MRC Short Guide: Trial Steering Committees (TSCs)

When is a study a Clinical Trial?

Clinical trials are studies evaluating the impact of interventions on human participants which meet the broad definition of a clinical trial used by the World Health Organization (WHO):

"any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes."

Interventions assessed in trials may include drugs or medicines, cells and other biological products, surgical procedures, radiological procedures, devices, behavioural treatments, changes to the care pathway, preventive care, or other treatments. Pilot and feasibility studies, or developmental clinical studies, which meet the above definition are also clinical trials.

Purpose of the TSC

Trials should have a Trial Steering Committee (TSC) to provide independence in oversight for the trial. It is part of the trial governance arrangements and provides assurance to the funder and Sponsor.

The standard arrangements for a TSC are described below and in the *MRC Guidance for Management of Global Health Trials*.

The MRC guidance on TSC membership and management should be followed for all trials funded or part-funded by the MRC, however the size, membership and frequency of meetings should also be proportionate to the risks of the trial.

Role and responsibilities of the TSC

The TSC has the following responsibilities:

- Ensuring scientific integrity
- **Assessing progress** of the trial against the timeline agreed with the Sponsor and funder
- **Assessing adherence** to the trial protocol and analysis plan
- **Assessing whether** drug trials are being conducted to the principles set out in the **ICH guidelines for Good Clinical Practice** (GCP)
- **Assessing patient safety -** considering recommendations from the Independent Data Monitoring Committee (IDMC)
- **Providing advice on major decisions** such as continuing or terminating the trial
- **Assessing whether action is needed in response to any new external information** that arises during the trial and potential impacts on the trial conduct and continued validity
- **Ensuring dissemination of results** – ensuring reporting by the trial team is transparent and timely, including reviewing any paper submitted for publication

- **Assume the role of a Data Access Committee** considering data re-use requests, where this is not covered by another dedicated committee
- **Overseeing the complaints procedure and compensation** for participants, should this be required
- **Advising the Trial Management Group** (TMG) on all aspects of the trial.

Membership of the TSC

As a group, TSC members should have the scientific, medical and clinical trial management experience to conduct and evaluate the trial.

At least 50% of TSC members, including the Chair, must be independent. Independent members are individuals who:

- are not involved directly in the trial
- are not employed by the trial Sponsor
- are not employed by the employing organisation of any of the trial investigators (unless this cannot be avoided)
- do not have any relationship with the trial investigators, funder(s) or Sponsor that might be perceived as allowing them to be influenced by these bodies.

The TSC membership should include:

- an independent Chair
- at least two additional independent members whose scientific, medical and methodological expertise is appropriate to the trial
- lay/public involvement representative(s)[1]
- the Chief Investigator
- one or two senior staff in the trial team (e.g. Co-Investigators/Principal Investigators, trial statistician, trials unit lead)

and

- *if appropriate:* Policy stakeholders from the Ministry/Department of Health in the proposed setting
- *if appropriate:* Members of relevant stakeholder groups, e.g. local NGOs operating in the field, representatives from user or community groups, other funders
- *for a trial involving more than one country and/or international collaborators:* Independent membership should be international (i.e. not all from a single country)
- *for a trial in a low income country:* One member should be an independent expert with experience of conducting trials in low income settings

[1] Lay representatives may not be appropriate to every trial but their involvement should always be considered.

The TSC meeting should also include:

- representatives of the Sponsor, host institution and/or funding organisation (who will usually be observers but may be full members)
- additional expert observers as required (e.g. trial manager).

Responsibilities of the TSC Chair

- To facilitate and summarise discussions, achieving consensus when possible
- To report to the Funder and Sponsor
- To ensure the patient or participant voice is taken into account
- To determine whether an unscheduled meeting should be held, when major issues are raised by the TMG or IDMC

TSC Meetings

The following meetings of the TSC should take place:

Meeting 1 (Before the start of the trial): This should be organised by the Chief Investigator (or co-ordinating trials unit) to approve the final protocol. Ideally this meeting should take place prior to Ethics Committee review. This may be an open meeting jointly with the iDMC.

Regular meetings (During the trial): These should take place **at least once per year**. More frequent meetings may be requested by the Chair of the TSC or the Chief Investigator and organised by the trial team. The frequency of the meetings is usually determined in relation to the trial risk assessment. More regular meetings are typically required during key stages of the trial such as trial set up. Additional meetings may be held at appropriate timepoints relating to the data collection or in response to critical milestones. Frequency of the meetings should be agreed between the Chief Investigator and TSC Chair.

Meeting papers should be circulated by the trial team well in advance of the meeting.

An accurate minute of the meeting should be prepared by the Chief Investigator (or their delegate) and agreed by all members, including the sponsor and funder representatives.

No unblinded information should be presented to the TSC, unless recommended by the independent Data Monitoring Committee (DMC). If the DMC recommends the TSC be unblinded to the accumulating comparative data, the independent members should initially review the information to protect the trial team from viewing unblinded data. If the independent members agree, then the non-independent members (or other attendees) can be shown the information.

Ensuring TSC arrangements are proportionate to the risk of the trial

Trial oversight arrangements should be proportionate to the risk of the trial.

When a trial is considered lower risk[2], then it may be appropriate to

- have a TSC with fewer members, or

[2] The Chief Investigator/Trial Management Group should agree with the Sponsor and funder whether a trial is lower risk.

- for the TSC to meet less frequently (but not less than once per year).

However, **the Chair and at least 50% of TSC members must be independent** and, if a funder representative does not attend every meeting, the funder should receive regular reports of each TSC meeting. TSC membership should be sufficient to cover all areas of expertise that are required.

Defining a trial as lower risk

To assess whether a trial is lower risk, a risk assessment should be undertaken. Consideration should be given to the intervention, safety implications, size and complexity of the trial. A trial can only be considered lower risk if:

- the intervention is low risk; examples might include a medicine used in regular clinical practice, a lifestyle or behavioural intervention, or a public health or health systems intervention
- the participant population are not considered to be a vulnerable group. Vulnerable groups include children, prisoners, individuals at risk of domestic or sexual violence, individuals who have lost capacity, individuals with mental health problems
- there is no expectation of disclosure of sensitive data
- the TMG are experienced in trial management
- the risk status is expected to remain at this level.

A pilot study or study with a small sample size should not be considered lower risk unless it also has the other features of a lower risk trial.

- If a trial is defined as lower risk, then the Trial Management Group (comprising the Chief Investigator and others who manage the trial day-to-day) and TSC Chair should propose a membership, meeting frequency and reporting arrangements (including to the funder), proportionate to the risk.

- The Chief Investigator, funder (MRC), Sponsor and independent TSC Chair must agree these arrangements before the first meeting of the TSC. If there is any disagreement or doubt about the trial being low risk, then it should not be defined a low risk trial.

- An annual meeting of the TSC may be adequate for monitoring some low risk trials, however TSC meeting frequency should always be appropriate to the needs of the trial. An accurate minute of all meetings should be prepared by the Chief Investigator (or their delegate) and agreed by all members. If it is agreed that funder and sponsor representatives will not attend, they must be provided with a written report (or minute) of each TSC meeting. This may be in the form of an annual report.

- 'Umbrella' TSCs (i.e. covering multiple trials) are an efficient use of membership and can also work well for low risk trials.

Further Resources

JA Lane, C Gamble, WJ Cragg, D Tembo, MR Sydes. A third trial oversight committee: Functions, benefits and issues. *Clinical Trials* 2020;17():106-112. https://doi.org/10.1177/1740774519881619

A template for a TSC Charter developed by MRC Clinical Trials Unit at University College London: https://www.ctu.mrc.ac.uk/our-research/other-research-policy/regulatory-information-toolkits-templates/

TSC membership for lower risk trials

Minimum requirements for TSC membership are:

- an independent Chair
- at least one additional independent member
- the Chief Investigator.

Additional members should be included in the TSC as required for the individual trial and following the membership recommendations for higher risk trials above. Involving a lay or patient representative should always be considered.

At least 50% of TSC members must be independent.

If it is agreed that funder and sponsor representatives will not attend, they must be provided with a written report or minute of each TSC meeting.