Clinical Trial/Study Management Group and Committees

Arrangements for the management of clinical trials/studies will vary according to their nature and requirements.

The Trial Management Group (TMG) will be responsible for all aspects of the day to day running of the trial/study from set-up to close down. Clinical trials/studies may also have a Trial Steering Committee (TSC) as well as a Data Management Committee (DMC). The DMC may also be referred to as the Data Safety and Monitoring Board (DSMB), Data Monitoring and Ethics Committee (DMEC) or Independent Data Monitoring Committee (IDSMC).

Any committee or group responsibilities stated in the protocol are to be followed including membership make up and frequency/time points of meetings.

Any key changes are to be modified via a protocol amendment and non-compliances are to be recorded on the central trial non-compliance log/documented on a file note.

1. Trial Management Group (TMG)

The TMG is made up of individuals responsible for the day-to-day management of the trial/study. The exact composition of this TMG will vary depending on the nature of the trial/study but it is typically the Chief Investigator (CI) and any of the following:

- Statistician,
- Clinical Trial Coordinator/Trial Manager,
- Data Manager,
- Programmer,
- Research Nurse,
- Pharmacist (for CTIMPs),
- Lab representative (for studies with research samples)
- Imaging specialist (for studies with endpoints related to specialist imaging)

Some of the participants may only attend at relevant time-points/for part of the meeting where applicable.

The remit of this group is to manage all aspects of the conduct of the trial/study, monitor its progress and quality of data collected, to ensure that the protocol is followed and that the safety and wellbeing of participants is upheld. Responsibilities of this group will include but are not limited to:

- Design of the trial/study
- Preparation of all trial/study documents (protocol, patient information sheet, leaflets, adverts etc.)

- Preparation of required documentation for submission to HRA, MHRA and local R&D approvals
- Design of data capture systems (paper and electronic)
- Overview of Data Management; collection of data generated during the study/trial, resolving queries on missing and inconsistent data and trend identification
- Overview of pharmacovigilance; Collection, reviewing and reporting of safety data to all appropriate parties. For example reviewing SAEs and if applicable AESI summary tables
- Preparation of progress, safety and funder reports
- Reviewing rate of participant recruitment rate against projected timelines
- Reviewing participant retention rate
- Discussing sample management/analysis plans, conduct and/or issues
- Reviewing non-compliances and overseeing the conduct of the trial to ensure that the approved protocol and procedures are adhered to
- Overview of any sponsor monitoring activity and issues raised
- Overview of any proposed amendments to the study
- Take appropriate action to ensure the safety and wellbeing of participants
- Oversee progress of study in relation to any funding milestones
- Analysis of data and publication of outcome

Minutes are to be taken during TMG meetings and filed in the TMF.

Frequency of TMG meetings is approved by the Chief Investigator and may be stated in the protocol.

2. Trial Steering Committee (TSC)

The role of the TSC is to provide overall supervision for the trial/study on behalf of the Sponsor and Funder as well as providing an element of expert advice that is independent of the CI and the Sponsor. The TSC is typically made up of members of the TMG (including the CI), project advisors, independent members e.g. clinicians, scientists, statisticians, patient representative(s) and should have an independent Chair (with no direct involvement in the conduct of the study). An observer from the Funder and Sponsor should be invited to their meetings. Involvement of independent members allows for an unbiased oversight of the management of the trial/study and ensures that key decisions are made objectively.

Not all trials/studies will require a TSC. The need and exact composition and arrangements for such a committee will depend on the complexity of the trial/study and could be considered as part of the risk assessment and monitoring strategy (for example risks associated with the IMP, safety

implications of assessments, size of the trial and whether it is single or multi-site, complexity of study/trial protocol).

If a trial/study requires a TSC, the procedures for its formation, agenda remit and membership should be detailed in the protocol and/or TSC charter (see CCTU/TPL027).Use CCTU/TPL096 TSC/DMC Agenda Template for consistency

Minutes taken during TSC meetings should be:

- Written using CCTU/TPL097 TSC/DMC Minutes template to ensure consistency
- Sent to the TSC Chair for approval and sign off
- Circulated to the TMG/TSC members
- Filed in TMF

3. Data Monitoring Committee (DMC)

The DMC is made up of a small number (3-4) of experts (clinicians, scientists, statisticians) that have relevant expertise and experience in the disease area, the intervention, clinical trials and statistics but are, ideally, completely independent of the conduct of the trial, the CI, the Sponsor or the Funder. The remit of this committee includes reviewing accumulating study/trial data (focusing on ethical, safety and efficacy end points), quality of trial conduct, trial progress, compliance as well as considering data emerging from other related studies, and making appropriate recommendations to the TSC and TMG. Members of DMC review interim reports prepared by the study statistician and can have access to un-blinded data. If they have serious ethical or safety concerns on the study conduct or assessments they can recommend changes to the trial conduct or even early termination.

Prepare an agenda for DMC meetings using CCTU/TPL096 TSC/DMC agenda template for consistency. The CTC may also need to help prepare progress reports for the committee. Following each meeting, the DMC will prepare a report with their comments and recommendations and send this to the TMG and TSC. Use CCTU/TPL097 TSC/DMC Minutes template for consistency. File a copy of the minutes in the TMF.

If members have access to unblinded data, care is to be taken to maintain the blind for the CI and any other blinded trial team members in attendance. The meetings should be separated into open and closed sessions, with only unblinded members attending the closed sessions.

Any unblinded reports should be named as such e.g. TRIAL_DMC_Unblinded_Report. These should be shared with unblinded members separate to the meeting link or two meeting links should be sent, one for the open and one for the closed session. The unblinded reports could be password

protected with the password only shared with unblinded members of the committee. Any emails containing unblinded data should have ***unblinded*** in the email subject. Care should be taken when forwarding or replying to emails to ensure any unblinded data is not sent to blinded trial team members.

If any unblinded data is shared with blinded team members, actions should be taken to maintain the blind such as instructing members to delete the emails and not open any attachments. If any unblinding does occur this should be reported to the regulatory team for CTIMPs or QA Manager for other trials.

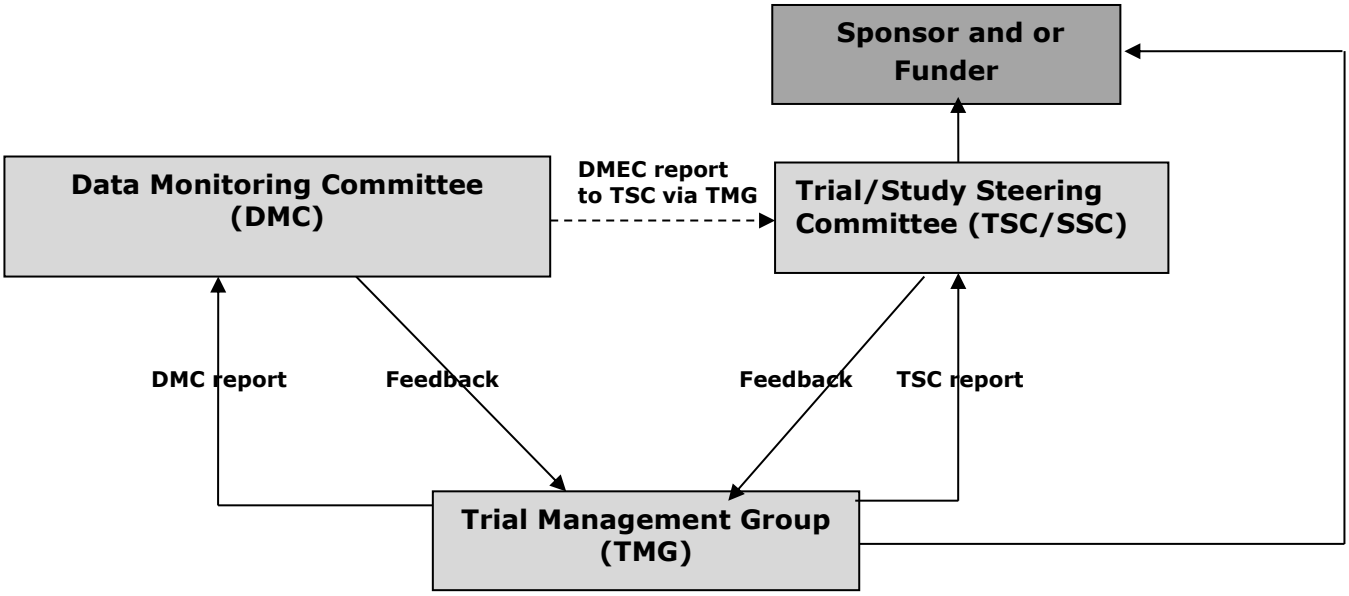
Not all trials/studies will require a DMC. The decision to have one will depend on the complexity and end-points of the trial/study and maybe considered as part of the risk assessment or funding arrangements For example any of the following factors may be taken into consideration when deciding the need for a DMC:

- The safety profile of IMP to be used
- Safety issues with study assessments
- Number of participants
- Whether single-site or multi-site
- End points and/or other data requiring regular review
- Potential for high morbidity or mortality during study
- Inclusion of vulnerable populations

If a trial/study requires a DMC, the procedures for its formation, remit and membership should be detailed in the protocol and/or a DMC charter (see CCTU/TPL010). The DAMOCLES study group published a template for a DMC charter (see reference in section 5.)

4. Relationship between various Study/Trial Committees

Every trial/study will have specific requirements and complexities and the need to have a TSC and/or a DMC and/or other committees will be made based on these as well as the risk assessment, the monitoring plan and funders' requirements. The relationship between the various committees that do exist for a trial/study and the reporting arrangements between them should be explained in the protocol or relevant committee charters. Below is an illustration as an example.



5. References

- CCTU/TPL027: Trial Steering Committee or Study Steering Committee Charter Template
- CCTU/TPL010: Data Monitoring Committee Charter Template
- The National Institute for Health Research - Research Governance Guidelines
- https://www.nihr.ac.uk/appendix-1-public-tscssc-member-role-description
- MRC Guidelines for management of global health Trials (2017)
- MHRA GCP Guide (2012)
- A proposed charter for clinical trial data monitoring committees: helping them to do their job well (DAMOCLES Study Group): The Lancet 2005, vol 365, 711-722