UNIVERSITY OF LINCOLN

STANDARD OPERATING PROCEDURE
Trial Management Group

Version Final 1.0 Date 01 May 2021

Effective Date: 01 August 2021

Next review: 2 years

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Version History	**Reason for change**

NOTE: All SOPs are subject to regular review.

Please ensure that the version of this SOP is the most up-to-date.

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1. PURPOSE

The purpose of this SOP is to set out the terms of reference for a Trial Management Group (TMG).

2. SCOPE

This SOP is applicable to the following groups of people involved in a trial/study (see flowchart at end of document):

- Trial Management Team/Group.
- TSC members and TSC Chair
- Data Monitoring Committee/Data Monitoring and Ethics Committee (DMC/DMEC)

3. BACKGROUND

3.1 All clinical trials and clinical studies should have a Trial Management Group (TMG).

3.2 For CTIMPS and all randomised clinical trials of devices, or other interventions, both a TSC and DMC are also required, and funders may have specific rules as to the recommended composition of these oversight groups. For large clinical studies which are not trials, it is generally recommended to have a TSC and TMG and this may also be stipulated by the funder. For small (non-randomised) clinical studies and where there is no requirement from the funder, it is at the discretion of the CI and sponsor as to whether a TSC and/or DMC are convened.

3.3 The CI is responsible for setting up the TMG and the TSC and DMC for trials and studies where they are required. The CI is also responsible for ensuring that the TMG communicates with the TSC and DMC and that the meetings of these groups are organised.

3.4 The SOP will define the general roles and responsibilities of members of the TMG and make recommendations for membership selection and decision-making processes.

3.5 The overall responsibility of a TMG is to ensure the smooth running, safety and attainment of the objectives of a clinical trial or similar study. TMG members should ensure the safe and effective conduct of the trial/study on a day to day basis and meet regularly. The TMG members should lead the writing of any publications or reports arising from the results of the study. In addition, the TMG can also make recommendations to the sponsor or funder if any changes are required in the trial/study processes.

3.6 The TMG should approve the protocol and any amendments, monitor the recruitment, review progress/completion of key milestones of the trial, review relevant information from external sources, consider the recommendations of the Data Monitoring Committee/Data Monitoring and Ethics Committee (DMC/DMEC) and funder, and resolve problems that they identify..

3.7 The TMG has a role in flagging up early issues that might indicate ethical dilemmas, such as deviation from the trial protocol, events that impact on patient safety, rights or wellbeing, and the potential effects of new external information. When such issues are identified, they should be fed back to the TSC and a course of action agreed on in a case-by-case basis. If considered necessary by the TSC or the trial Sponsor, then issues may also be discussed further with the Ethics Committee

4. CROSS REFERENCES

4.1 CG-QMS Data Monitoring Committee

4.2 CG-QMS Trial Steering Committee

5. PROCEDURE

ROLE OF THE TMG

The general roles of the TMG are as follows:

5.1 To develop the protocol and associated trial documentation so that the trial/study can commence and continue in accordance with the pre-planned time schedule.

5.2 To recruit participants and monitor progress of the trial in terms of patient/participant recruitment, adherence to the protocol, completion of milestones (as expected by the funder or defined in the study Gantt Chart and/or funding application) and patient safety.

5.3 To consider any new information that is published in relation to the trial/study research question and evaluate the impact of that on the continuation of the trial/study and related procedures. This is important, particularly if the new information highlights any safety issues or gives compelling evidence that the treatment/intervention under investigation is unsafe or ineffective. Under such circumstances, it would be wise to discuss this with the TSC and if needed, review the protocol and new information with advice from the ethics committee and sponsor. Such action could help ascertain whether the study/trial protocol should/could be amended or (in extreme circumstances), whether the study should be suspended or even stopped.

5.4 To have oversight of the safety and well-being of the trial participants.

5.5 To consider the advice of the TSC (where convened), DMC/DMEC (where convened), ethics committee and Sponsor in relation to any review they conduct of any complaints by participants, or any adverse events and deaths as defined by the protocol.

5.6 To provide information and advice to the Chief Investigator (CI), the trial Sponsor and the trial funder on all aspects of the trial.

TASKS TO BE UNDERTAKEN BY THE TMG

The specific <u>protocol, documentation and publication-related tasks</u> to be undertaken by the TMG include but are not limited to the following:

5.7 To record minutes of all TMG meetings.

5.8 To draft amendments to the protocol.

5.9 To propose or develop changes to the design of the trial, including additional sub-studies.

5.10 To have responsibility for the timely reporting of trial results in accordance with the study Gantt chart/ milestones as described in the protocol or funding application.

5.11 To help to develop, comment upon and ultimately approve, the statistical analysis plan.

5.12 To help to develop, comment upon and ultimately approve, any publication and dissemination plans for the study/trial.

5.13 To help to develop, comment upon and ultimately approve, the final reports for the funder, ethics committee and any arising publications.

5.14 To approve external or early internal requests for release of data or subsets of data or samples including clinical data and stored biological samples.

The specific <u>progress monitoring tasks</u> to be undertaken by the TMG are as follows:

5.15 To collate and monitor recruitment figures and work with the TSC to develop strategies to deal with any recruitment problems.

5.16 To collate and monitor the completeness of data and work with the TSC to develop strategies for improving satisfactory data collection for the trial.

5.17 To record and monitor follow-up and withdrawal rates at all study sites and advise the TSC if improvements or protocol changes are needed.

The specific TMG tasks relating to the <u>safety and well-being of trial participants</u> are as follows:

5.18 To propose strategies to deal with problems including sites that deviate from the protocol.

5.19 To regularly review summary data on the number of adverse events, deaths and withdrawals of trial participants.

5.20 To agree a pre-defined format for DMC/DMEC reports in collaboration with the DMC/DMEC.

5.21 To receive feedback from the DMC/DMEC and make any necessary changes to the protocol or study processes which improve participant safety or enhance safety reporting.

5.22 To make decisions if needed as to the future continuation (or otherwise) of the trial.

TMG MEMBERSHIP

5.23 The CI or PI would normally chair the TMG meetings. Membership should include all research team members who take part in the day-to-day participant recruitment, project management, data management, data collection and project administration such as (but not limited to) the following people:

- Research staff
- Research nurses
- Clinical staff
- Allied Health professionals
- Technical staff
- Data managers
- Project Administrators
- PPI advisors (these may be incorporated -especially in projects where there is no TSC)
- Any other experts providing support or guidance to the project

TMG MEETINGS AND AGENDAS

5.24 TMG meetings should be held at the intervals specified in the project proposal or Gantt Chart. Normally these meetings shall occur on a regular and pre-determined basis but may be needed more frequently for example, during the set-up phase of a study or when there is an urgent need for extra discussion. The Agenda of TMG meetings should be flexible to accommodate the design and phase of the study in question. It should allow for discussion/review of but not be limited to, the following items:

- **Protocol changes**: Any protocol amendments and sub-studies
- **Recruitment progress**: Actual recruitment versus final target
- **Acceptance rate:** as a proportion of those invited to participate, and (if known), all eligible participants
- **Follow-up and loss to follow up**: Percentage of participants proceeding through each trial stage to allow monitoring of the recruitment and retention, including missing outcome data. This information does not necessarily need to be split by treatment/intervention arm, but CONSORT style diagrams may be helpful to present this information.
- **Overall withdrawal rate and level of withdrawal**: summarising those patients who have withdrawn from treatment but are still in follow-up and those who withdraw with no future contact.
- **Data management metrics (if needed)**: e.g. rate of returns of questionnaires, forms or scans, volume of queries, time to return, enhanced metrics via electronic data capture
- **Completeness of data collected**
- **Summary of adherence to treatment/intervention.** Not split by treatment/intervention arms (to avoid unblinding and bias while study in progress).
- **Summary of adverse events** (including any deaths, adverse events, serious adverse events and suspected unexpected serious adverse reactions). This can be split by treatment arm as long as the actual treatment allocation is kept blinded (for example, the arms could be called “A” and “B”).
- **Review of existing publication plans and progress**
- **Review of existing statistical analysis plans and progress**

- **Updates on any planned publications and presentations**
- **Review of any protocol deviations overall and by site**
- **Summary of any data monitoring and ethics committee (DMC/DMEC) recommendations**
- **Any organisational problems or other trial issues**

The above list is not exhaustive but is largely based on the list provided in the following publication: *Exploring the role and function of trial steering committees: results of an expert panel meeting. Harman et al. Trials (2015) 16: 597.*

6. FLOWCHART

Oversight and Management Structure Diagram:

This oversight and management structure should be followed unless otherwise agreed with the Sponsor, funder and Trial Management Group: