

TERMS OF REFERENCE

Data Safety and Monitoring Board (DSMB)

Purpose of the DSMB

An independent and multidisciplinary group established to provide oversight of investigator initiated clinical trials (IICTs) of which Macquarie University is a sponsor. This includes clinical trials which include non-pharmacological, behavioural and lifestyle interventions.

The DSMB will review, at intervals, accumulating clinical trial data, in order to monitor the progress of the trial and to make recommendations on whether to continue, modify or stop the trial for safety or ethical reasons.

The duration of the function of individual DSMBs should be stated in the protocol and could vary from study to study depending on the requirements and key time points in the study.

1. Responsibilities:

- 1.1 Provide independent, sound, and timely review of IICTs data.
- 1.2 Advise investigators on whether to continue, modify or stop the clinical trial for safety or ethical reasons.
- 1.2 Safeguard the interests of the study participants.
- 1.3 Oversee the timely analysis, review, and publication of the main IICTs results.
- 1.4 Ensure ongoing scientific validity, integrity, and clinical and scientific relevance of the study.

2. Composition of the DSMB

2.1. The composition of Data Safety Monitoring Board will comprise of the following core members:

- Independent biostatistician.
- Medically qualified person(s) with scientific expertise in the clinical aspects of the disease/patient population being studied.
- Pharmacologist or pharmacist.
- Member/s with practical experience and expertise in current clinical trial conduct and methodology.

2.1.1. Independence of the DSMB

- Members of the DSMB must be independent to the study.
- Members should have no financial or other connections that could influence (or be perceived to influence) their objectivity in evaluating the study data.
- Members should have no vested interest in the outcome of the trial and are therefore free from material conflicts of interest.

If there are conflicts of interest and these are minor, they must be disclosed and managed.

2.2. Support structure:

- Executive officer or Secretariat (a non-voting member).

3. Appointment of DSMB Members and Terms of Appointment

3.1. Members of the DSMB shall be appointed in consultation with the MQ Health Clinical Research Executive and other MQ Institutional officers, as deemed appropriate.

- 3.1.1. For each individual IICT, a separate DSMB will be established upon determination by the Clinical Research Executive.
- 3.1.2. The terms of appointment of the DSMB will be for the length of the project.
- 3.2. Upon appointment members of DSMB will be required to provide an up-to-date CV and sign a statement undertaking:
 - That all matters that he/she becomes aware of during the course of their membership will be kept confidential.
 - That any conflict of interest which exists or arises during the members tenure will be declared.
- 3.3. Members of the DSMB should be suitably trained and inducted into their roles.
- 3.4. Members should be able to balance necessary expertise with conflict of interest requirements.

4. Meetings

- 4.1 Meetings will be held in person or via video conference when deemed necessary.
- 4.2 A quorum shall exist for each research study under review when at least three members have provided input.

5. Procedures

- 5.1 The DSMB will review the trial data and advise investigators on whether to continue, modify or stop the clinical trial for safety or ethical reasons.
- 5.2 Identify through the review any serious emerging safety concerns, to minimise the time that participants may be placed at excess risk. By reviewing of interim, unblinded, comparative data to develop a clear picture of the emerging balance of risks and benefits.
- 5.3 Following interim analysis, the DSMB should recommend continuation, modification or stopping the trial based on the predetermined stopping rules.
- 5.4 Maintain confidentiality of unblinded interim results and provide an objective and unbiased assessment of those results.
- 5.5 Contribute to the successful completion of a trial by periodically reviewing accumulating trial data, to inform trial conduct decisions. By reviewing:
 - Recruitment rates and
 - Protocol compliance
 - Identify problems and recommend to the MQ Health Clinical Research Executive any relevant actions.

6 Definitions:

Clinical trial as per the *ICG GCP* definition is: Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy. The terms clinical trial and clinical study are considered synonymous.

Data Safety Monitoring Board (DSMB) - An independent and multidisciplinary group established by the trial sponsor to review, at intervals, accumulating trial data, in order to monitor the progress of a trial and to make recommendations on whether to continue, modify or stop the trial for safety or ethical reasons.

Investigator Initiated Clinical Trial (IICT) has the following characteristics:

- An investigator initiates and organises the trial, he or she may be defined as the sponsor of the trial and will be responsible for the sponsor's functions or the investigator's institution (e.g. hospital, research institute or university) is defined as the sponsor with the same functions;
- The principal investigator or the Hospital/Institution is the primary author and custodian of the clinical trial protocol.
- A pharmaceutical/device company is not acting as the sponsor for the purposes of the CTN application.
- The clinical trial addresses relevant clinical questions and not industry needs.
- Another party (usually a pharmaceutical or medical device company) provides the medicinal product or device used in the clinical trial, but has no other involvement in the conduct of the trial.

(References: Australian Clinical Trials website: <https://www.australianclinicaltrials.gov.au/industry-and-sponsors/sponsorship>) and Melbourne Health SOP No.011)

Adverse Event - Any untoward medical occurrence in a patient or clinical trial participant administered a medicinal product and that does not necessarily have a causal relationship with this treatment. (Ref: *Safety monitoring and reporting in clinical trials involving therapeutic goods, NHMRC, 2016*)

Clinical Research Executive (CRE) is a delegate of the MQ Health Executive group and includes membership from the following areas: clinical medicine, clinical trials, academic, nursing, clinical and research governance, research practice and management.

Sponsor - An individual, organisation or group taking on responsibility for securing the arrangements to initiate, manage and finance a study.

Serious Adverse Event - Any untoward medical occurrence that at any dose:

- results in death,
- is life-threatening,
- requires inpatient hospitalization or prolongation of existing hospitalization,
- results in persistent or significant disability/incapacity,

Or is a congenital anomaly/birth defect.