**Clinical Directorate Clinical Research Governance Team**

**Trial name**

**Trial Steering Group**

**Terms of Reference**

**Version X.Y - dd/mm/yyyy**

**Guidance notes [delete before finalisation of the terms of reference].**

Please take care when completing this template and ensure all text is relevant to your proposed trial.

Some sections will not be applicable to all studies and some studies will require extra sections. The template has been provided with the below;

|  |  |  |
| --- | --- | --- |
| **Text** | **Purpose** | **Action to be taken** |
| Standardised Text | Provided by the University of Liverpool for organisational compliance | Review and ensure it applies to your study. Delete if not applicable and rewrite for your study. |
| Guidance notes | Provided for specific support, and where study specific information needs to be completed/updated | Reviewed and deleted once ToR is finalised. |

Please ensure to remove guidance notes as above, any TEMPLATE watermarks and ensure the Version Number and Date is present in the footer.

If you require any assistance please contact [sponsor@liverpool.ac.uk](mailto:sponsor@liverpool.ac.uk)

|  |  |
| --- | --- |
| **Trial Specific Information** | |
| **Trial Acronym:** |  |
| **Full Trial Name:** |  |
| **Protocol registrations (ISRCTN, EudraCT etc)** |  |
| **Sponsor:** |  |
| **Chief Investigator:** |  |

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## Introduction

The document will define the roles and responsibilities of the Trial Steering Committee (TSC) for the trial name trial, its relationship with other trial committees, its membership, and the purpose, timing and quoracy of its meetings. The ToR will also provide an outline of the content of the reports that will be provided to the TSC.

TSC members should formally register their agreement to join the committee by confirming (1) that they agree to be a member of the TSC and (2) that they agree with the contents of this Terms of Reference. Any potential competing interests should be declared at the same time. Independent Members should complete and return Appendix 1. Non-Independent Members should complete and return Appendix 2.

Any observers must sign a confidentiality agreement on the first occasion they attend a meeting (Appendix 3) and **PRIOR** to receiving any meeting documentation (e.g. minutes of previous meetings, reports, etc.). This will not apply to individuals who are existing members of either the TMG or IDSMC who have already signed a ToR/Charter, as these contain confidentiality agreements.

If a conflict of interest is declared by a TSC member during the course of the trial, the Trial Manager will report this to Sponsor and funder to review and advise if they are happy for the member to serve on the committee in the planned capacity or whether they should resign from the committee.

## Roles And Responsibilities

The role of the TSC is to provide overall and independent oversight of the trial. In particular, the TSC in the development of this protocol and throughout the trial, will take responsibility for:

*amend as appropriate, the list is not extensive and should be adapted to address the specific needs of the trial – consider specifically trials where a separate IDSMC is not convened and the TSC undertakes the role of unblinded data quality and participant safety oversight*:

* decisions such as a need for a major change to the protocol;
* reviewing and approving any substantial protocol amendments;
* monitoring the progress of the trial;
* reviewing relevant information from other sources;
* considering recommendations from the Independent Data and Safety Monitoring Committee (IDSMC);
* advising the Trial Management Group (TMG) on all aspects of the trial;
* making recommendations to the funder/Sponsor;
* ensuring that the trial is conducted at all times in adherence to the protocol and the principles Good Clinical Practice (GCP).
* The TSC Chair is expected to facilitate and summarise discussions. The TSC statistician will provide independent statistical expertise. The TSC clinician will provide independent clinical expertise.

Day to day management of the trial is the responsibility of the CI and a separate TMG has been set up to assist with this function.

**Patient Rights & Safety**

In all the work undertaken by the TSC the rights, safety and wellbeing of the trial participants are the most important considerations and should prevail over the interests of science and society. The TSC should satisfy themselves that processes are in place to ensure that;

*amend as appropriate*

* freely given informed consent is obtained from each trial participant/appropriate deferred consent processes are in place;
* participant safety is being appropriately monitored.

The TSC should advise the investigators on the completeness and suitability of the patient information provided.

**Consideration of New Information**

The TSC should consider new information relevant to the trial including reports from the IDSMC It is the responsibility of all members of the TSC to bring results from other studies that may have a direct bearing on future conduct of the trial to the attention of the TSC.

On consideration of this information the TSC should recommend appropriate action, such as changes to the protocol, additional patient information, or stopping the trial. The rights, safety and well-being of the trial participants should be the most important consideration.

## Membership Of TSC

*Consideration should be given to the funding source of the trial as each funder will have their own specific requirements outlined in the contract of funding and may wish to approve specified members. This should be detailed here and/or the below example wording adapted.*

The membership of the TSC is limited. The appointed TSC members will possess voting rights and includes the following:

* Independent[[1]](#footnote-1) members:
  + An independent Chair
  + An Independent Statistician
  + An Independent individual with expertise relevant to the trial
  + An independent lay/consumer representative
  + Two or more other independent expert members (one being a statistician) with expertise relevant to the project
* Non-Independent member:
  + Chief Investigator

TSC membership is to be for the duration of the clinical trial. If any members leave the TSC during the course of the trial, the Sponsor/funder will promptly appoint their replacements.

In addition to the TSC members listed above, individuals from the TMG and others involved in running the trial will be required to attend meetings to provide reports and updates. Usually this will be the Trial Manager and the Sponsor Representative. Occasionally, observers may also be invited by the Chair. None of these individuals are considered TSC members however and they do not possess any voting rights.

Members of the TSC are detailed in the trial title Oversight Committee Membership Log.

## Organisation Of TSC Meetings

**Attendance of meetings**

The Trial Manager will liaise with TSC members and other required non-member attendees/observers to ensure that the meeting date is suitable for all to attend. Individuals who cannot attend in person should be encouraged to attend by teleconference.

If there is no suitable date for all required individuals or individuals can no longer attend and the meeting cannot be rescheduled then the TSC may still meet if quorate for decision-making. If the TSC is considering recommending major action after such a meeting the TSC Chair should talk with any absent members as soon after the meeting as possible to check they agree. If they do not, the Chair must communicate this to the Trial Manager and a further teleconference should be arranged with the full TSC.

If a member does not attend and does not send apologies for a meeting, every effort will be made to ensure their availability for the next meeting. If a member does not attend nor send apologies for the following meeting and/or do not engage in discussions outside of the TSC meetings, they may be asked if they wish to remain a member of the TSC.

**Format of TSC Meetings**

Meetings will be organised by the Trial Manager. Papers for the meeting will be circulated in advance.

**Frequency of Meetings**

The trial was designed and risk assessed to have meetings *specify frequency*. The TSC will meet shortly after the IDSMC has met, although there may be periods when more frequent meetings are necessary, in person or by teleconference. Major trial issues may need to be dealt with between meetings, by phone or by email. TSC members should be prepared for such instances.

## Initial TSC Meeting

During the first TSC meeting, members will be asked to:

* Review and approve a draft of the TSC ToR;
* Confirm that they have read and agreed the protocol, either during the meeting or via email. Ideally the protocol review should take place prior to submission for ethical and regulatory approval however if this is not possible a copy of the final version of the protocol submitted to ethics and/or regulatory authorities should be provided with an opportunity to comment at the next meeting. Any suggested revisions will either trigger an amendment or be implemented at the next amendment, whichever is appropriate;
* Agree on the frequency of future meetings;
* Agree on a timeframe for being notified of any suspected unexpected serious adverse reactions (SUSARs)/related unexpected serious adverse events (RUSAEs) and document the outcome in section 8 of the ToR;
* Ensure that an IDSMC has been established, comprising members who are independent of both the trial and the TSC
* Decide how far in advance of future meetings they wish to receive reports and any supporting documentation.

## Final TSC Meeting

Final analysis of the primary and secondary outcome measures will be carried out at study closure. A final meeting will be held in-person/held by teleconference upon the availability of the final study analysis.

## TSC Meeting Documentation

**Agenda & Minutes**

The TSC agenda and relevant supporting documents, including minutes of the previous meeting, will be circulated before the meeting to allow time for the review. The TSC Chair will decide how far in advance of meetings they wish to receive papers.

The Trial Manager or delegated other will be responsible for taking minutes of the meetings. The minutes will describe the proceedings in the TSC meeting and will summarise any recommendations to Sponsor. The TSC Chair will be responsible for ratifying draft minutes.

**Reports**

Each TSC meeting should be scheduled to follow on shortly after each Independent Data Safety Monitoring Committee (IDSMC) meeting. Therefore, the TSC will usually be provided with the open IDSMC report. When close scheduling is not possible, or where the TSC require additional/alternative reports, this will be agreed by the Chair and documented in the minutes.

The TSC members will not be privy to accumulating outcome measure data by trial arm; this will be reviewed by the Independent Data Safety Monitoring Committee (IDSMC) only.

**Confidentiality of Meeting Documentation**

TSC members, attendees and observers are required to securely store copies of the TSC reports, agendas and minutes, as well as copies of communications between meetings. All documentation should be considered confidential to those unconnected with the trial.

The *<insert organisation/person responsible>* will keep a central record of all agendas, minutes, reports and correspondence by trial committees in the Trial Master File (TMF).

## Safety Reporting

It is the responsibility of the CI to notify the TSC of any <amend as appropriate suspected unexpected serious adverse reactions (SUSARs)/related unexpected serious adverse events (RUSAEs)> occurring during the course of the trial. This task is usually delegated to insert organisation/person responsible and is detailed in the subcontract between Sponsor and insert organisation/person responsible.

<The timeframe of notifying of the TSC/SSC of these reports should be described here and will be determined at the first meeting of the TSC/SSC>

## Decision Making

The TSC is considered quorate for decision making if <consideration should be given to the funding source of the trial as each funder will have their own specific requirements for quoracy outlined in the contract of funding. This should be detailed here>.

Every effort should be made to achieve consensus. The role of the Chair is to summarise discussions and encourage consensus; therefore, it is usually best for the Chair to give their own opinion last. It is important that the implications (e.g. ethical, statistical, practical or financial) for the trial be considered before any decision is made. If a consensus cannot be reached the decision will be put to a vote.

The possible recommendations are numerous and could include:

* No action needed, trial continues as planned
* Early stopping due to, amongst other things, safety concerns, slow recruitment, or external evidence[[2]](#footnote-2)
* Stopping recruitment within a subgroup
* Extension of recruitment or follow-up
* Stopping one of the treatment arms
* Advising on or proposing protocol changes

## Organisational Diagram

The TMG is responsible for overseeing the day-to-day running of the trial and reports to the TSC.

The TSC is the independent oversight body for the trial and must be composed of independent members. In addition to the independent members, the Chief Investigator will be a non-independent voting member.

The IDSMC is the independent body responsible for maintaining oversight of data quality and participant safety and must be composed of independent members. The IDSMC will be privy to unblinded data in their closed sessions. The IDSMC are advisory to the TSC.

Membership of the committees are detailed in the trial title Trial Oversight Committee Membership Log.

The following diagram shows the flow of information between the TSC and the other committees and functional areas involved in the trial.

*<please adapt diagram as required for your trial>*

**IDSMC open report & recommendations**

**Report**

**TSC**

**Feedback**

**IDSMC**

**TSC**

**TMG**

**Questions/Feedback**

**Report**

**TSC**

**Feedback**

## Disagreement Between IDSMC And TSC

The TSC has ultimate responsibility for the trial. However, the TSC should report back to the IDSMC how they have acted upon the IDSMC recommendations. If the IDSMC has serious concerns with the TSC decision, a joint meeting of these groups should be held. The information to be shown would depend upon the action proposed and the IDSMC concerns.

The meeting should be chaired by an external expert who is not directly involved with the trial.

Depending on the reason for the disagreement confidential data may have to be revealed to all those attending such a meeting. For any individuals who have not already signed a confidentiality agreement or the trial (e.g. TMG or IDSMC members), a confidentiality agreement will be required to be signed prior to the meeting or receiving any documentation (see Appendix 3).

## Dissemination And Implementation Of Results

The publication and presentation policy should be agreed at the start of the trial by the TSC and should ideally form part of the protocol. The publication policy will define arrangements for authorship. Large trials may have group authorship, with a list of contributors giving details of who did what, for example: TSC, collaborating investigators and acknowledging participants.

One of the first publications from the trial may be the trial protocol. The protocol should be submitted, ideally, at the start of the trial but protocols will be accepted up to the end of participant recruitment by, e.g. Trials journal.

The TSC should ensure that appropriate efforts are made to ensure that the results of the trial are adequately disseminated and due consideration is given to how the recommendations will be implemented in clinical practice.

No publications or presentations with trial outcomes should be produced before the primary paper has been agreed and accepted for publication, without the prior approval of the TSC. It is, however, often possible to publish baseline or sub study papers prior to the main trial publications. It should be noted that many funders will require notification (and possibly approval) of any publications arising from their funding.

**Post-publication Constraints**

TSC members must keep any issues from their involvement confidential for a period of 12 months following publication of the primary results.

## Appendix 1: Agreement and competing interests form for independent members

**Trial name Trial Steering Group: Agreement to join the Trial Steering Group as an independent member and disclosure of potential competing interests**

By signing below, I agree to the following statements:

1. I have read and understood the TSC Terms of Reference (version and date as per the foot of this page);
2. I agree to join the TSC for this trial as an independent member;
3. I agree to treat all information and sensitive trial data and discussions confidentially.

The avoidance of any perception that independent members of a TSC may be biased in some fashion is important for the credibility of the decisions made by the TSC and for the integrity of the trial.

Potential competing interests should be disclosed via the <insert organisation/person responsible>. In many cases simple disclosure up front should be sufficient. Otherwise, the (potential) independent TSC member should remove the conflict or stop participating in the TSC. Table 1 lists potential competing interests.

|  |  |
| --- | --- |
|  | No, I have no potential competing interests to declare |
|  | Yes, I have potential competing interests to declare (please detail below) |
| Please provide details of any potential competing interests: | |
|  | |
|  | |

|  |  |
| --- | --- |
| Name: | Name of Institution: |
| Signed\*: | Date: |

*\*Signatures may be wet-ink or electronic (e.g. ADOBE Sign)*

**Once completed, please return completed appendix to trial email address.**

**Table 1: Potential competing interests for independent members**

|  |
| --- |
| * Stock ownership in any commercial companies involved |
| * Stock transaction in any commercial company involved (if previously holding stock) |
| * Consulting arrangements with the Sponsor/Funder |
| * Ongoing advisory role to a company providing vaccines to the trial |
| * Frequent speaking engagements on behalf of the intervention |
| * Career tied up in a product or technique assessed by Trial |
| * Hands-on participation in the Trial |
| * Involvement in the running of the Trial |
| * Emotional involvement in the Trial |
| * Intellectual conflict e.g., strong prior belief in the Trial’s experimental arm |
| * Involvement in regulatory issues relevant to the Trial procedures |
| * Investment (financial or intellectual) or career tied up in competing products |
| * Involvement in the writing up of the main Trial results in the form of authorship |

## Appendix 2: Agreement and competing interests form for non-independent members

**Trial name Trial Steering Group: Agreement to join the Trial Steering Group as a non-independent member and disclosure of potential competing interests**

By signing below, I agree to the following statements:

1. I have read and understood the TSC Terms of Reference (version and date as per the foot of this page);
2. I agree to join the TSC for this trial as an non-independent member;
3. I agree to treat all information and sensitive trial data and discussions confidentially.

The avoidance of any perception that independent members of a TSC may be biased in some fashion is important for the credibility of the decisions made by the TSC and for the integrity of the trial.

Potential competing interests should be disclosed via the <insert organisation/person responsible>. In many cases simple disclosure up front should be sufficient. Otherwise, the (potential) independent TSC member should remove the conflict or stop participating in the TSC. Table 1 lists potential competing interests.

|  |  |
| --- | --- |
|  | No, I have no potential competing interests to declare |
|  | Yes, I have potential competing interests to declare (please detail below) |
| Please provide details of any potential competing interests: | |
|  | |
|  | |

|  |  |
| --- | --- |
| Name: | Name of Institution: |
| Signed\*: | Date: |

*\*Signatures may be wet-ink or electronic (e.g. ADOBE Sign)*

**Once completed, please return completed appendix to trial email address.**

**Table 1: Potential competing interests for non-independent members**

|  |
| --- |
| * Stock ownership in any commercial companies involved |
| * Stock transaction in any commercial company involved (if previously holding stock) |
| * Consulting arrangements with the Sponsor/Funder |
| * Ongoing advisory role to a company providing drugs to the trial |
| * Frequent speaking engagements on behalf of the intervention |
| * Intellectual conflict e.g. strong prior belief in the Trial’s experimental arm |
| * Involvement in regulatory issues relevant to the Trial procedures |
| * Investment (financial or intellectual) in competing products |

## Appendix 3: Confidentiality agreement for observers

**Trial name Trial Steering Committee: Agreement to attend the Trial Steering Committee and treat all information confidentially**

By signing below, I agree to the following statements:

1. I have read and understood the Trial name TSC Terms of Reference (version and date as per the foot of this page);
2. I agree to treat as confidential all information and documentation obtained by attending the Trial name TSC unless explicitly permitted otherwise.

|  |  |
| --- | --- |
| **Name:** | **Name of Institution:** |
| **Signed\*:** | **Date:** |

*\*Signatures may be wet-ink or electronic (e.g. DocuSign or Adobe Sign)*

**Once completed, please return completed appendix to trial email address.**

1. *not be involved with the trial in any other way or have any competing interest that could impact on the trial* [↑](#footnote-ref-1)
2. External evidence will be collated and presented to the TSC members by the Trial Statistician, however the TSC may also present external data of which they have become aware. [↑](#footnote-ref-2)