[TRIAL NAME]

**Chief Investigator**:

**Sponsor**:

**ISRCTN No**: [IF APPLICABLE],

**CT.gov No**: [IF APPLICABLE],

**REC No:**

**EudraCT No:** [IF APPLICABLE],

**Trial Steering Committee Charter**

Version x.x, [DATE]

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| **Version** | **Date** | **Amendments by** | **Amendments** |
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# 1. INTRODUCTION

The role of the Trial Steering Committee (TSC) is to provide overall supervision for [TRIAL NAME], to take steps to reduce deviations from the protocol to a minimum, periodic review of the trials progress, to review safety data (including unblinded data) and to help resolve any differences within the research team or between the team and trial sponsor. The TSC operates on behalf of the Trial Funder, Trial Sponsor and is to ensure that the trial is conducted according to the UK Research Governance Frameworks for Health and Social Care, the principles of Good Clinical Practice (GCP) and all relevant regulation and local policies.

The background to this trial including all objectives, assessments, interventions and analyses are described in the study protocol.

The TSC will have ultimate responsibility for the trial and will assume primacy over the Data Monitoring Committee (DMC) or Chief Investigator (CI). The sponsor and CI will agree the charter of the TSC prior to the start of the research project.

The main objective(s) of the trial are…..

[Insert flowchart of trial design here]

The purpose of this charter is to define the roles and responsibilities of members of the [TRIAL NAME] TSC and to guide its activities, including the timing of meetings, methods of providing information to and from the TSC, frequency and format of meetings, statistical issues and relationships with other committees. This charter also describes procedures for ensuring confidentiality and proper communication to and from the TSC and provides and outline of reports to be provided to the TSC.

# 2. ROLES AND RESPONSIBILITIES

The aims of the TSC are to safeguard the interests of trial participants, potential participants, investigators and Sponsor; to assess the safety and efficacy of the trial’s interventions, and to monitor the trial’s overall conduct, and protect its validity and credibility. In discharging its safety role the TSC will work in conjunction with the DMC. The [TRIAL NAME] TSC will also act as a Data Monitoring and Ethics Committee (DMC) for this trial (optional).

## Terms of reference

The [TRIAL NAME] TSC will oversee the monitoring of the progress and objectives of the trial by the Trial Office and the Trial Management Group (TMG), which will include:

[LIST TO BE ADAPTED FOR THE TRIAL]

* Ensuring that all relevant approvals are obtained before the project commences.
* Ensuring that the rights, safety and wellbeing of participants remain the most important considerations regardless of the interests of science and society.
* Assessing data quality, including completeness.
* Monitoring recruitment figures and losses to follow-up.
* Monitoring compliance with the protocol by participants and investigators.
* Monitoring evidence for treatment differences in the main efficacy and safety outcome measures – and thus recommending action when / whether the main trial question has been answered.
* Monitoring evidence for treatment harm (fatal and non-fatal serious adverse events).
* Recommending whether the trial should continue to recruit, terminate or adapt based on safety or efficacy considerations.
* Responding to advice provided by the trial DMC.
* Recommending any substantial amendments to the protocol, where necessary.
* Advising on and/or endorsing any substantial amendments suggested by investigators or Sponsors.
* Assessing the impact and relevance of any external information provided to the committee.
* Monitoring compliance with previous TSC recommendations.
* The TSC should inform the TMG of any concerns regarding the safety of participants, trial failing to indicate a clear benefit, accrual rate too low to provide meaningful results.

A specific role of the TSC will be… (complete if applicable)

In the event that unblinding is required the [TRIAL NAME] Independent Statistician will [Insert details of trial unblinding procedure].

The TSC will **not** have a role in increasing or decreasing the planned sample size as it is not blind to the current results of the trial.

The TSC will be asked to make recommendations to the TMG, Funder and Sponsor as required, but will not be empowered to make decisions on behalf of the trial.

# 3. MEMBERSHIP AND PRIMARY RESPONSIBILITES

Membership will include representation from [clinical and other specialties e.g. surgery, radiation oncology] two lay members and an independent statistician. Representatives of both Funder and Sponsor will be invited to the TSC. Members have been chosen because they are experienced in trials and/or the disease area. The members should ideally be independent of the trial (e.g. should not be involved with the trial in any other way or have some involvement that could impact on the trial).

Members should not serve on TSCs of similar, concurrently active trials as this could compromise the independence of the trial and possibly the confidentiality of the results of the individual trials. Any competing interests, both real and potential during the next x years, should be declared.

The Chair’s role will be to facilitate and summarise discussions, to oversee meetings, write the agenda for each meeting, and to represent and report the views of the committee. The Chair will agree with the CI the content of the charter and the schedule of meetings for the TSC. The Chair will also establish clear reporting lines to the Funder, Sponsor and TMG. The Chair will also provide an independent opinion (and seek advice where required) if conflicts arise between the investigators, Funder, Sponsor or other parties involved in the trial.

The TSC membership includes a statistician to provide independent statistical expertise and to further guide the other TSC members through the report. The TSC statistician will not prepare the TSC documentation. This will usually be provided by the Trial Manager (TM) with the help of the trial statistician and other parties as required.

The responsibilities of the TSC independent statistician will include assessment of …

[Provide details of any stopping rules] In such instances recommendations will likely be further protocol training and either withdrawal of the trial centre or early trial termination of the trial.

The [TRIAL NAME] TM will act as secretary and coordinate meetings and minutes. The TM will also be able to clarify any queries arising during a meeting. The Chair may also request that additional members of the TMG be available to attend meetings to seek clarification of the data or confirm the TSCs understanding of the data.

Members of the TSC should declare their agreement to be a committee member, agreement to this charter’s contents, confidentiality of all meeting matters and conflicts of interest by completing the agreement in the appendix.

The membership of the TSC in [MONTH, YEAR] is shown in Table 1.

|  |  |  |
| --- | --- | --- |
| **Name** | **TSC role** | **Job title** |
|  | Chairman |  |
|  | [Clinician / surgeon / etc] |  |
|  | Independent Statistician |  |
|  | Lay member 1 |  |
|  | Lay member 2 |  |
|  | [TRIAL NAME] Chief Investigator |  |
|  | Secretary |  |
|  | [TRIAL NAME] statistician |  |
|  | Sponsor Representative |  |
|  | Funder Representative |  |

***Table 1: TSC members (amend as required)***

The responsibility for convening and organising TSC meetings sits with the CI and the Chair of the TSC. The Chair will approve the appointment of committee members at the first meeting. The Funder and Sponsor will be invited to attend and will be made aware of the committee membership.

Membership to the TSC is for the duration of the trial. However, should any member leave or be unable to participate regularly in meetings, the TMG shall be approached by the TSC to suggest replacements who will be appointed by the Chair.

**The TSC membership has indemnity coverage via the University of xxxxx Professional Indemnity insurance. This is in the event of the TSC being sued by a trial participant (or family member) for example.**

# 4. TSC MEETINGS

All potential TSC members will have reviewed the protocol and this charter before agreeing to join the committee. Before recruitment begins the trial will have obtained a Sponsor, completed peer review by the funding body, scrutiny by the TMG and will be approved by a REC and have obtained R&D and other permissions as appropriate to proceed. If proposed TSC members have major reservations regarding trial design they should report these to Swansea Trials Unit (STU). Potential TSC members should be independent and constructively critical of the ongoing trial, but also supportive of aims and methods of the trial.

The first TSC meeting should be held prior to the start of participant recruitment. Ideally it should be held face-to-face to discuss, revise and finalise the terms of reference, agree the content of this charter and sign any agreements. The second meeting should be within one year of commencing data accrual.

TSC members should be reimbursed for any reasonable travel, accommodation or other costs (e.g. telephone) incurred. The lay members will be reimbursed in accordance with Involving People guidelines.

The committee will only be quorate when the Chair, the statistician and one clinician participate, either in person or remotely (unless otherwise agreed). If the TSC is discussing major issues or amendments the Chair should communicate the information to absent members as soon as possible after the meeting to determine if all agree. If there is disagreement a further meeting should be convened with the full TSC at the earliest opportunity.

The TMG may request that the TSC meet outside their planned meeting schedule, should the need arise.

# 5. RELATIONSHIPS

The responsibilities of the TSC in relation to the TMG, STU and Sponsor are presented in the protocol.

TSC members MUST disclose information about any conflict of interests by completing the Agreements and competing interests form in the appendix and returning it to the Trial Manager (TM). These are not restricted to financial matters – involvement in other trials or intellectual investment could be relevant. Although members may well be able to act objectively despite such connections, complete disclosure enhances credibility.

The TSC will report its recommendations in writing to the TM, and a copy sent to STU, to coincide with TMG meetings. If the trial is to continue largely unchanged then it is often useful for the report from the TSC to include a summary paragraph suitable for trial promotion purposes.

# 6. ORGANISATION OF MEETINGS

The TSC meeting arrangements will be as agreed at the first meeting, which is likely to be twice per year from study commencement. The date and place of the meeting will be decided at the close of the preceding meeting where possible. Videoconference and/or teleconference facilities may be provided. Failure to attend three consecutive meetings will result in the member being removed from the group.

The first meeting will be face-to-face if possible. It is recommended that all subsequent meetings should be face-to-face too, with teleconference as a second option.

TSC meetings will consist of open and closed sessions as part of the agenda.

* **Closed session**: The Chair may ask that only the independent members participate in a closed session. This may involve one or more of the [TRIAL NAME] trial team being asked to leave during that time.
* **Open session**: Attended by those at the closed session, plus any other attendees invited for the purpose of that meeting. Those attending only the open session may join in person or, if appropriate by phone.

The format will be:

1. **Closed session**: All parts of the report are discussed, and TSC discussion.
2. **Open sessions**: Discussion with other attendees on any matters arising from the closed session (assumes that others will have read the “open” report in advance).
3. **Closed session**: Extra closed session if necessary.

The content will be:

1. **Closed session**: Efficacy and safety data by treatment group.
2. **Open session:** Recruitment and data quality and the total numbers of events for the primary outcome measure and other outcome measures

In a blinded trial, TSC meetings to review unblinded data will be “closed” meetings at which the Sponsor and trial team will not be present. The TSC may also hold “open” meetings with the Sponsor to discuss its conclusions and recommendations.

Extraordinary meetings can be convened by the CI, Chair or Sponsor if required.

The final TSC meeting will be arranged when recruitment is completed and the database has been hard locked. Discussions will centre on completed data interpretation and publication timelines. If the trial is terminated early, no final TSC meeting is required,

Identification and circulation of external evidence (e.g. from other trials / systematic reviews) is not the responsibility of the TSC members. The TM will accumulate and prepare this information.

TSC members must **not** share confidential information with people outside the TSC, including the CI, where instructed not to.

The TSC members should store the papers safely after each meeting so they may check against the next report. After the trial is reported, the TSC members should destroy all interim reports.

# 7. MEETING DOCUMENTATION

An outline of the contents of the TSC report to be provided by the TM is given below:

[LIST TO BE ADAPTED FOR THE TRIAL]

* Outline of the study design and sample size sought
* Current available evidence
* Major protocol amendments
* Patient screening
* Study accrual by month/total, usually split by site
* A CONSORT diagram
* Completeness and quality of data collected into the trial database
* Quality controls
* Baseline characteristics of participants
* Safety reporting
* Follow up data available
* Protocol violations by investigators or participants. For example
  + Eligibility violations
  + Treatment violations
* Any matters affecting the trial
* Compliance by patients to clinic visit
* Withdrawals (and reasons for them)

Information not included above required by the TSC should be requested by the Chair in a timely manner**.** Meeting documentation will be circulated xx weeks before the meeting by the TM.

# 8. DECISION MAKING

The possible recommendations are numerous and could include:-

* No action needed, trial continues as planned.
* Early stopping due to, amongst other things, clear benefit or harm of a treatment, safety concerns on secondary outcome, futility, slow recruitment, or external evidence.
* Stopping recruitment within a subgroup.
* Extension of recruitment or follow-up.
* Advising on or proposing protocol changes. Note: The TSC will not advise on changes to the target sample size that are based on emerging differences between the trial arms.
* The role of formal statistical methods, specifically which methods will be used and whether they will be used as guidelines or rules

A recommendation to discontinue recruitment, in all patients or in selected subgroups, will be made only if the result is likely to convince a broad range of clinicians, including those supporting the trial and the general clinical community.

No formal interim statistical analyses of the principal outcome measure are planned in this feasibility trial. It is expected that the trial will terminate when the intended sample size has been achieved.

The role of the Chair should be to summarise discussions and encourage consensus. In each area of discussion the Chair should give their own opinion last.

Every effort should be made for the TSC to reach a consensus. If the TSC cannot achieve consensus, a vote should be taken, although details of the vote should not be routinely included in the report.

If the TSC is considering recommending major action after such a meeting the Chair should talk with the absent members as soon after the meeting as possible to check they agree. If they do not, a further teleconference should be arranged with the full TSC.

# 9. TSC REPORTING

The TSC should make any recommendations in writing to the TMG, usually within x weeks after the meeting. This should be copied to STU and Sponsor if required. Unless the TSC is recommending that the trial protocol be change in some way, the report to the TMG should not usually reveal any confidential information, unless a substantial protocol amendment is required. In such instances the information provided and dissemination should be minimal. Minutes from the meeting should be accurate and detail main discussion points, recommendations and actions. Separate minutes of open and closed session will be made if the meeting is run in this format. The minutes for each session should be made only by someone who attends that session unless a digital recording is made. It will usually be the TM who takes the minutes, however there may be a requirement for a secretary or a TM from a different trial to clerk the meeting if major discussions are expected. All members of the TSC should see and comment on the minutes. The Chair will be responsible for signing off all minutes.

The TMG has ultimate responsibility for the trial on behalf of the Sponsor. However, the TMG should report to the TSC how they have acted upon the TSC’s recommendations.

If the TSC has serious problems or concerns with the TMG decision, a meeting of these groups including Sponsor involvement should be held. The information to be shown would depend upon the action proposed and the TSCs concerns. The meeting should be chaired by a senior member of STU or external expert who is not directly involved with the trial. Depending on the reason for the disagreement confidential data will often have to be revealed to all those attending such a meeting.

# 10. AFTER THE TRIAL

The CI on behalf of the Sponsor has responsibility for ensuring that trial results will be published in a correct and timely manner.

Information about the TSC will be included in published trial reports, TSC members will be named (unless they specifically request not to be) and their affiliations acknowledged in the published report. A brief summary of the timings and conclusions of TSC meetings should be included in the body of this paper.

The TSC members should be given at least x weeks to read and comment on any draft publications that report outcome measures and/or details of the TSC. This may be done simultaneously to other groups reviewing the draft manuscript.

The results of the trial will be disseminated on the trial website in the first instance. Participants will be made aware of this to allow them to access information.

**Appendix 1 - Agreement and competing interests form for independent members of the [TRIAL NAME] Trial Steering Committee**

Please complete the following document and return to: [NAME AND ADDRESS OF SECRETARY]

|  |  |
| --- | --- |
|  | I have read and understood the TSC charter **Vx.x** dated **[date]** |
|  | I agree to join the TSC for this trial as an independent member |
|  | I agree to treat all sensitive trial data and discussions confidential |

The avoidance of any perception that members of the 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. Possible competing interest should be disclosed via the trials office. In many cases simple disclosure up front should be sufficient. Otherwise, the (potential) TSC member should remove the conflict or stop participating in the TSC. Table 2 lists potential competing interests:

|  |
| --- |
| 1. Stock ownership in any commercial companies involved.  2. Stock transaction in any commercial company involved (if previously holding stock)  3. Consulting arrangements with the Sponsor  4. Frequent speaking engagements on behalf of the intervention  5. Career tied up in a product or technique assessed by the trial  6. Hand-on participation in the trial  7. Involvement in the running of the trial  8. Emotional involvement in the trial  9. Intellectual conflict e.g. strong prior belief in the trial’s experimental arm  10. Involvement in regulatory issues relevant to the trial procedures  11. Investment (financial or intellectual) in competing products  12. Involvement in the publication |

**Table 2: Potential competing interests for independent members**

|  |  |
| --- | --- |
|  | **NO,** I have no competing interests to declare |
|  | **YES,** I have competing interests to declare (please detail below) |
|  |  |
|  |  |
|  |  |

Full name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Signed: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_