**Clinical Directorate Clinical Research Governance Team**

**Trial name**

**Independent Data & Safety Monitoring Committee Charter**

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

**Guidance notes [delete before finalisation of the charter].**

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;

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| --- | --- | --- |
| **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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## 

## Scope Of IDSMC Charter

The charter will define the roles and responsibilities of the Independent Data and Safety Monitoring Committee (IDSMC) for the trial title trial, its relationship with other trial committees, its membership, and the purpose and timing of its meetings. The charter will also provide the procedures for ensuring confidentiality and proper communication, the monitoring guidelines to be implemented by the IDSMC, and an outline of the content of the open and closed reports that will be provided to the IDSMC.

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

Any observers must sign a confidentiality agreement on the first occasion they attend a meeting (Appendix 2) 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 Trial Management Group or Trial Steering Committee who have already signed a Terms of Reference document, as these contain confidentiality agreements.

**Conflict of Interest**

The IDSMC membership has been restricted to individuals free of apparent significant conflicts of interest. The source of these conflicts may be financial, scientific or regulatory in nature. Involvement in other trials or intellectual investment could be relevant. Thus, neither study investigators nor individuals employed by the sponsor, nor individuals who might have regulatory responsibilities for the trial products, are members of the IDSMC. Members will have to sign Appendix 1 which states that members do not have any conflicts of interest and that all information discussed within the closed reports will remain confidential to the IDSMC members and the Trial Statisticians who attend closed meetings.

If a conflict of interest is declared by an IDSMC member during the course of the trial, the Trial Manager should 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

**Role of the IDSMC**

The role of the ISDMC is to monitor project data at specified timepoints, including the following *amend as appropriate*:

* 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 efficacy and safety outcome measures
* recommending or advising on any major changes to the protocol, where necessary (e.g. changes to the recruitment procedures, inclusion criteria, endpoints, data collection etc.)
* requesting additional data analyses for monitoring purposes of the IDSMC
* assessing the impact and relevance of any external evidence provided
* monitoring compliance with previous IDSMC recommendations
* monitoring planned sample size assumptions
* recommending whether the trial should continue to recruit or follow-up (see section on decision-making)

The IDSMC Chair is expected to facilitate and summarise discussions. The IDSMC statistician will provide independent statistical expertise. The IDSMC clinician will provide independent clinical expertise.

The IDSMC is the only oversight committee to have access to unblinded comparative data during the course of the research project.

The IDSMC will be advisory to the Trial Steering Committee (TSC). The TSC will be responsible for promptly reviewing the IDSMC recommendations, to decide whether to continue or terminate the trial, and to determine whether amendments to the protocol or changes in study conduct are required.

## Membership Of The IDSMC

**IDSMC Members**

*In addition to the below example wording, 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 wording adapted.*

Membership of the IDSMC is comprised of 3 or 4 independent[[1]](#footnote-1) members, of whom one person is appointed as Chair. This is a multidisciplinary group consisting of at least one statistician and at least one clinician that, collectively, have experience in the management of <area of medicine that is subject of study> and in the conduct of randomised clinical trials.

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

Members of the IDSMC are detailed in the trial name Oversight Committee Membership Log.

**Other Attendees/Observers**

In addition to the IDSMC members noted above, other persons may attend IDSMC meetings. None of these individuals are considered IDSMC members however and they do not possess any voting rights.

The trial name database will be managed by <*insert details of database management here*>. The trial statistical team, led by the Lead Trial Statistician, is responsible for the production of the reports to the IDSMC (OPEN and CLOSED), will guide the IDSMC through the reports, and may participate in IDSMC discussions.

The Chief Investigator should also be available to attend open sessions of the IDSMC meeting.

In addition to the above attendees, individuals from the Trial Management Group and others involved in running the trial may be required to attend meetings to provide reports and updates. Usually this will be the Trial Manager. Occasionally, observers may also be invited by the Chair.

## Organisation of IDSMC meetings

**Attendance at IDSMC Meetings**

The Trial Manager will liaise with IDSMC members to ensure that the meeting date is suitable for all members to attend. Members who cannot attend in person should be encouraged to attend by teleconference. The CI must try to attend all meetings, especially if major actions are anticipated.

If there is no suitable date for all IDSMC members or members can no longer attend and the meeting cannot be rescheduled then the IDSMC may still meet if quorate for decision-making (see section 10 for details). If the IDSMC is considering recommending major action after such a meeting the IDSMC Chair should talk with the 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/or Trial Statistician and a further teleconference should be arranged with the full IDSMC.

**Frequency of IDSMC Meetings**

The IDSMC should meet at least annually however the frequency of meetings can be increased if required by the risk assessment or planned analyses outlined in the protocol. Meetings should be scheduled prior to the date of the TSC meetings so that the IDSMC Chair can write to the TSC Chair confirming whether any recommendations have been made regarding safety and efficacy. Major trial issues may need to be dealt with between meetings by teleconference or email.

## Format of IDSMC Meetings

Meetings will be arranged by the Trial Manager and will either be face-to-face meetings, tele- or video- conference. To provide a forum for exchange of information among various parties who share responsibility for the successful conduct of the trial, a format for open sessions and closed sessions will be implemented. The intent of this format is to enable the IDSMC to preserve confidentiality while at the same time providing opportunities for interaction between the IDSMC and others who have valuable insights into trial-related issues.

**Open sessions**

The open session may be attended by all attendees of the IDMSC meeting. Contents of the open reports will be agreed in advance between the IDSMC members and the trial statistical team producing the report.

**Closed sessions**

The IDSMC is the only committee that may have access to unblinded comparative data. Closed meetings of the IDSMC will be limited to the independent members of the IDSMC and statisticians and should be conducted separately to the open meeting. Other attendees will not attend this session.

Closed reports will be available only to the IDSMC members attending the closed sessions of the IDSMC meeting. The contents of the report will be agreed in advance between the IDSMC members and the trial statistical team producing the report.

At the end of each closed session, the IDSMC will develop a consensus on its list of recommendations, including that relating to whether the trial should continue.

IDSMC members and trial name statistics team must not share confidential information (closed report and discussion within closed sessions) with anyone outside the IDSMC, including the Chief Investigator.

## Initial IDSMC Meeting

During the first IDSMC meeting members will be asked to:

1. Nominate/Confirm a chair;
2. Decide whether they will be unblinded in their assessment of safety data;
3. Review and approve a draft of the IDSMC charter;
4. 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;
5. Agree on the frequency of future meetings;
6. 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 9 of the charter;
7. Decide how far in advance of future meetings they wish to receive reports and any supporting documentation.

Whether the first meeting has open or closed sessions will be decided in advance of the meeting by the IDSMC members.

## Final IDSMC 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.

## IDSMC Meeting Documentation

**Agenda, Minutes & Reports**

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

The report format and content (both open and closed) will be agreed in advance between the IDSMC members and the trial statistical team producing the report. Closed reports will be available only to the IDSMC members attending the closed sessions of the IDSMC meeting.

The Trial Manager (or agreed delegate) will normally provide minutes of the open meetings however this should be confirmed before the start of the meeting. The open minutes will describe the proceedings in the open session of the IDSMC meeting, and will summarise all recommendations by the IDSMC. The minutes will be stored in the main Trial Master File (TMF).

The Trial Statistician will minute the closed IDSMC meetings and agreement of their accuracy must be sought from all members of the closed session. As these closed minutes may contain unblinded comparative information, it is important that they are not made available to anyone outside the closed IDSMC. The Trial Statistician will store the closed minutes in the closed section of the Trial Statistics File.

The IDSMC Chair will be responsible for ratifying draft minutes (both OPEN and CLOSED).

**Confidentiality of Meeting Documentation**

IDSMC members, attendees and observers are required to securely store copies of the 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 name of responsible organisation/person* will keep a central record of all agendas, minutes, reports and correspondence by trial committees in the TMF (closed reports and minutes will be stored in the closed section of the Trial Statistical File).

## Safety Reporting

It is the responsibility of the CI to notify the IDSMC of any 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 the *insert name of responsible organisation/person* and is detailed in the agreement between Sponsor and *insert name of responsible organisation/person*.

*The timeframe for notifying the IDSMC of these reports should be described here and will be determined at the first meeting of the IDSMC*.

## Decision Making

The IDSMC 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*.

The chair should 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 IDSMC to reach a consensus. If the IDSMC cannot achieve consensus, a vote should be taken, although details of the vote should not be routinely included in the report to the TSC, as it may inappropriately convey information about the state of the trial data.

**Possible Recommendations**

At each meeting of the IDSMC during the conduct of the trial, the IDSMC will make recommendations to the TSC. The possible recommendations are numerous, will be guided in part by statistical monitoring guidelines defined in the trial protocol 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; the IDSMC will be notified of all changes to the protocol or to study conduct. The IDSMC concurrence will be sought on all substantive recommendations or changes to the protocol or study conduct prior to their implementation.

The IDSMC will make a recommendation on the target sample size of the trial if an internal pilot has been undertaken.

The IDSMC Chair should report in writing to the TSC Chair, usually within three weeks after the meeting. This should be copied to the trial account who will ensure they are forwarded to the Chief Investigator and Lead Trial Statistician. The letter to the TSC should not reveal any confidential information.

The TSC is jointly responsible with the IDSMC for safeguarding the interests of participating patients and for the conduct of the trial. Recommendations to amend the protocol or conduct of the study made by the IDSMC will be considered and accepted or rejected by the TSC. The TSC will be responsible for deciding whether to continue or stop the trial based on the IDSMC recommendations.

Recommendations from the IDSMC meetings to *insert name of responsible organisation/person* will also be attached to the Annual Safety Update Report, when appropriate, in accordance with European Commission guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medical products for human use.

**Formal Statistical Stopping Guidelines**

*IDSMC review the trial data and make recommendations to the TSC about what they have seen. To complete from trial protocol or remove section if not applicable for the trial*.

## 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 Oversight Committee Membership Log.

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

*please adapt diagram as required for your study*

**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 to 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 TSC members), a confidentiality agreement will be required to be signed prior to the meeting or receiving any documentation (see Appendix 2).

## After The Trial

**Publication of Results**

The Chief Investigator has responsibility for ensuring that trial results will be published in a correct and timely manner. The TSC is the committee that should oversee this process

**Post-publication Constraints**

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

**IDSMC Information for Trial Reports**

IDSMC members will be named (unless they specifically ask not to be) in the primary published report. A brief summary of the timings and conclusions of IDSMC meetings should be included in the body of this paper.

**IDSMC Review of Publications**

The IDSMC members should be given at least two weeks, and if possible a month, to read and comment on any draft publications that report outcome measures and/or details of the IDSMC. This may be done simultaneously to other groups reviewing the draft manuscript (e.g. TSC, trial investigators).

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

**Trial name Independent Data Safety Monitoring Committee: Agreement to join the Independent Data Safety Monitoring Committee as an independent member and disclosure of potential competing interests**

By signing below, you agree to the following statements:

1. I have read this Charter (version and date as per the foot of this page), I understand it, and I will work according to it. I will also work consistently with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable laws and regulations.
2. I agree to keep in confidence all information generated as result of or related to the trial, including without limitation safety data, study observations, study progress and relations to third parties, including regulatory authorities and ethical committees. The undertaking and obligation to maintain confidentiality shall survive the term of this agreement by five years. This provision shall not preclude either the Member nor Institutions from informing third parties about Member’s membership of the Committee.
3. My obligation to maintain confidentiality shall not apply to communications between or among Committee members, Committee members and Institutions directors and/or officers, and/or – at the request of Institutions – Committee members and regulatory authorities or other relevant third parties authorised by Institutions, provided that the Committee members in any communication with any regulatory authority or authorised third party shall instruct the authority or the third party to maintain confidentiality to the extent permitted by law.
4. The obligation to maintain confidentiality as set out in clause 3 shall not apply to information, which by other interests than the recipient, and without the recipient disclosing any information to such interests, has been:
5. made generally available to the public by third parties or the disclosing party;
6. published by or with the consent of the disclosing party, e.g. by publication in scientific periodicals or at meetings, seminars or symposiums;
7. made available to the public by a third party who did not acquire directly or indirectly the information from the Member and/or Institutions;
8. required by any law, rule, regulation, decision, order, subpoena or other process to be disclosed. If such disclosure is requested, the party receiving such a request will promptly notify the other party of such request.

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

|  |  |
| --- | --- |
|  | No, I have no potential competing interests to declare. The source of these conflicts may be financial, scientific or regulatory in nature. I confirm that I am not involved in any other trial or intellectual investment that could be relevant. I confirm that I will not trade in stock of companies affected by the trial until the results are public knowledge. I confirm that I do not have regulatory responsibilities for the trial products. If I develop any significant conflicts of interest during the course of the trial I should resign from the IDSMC. |
|  | 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.**

## Appendix 2: Confidentiality agreement for observers

**Trial name Independent Data Safety Monitoring Committee: Agreement to attend the Independent Data Safety Monitoring Committee and treat all information confidentially**

By signing below, I agree to the following statements:

1. I have read and understood the Trial name IDSMC Charter (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 IDSMC 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. *Should 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 IDSMC members by the trial statistician, however the IDSMC may also present external data of which they have become aware. [↑](#footnote-ref-2)