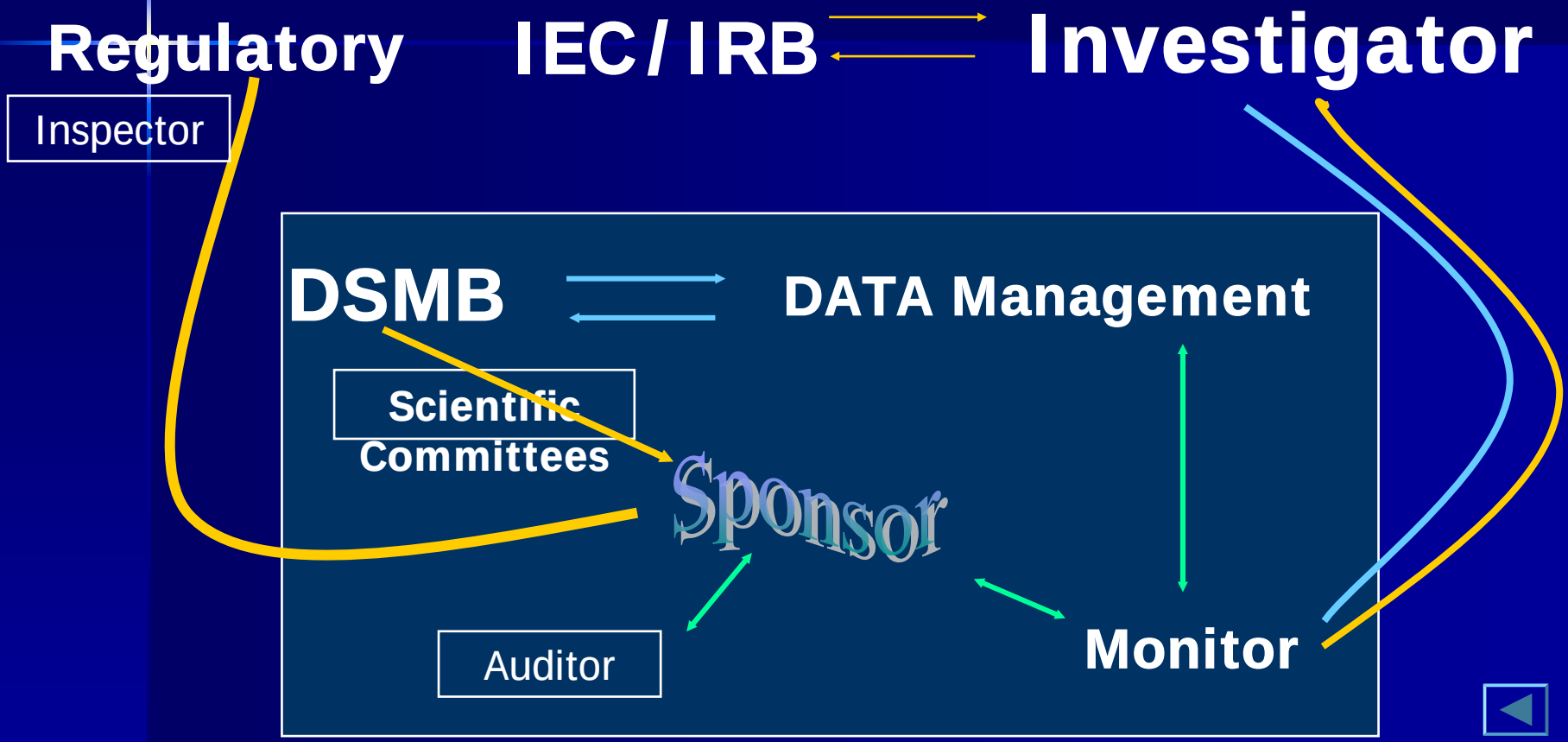
Constituting a DSMB

- The sponsor is responsible for establishing the DSMB Charter, which should be included in (or referred to by) the study protocol. This may be undertaken with advice from the investigator(s) or other parties involved in the study.
- The sponsor is responsible for the selection and appointment of DSMB members as well as ensuring that the DSMB has the means and resources to function well.

DSMB Charter

- Scope of DSMB
- Responsibilities of the DSMB
- Organization of DSMB
- Membership of DSMB/Quorum requirement
- Data that will be reviewed by the DSMB and statistical plan
- Intervals at which the DSMB will review
- The materials to be forwarded to the DSMB
- The process and format of the meeting
- The procedures for maintaining study integrity & confidentiality
- The format and content of DSMB reports
- Procedure for the distribution of report
- Procedure for record keeping and archiving.
- The procedure for amending the DSMB charter
- the procedure for auditing and/or inspection of the DSMB

Organization Flow Chart



Operation of DSMB

- Selection and appointment of DSMB members
  - Procedure for selecting/appointing members
  - Procedure for identifying conflicts of interest
- Terms of Appointment
- Condition of appointment
- Education for DSMB members
- Procedures to define the offices for the good function of DSMB
- Independent Consultants
- Procedure for reporting and addressing potential conflict of interest
- Staff – to support the DSMB's work

Operation of DSMB

- Quorum requirement
- Meeting requirements
- Meeting procedures
- Format of meetings
- DSMB review of the sponsor's report
- Arriving at recommendations
- DSMB recommendation(s) distribution

Operation of DSMB

- Minutes of the DSMB meeting
  - Minutes of Open session
  - Minutes of Closed session
- Communicating the DSMB recommendation
- Documentation and achieving

DSMB Fundamentals

- Has **GLOBAL** overview, whereas IECs / IRBs only have local overview
- Knowledgeable, **independent** group of experts
  - Often including a bio-statistician, medical experts and a bio-ethical expert
- Will assess:
  - Efficacy, safety and trial design questions / issues

DSMB Fundamentals – *cont'd*

- Part of the overall **RISK MANAGEMENT** program for a product during development
- Contribute to the integrity of the trial(s) and protection of patients' well being
- May see unblinded data, so must ensure independency from the trial
- Ensure that regular data reviews are taking place

When to Use DSMB

- Length of trial

(long term data can show a different efficacy / safety profile)

- Number of patients enrolled globally
- Vulnerable populations
  (paediatrics, elderly, pregnant, etc.)
- Life–threatening diseases
- If previous data in another indication presented issues
- Double blind randomised control trial

The Protocol:

"A group of independent experts will form an independent DSMB. The committee will be responsible for monitoring on an approximately semi-annual basis the safety data of the clinical trial and the safety of the patients. The drug safety committee will provide recommendations on the progress of the trial and the safety of the patients after each meeting. This review will continue until the last patient has finished treatment.

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DSMB – who are they?

The DSMB will consist of **independent experts** not involved in the trial, including **statistician**, **Clinician, Clinical pharmacologist** and an **expert in clinical research ethics**.

Representatives from the sponsor may participate in the open session of DSMB meetings as non-voting members in order to discuss any question that might arise;

But representatives from the sponsor will **not** be allowed to participate at the closed DSMB sessions and may **not** review and discuss the data provided to DSMB.

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Examples:

- Double Blind Randomised placebo Control Trial of antibiotics in Chronic Bronchitis
- Comparative, randomised Clinical trial of antimalarials in multidrug resistant malaria, a 2-year study

The report

Sponsor provides report to DSMB

- summary tables on demographic data
- adverse events, serious adverse events
- laboratory abnormalities, shifts in laboratory values,
- Clinical response
- withdrawals from study medication and deaths by treatment arm.

The independent DSMB will review

- safety listings
- DSMB will meet after x days after the initiation of the study and review the safety of patients in both arms
- Recommendation to sponsor

What could happen?

- Reviews by the DSMB may lead to protocol amendment – introduction of additional safety parameters, etc.
- **Stop or suspension of the trial**
- All IECs / IRBs should be informed

- Any question???