SCOPE

This procedure applies to any study that justifies the set-up of a DSMB.

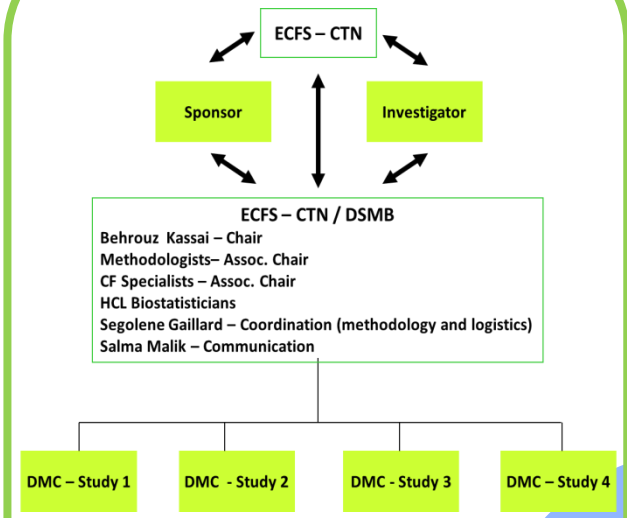
When is a DSMB usually needed?

1. New product
2. Product with an unknown safety profile
3. Long-term/longitudinal studies
4. Studies with a large sample size
5. The kind of population enrolled in a clinical trial might be an argument for setting up a DSMB :
   - ○Population at risk for whom the risk or the occurrence of major morbidity or mortality are the main criterion of evaluation
   - ○Pediatric studies, even for non-critical indication. In this case, a DSMB might be useful considering that children are not able to express themselves in the same way as adults do and in order to detect any potential harm to the patient as soon as possible
   - ○Intellectually-disabled patients.

…etc…

At implementation of a clinical trial the sponsor should consider the need for a DSMB

Give instructions to sponsors on how to apply to the ECFS-CTN for the constitution of a DSMB
Define the composition, the role and the Functioning of a DSMB in a study



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STANDARD OPERATING PROCEDURE

ECFS-CTN DSMB

Constitution and Management of an Independent Data Safety Monitoring Board through the European Cystic Fibrosis Society – Clinical Trial Network

ECFS - CTN / DSMB
CIC - EPICIME LYON

epicime

ripps

ecfs ctn Clinical Trials Network

Hospices Civils de Lyon

DSMB ROLE

The role of the DSMB is to:

○Evaluate the safety and the relative efficacy of the study treatment during the course of the study

○Ensure and control the global quality of the study conduct

○Submit recommendations to the sponsor or the scientific committee of the study

DSMB RECOMMENDATIONS

The DSMB may recommend termination of the trial in the following situations

○Occurrence of unanticipated adverse events which may pose a serious risk for participating patients

○Demonstration of efficacy before the planned accrual

○Because of « futility » (the most difficult situation), i.e. in absence of a reasonable probability that the trial may reach a conclusion within its planned frame

DSMB COMPOSITION

The DSMB is an independent multidisciplinary group consisting of at least three to five members:

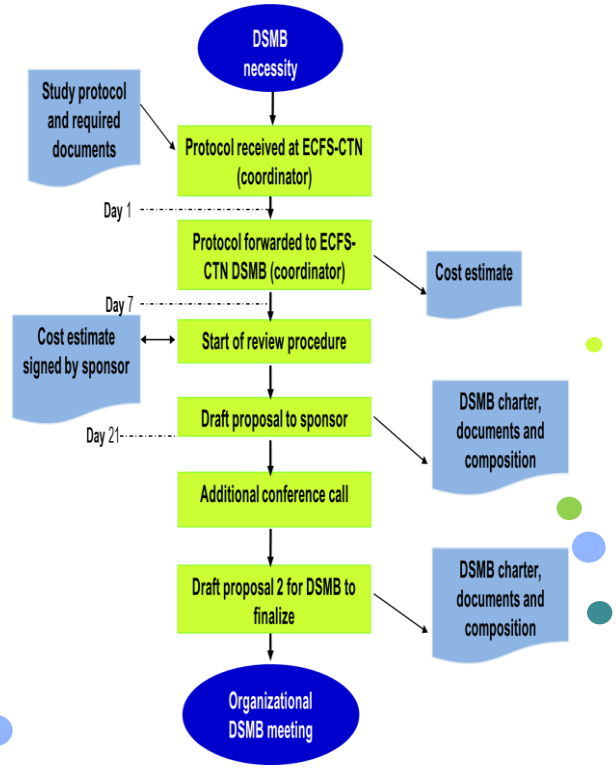
○At least one qualified physician specialized in the specific disease area being studied to assess the clinical aspects of safety and/ or efficacy monitoring

○A pharmacologist expert in clinical research methodology

○If ethical issues are raised (especially in safety monitoring), one member could be chosen for his expertise in ethics

○An independent statistician: As statistical methods are applied in the monitoring process, biostatistician expertise should also form part of a DSMB. The statistician prepares the analyses required by the committee. He should be present during the DSMB meeting but shall not participate in the vote

Steps for submission of protocols to the ECFS-CTN DSMB



REQUIRED DOCUMENTS

1. Study protocol, current version, not yet approved by Institutional Review Board and Health Authorities
2. Informed consent forms (English).
3. Data and Safety Monitoring Plan including the following elements:

- The content and frequency of planned interim reports
- The planned statistical methods, interim stopping rules, as appropriate, and rules that would trigger immediate DSMB review of safety outcomes

4. Draft versions of the Case Report Form (CRFs) and Data Management Plan

TIMELINES

- **First contact:** Signature of Confidentiality Disclosure Agreement (CDA) as required by the sponsor or PI
- **Day -7**: Study protocol and required documents received at ECFS-CTN DSMB
- **Day -2:** Estimation of costs by ECFS-CTN DSMB and draft proposal provided to sponsor or PI
- **Day 0:** At signature of estimate signed by the sponsor: **Start of review procedure**
- **Day 21:** Proposal to the sponsor or PI including:
  - DSMB charter draft
  - Name of DSMB members
  - DSMB draft documents
- **Conference call:** Proposed to the sponsor to answer questions and subsequent issues raised by the proposal
- **The organizational meeting of the study DSMB:** At the end of the process, organizational meeting of the study DSMB can be scheduled and organized by the ECFS-CTN DSMB.