The [Study Title] Data Monitoring Committee Charter

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| **Study Title:** |  |
| **Chief Investigator:** |  |
| **EudraCT Number:** |  |
| **Sponsor:** | University of Edinburgh & NHS Lothian |

*This Data Monitoring Committee (DMC) charter template will be used for studies that are sponsored or co-sponsored by the University of Edinburgh and/or NHS Lothian only.*

*As a template, sections may be adapted to suit the requirements of each study and some sections may not apply to all studies and can therefore be removed.*

*This charter template is based on the DAMOCLES Study Group. A proposed charter for clinical trial data monitoring committees: helping them to do their job well. The Lancet 2005; vol 365: 711-722*

*It should be noted that there are various models for statistical input, of which two are:*

*An unblinded statistician prepares unblinded DMC reports but does not advise the Trial Steering Committee (TSC). The blinded statistician who advises the TSC is often the senior trial statistician.*

*An unblinded statistician prepares the unblinded DMC reports and also advises the TSC.*

*The template is written with the first model in mind however, authors of DMC charters can adapt this template to fit the second, or other models, as required.*

**Approval Signatures:**

The following individuals, by providing their signatures, indicate their understanding of and willingness to comply with the roles and responsibilities assigned to them in this Charter.

1. DMC Chair:

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PRINT NAME SIGNATURE DATE

1. DMC Member:

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PRINT NAME SIGNATURE DATE

1. DMC Member:

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PRINT NAME SIGNATURE DATE

1. Chief Investigator:

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PRINT NAME SIGNATURE DATE

1. [Trial/Unblinded] Statistician: Consider model to be followed as detailed in preamble

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# Introduction

* Objectives of trial, including interventions being investigated from the protocol
* Outline of scope of charter. Illustrative example;

*The Charter will define the primary responsibilities of the DMC, its membership, and the purpose and timing of its meetings. The Charter will also provide the procedures for ensuring confidentiality and proper communication, the statistical monitoring guidelines to be implemented by the DMC, and an outline of the content of the Open and Closed Reports that will be provided to the DMC.*

Roles and Responsibilities

* A broad statement of the aims of the committee.
* Terms of reference
* Specific roles of DMC. Illustrative example;

*The DMC will be responsible for safeguarding the interests of trial participants, potential participants, investigators and sponsor; assessing the safety and efficacy of the interventions during the trial; reviewing external evidence with an impact on risk/benefit balance and for monitoring the overall conduct of the clinical trial. Generally the CI identifies any relevant external evidence and passes this to the DMC Chair for review by the DMC. The DMC will provide recommendations about stopping, modifying or continuing the trial to the Trial Steering Committee (TSC). To contribute to enhancing the integrity of the trial, the DMC may also formulate recommendations relating to the selection, recruitment, or retention of participants, or their management, or to improving their adherence to protocol-specified regimens and retention of participants, and the procedures for data management and quality control.*

*The DMC will be advisory to the TSC. The TSC will be responsible for promptly reviewing the DMC 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.*

Before or early in the trial

* Whether the DMC will have input into the protocol. All potential DMC members should have sight of the protocol/outline before agreeing to join the committee. Before recruitment begins the trial will have undergone review by the funder/sponsor (e.g. peer review for public sector trials), scrutiny by other trial committees and a research ethics committee. Therefore, if a potential DMC member has major reservations about the trial (e.g. the protocol or the logistics) they should report these to the trial office and may decide not to accept the invitation to join. DMC members should be independent and constructively critical of the ongoing trial, but also supportive of aims and methods of the trial.
* Whether the DMC will meet before the start of the trial. It is recommended that, if possible, the DMC meets before the trial starts or early in the course of the trial, to discuss the protocol, trial, analysis plan, future meetings and have the opportunity to clarify any aspects with the Principal Investigators (PIs). The DMC should meet within one year of recruitment commencing. The DMC charter should be signed by members prior to Sponsors Authorisation to Open (SATO) being issued.
* Any specific regulatory issues. The DMC should be aware of any regulatory implications of their recommendations.
* Any other issues specific to the trial (e.g. Phase I studies, dose escalation communication plan to the Sponsor and Investigator Team(s), and if applicable relevant trial committees e.g. TSC/TMG).
* Whether members of the DMC will have a contract. Members of a DMC may be advised to have a contract making clear the need for confidentiality and the liability status of the DMC members. When there is no such contract, DMC members could formally register their assent by confirming (1) that they agree to be on the DMC and (2) that they agree with the contents of this Charter by signing.

Composition

* Membership and size of the DMC. The DMC chair must have experience of serving on previous DMC(s). Illustrative example;

*The DMC is an independent multidisciplinary group consisting of [clinicians, statisticians] that, collectively, have experience/expertise in the management of patients with [condition(s) relevant to study and anticipated adverse effects] and in the conduct and monitoring of randomised clinical trials. University of Edinburgh insurance indemnifies DMC members for their work on the committee. As stated in the preamble, this template applies to University of Edinburgh/NHS Lothian sponsored or co-sponsored studies only.*

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| --- | --- | --- |
| **Name of Member** | **Role on DMC** | **Responsibility** |
| *[Insert name]* | Chair of DMC | *[Insert basic responsibility]* |
| *[Insert name]* | Independent DMC statistician | *[Insert basic responsibility]* |
| *[Insert name]* | Independent clinician [insert specialty] | *[Insert basic responsibility]* |
| *[Insert name]* | *[Other members]* | *[Insert basic responsibility]* |

# Relationships

* Relationships with PIs, other trial committees (e.g. TSC or Executive committee), Sponsor and regulatory bodies.
* Clarification of whether the DMC are advisory (make recommendations) or executive (make decisions).
* Any payments to DMC members (e.g. travel/accommodation).
* The need for DMC members to disclose information about any competing interests. Illustrative example;

*DMC membership is restricted to individuals free of relevant significant conflicts of interest. The source of these conflicts may be financial, scientific or regulatory in nature. Individuals who fulfil any of the following criteria are automatically disqualified from membership: the study Investigators, individuals with conflicts of interest as determined by the Chair of the DMC.*

*The DMC members will disclose to fellow members any consulting agreements or financial interests they have with University of Edinburgh, NHS Lothian or the manufacturing license holder of an Investigational Medicinal Product (IMP)/medical device subject to investigation during the study. The DMC will be responsible for deciding whether these consulting agreements or financial interests materially impact their objectivity.*

*The DMC members will be responsible for advising fellow members of any changes in these consulting agreements and financial interests that occur during the course of the trial. Any DMC member who thinks they may have developed a relevant significant conflict of interest during the course of the trial must declare this. If the other DMC members consider it to be a relevant significant conflict of interest, the member should resign from the DMC.*

*DMC membership is normally for the duration of the clinical trial. If any member leaves the DMC during the course of the trial, the Sponsor, in consultation with the TSC and/or Investigators will promptly appoint their replacement.*

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# Organisation of DMC Meetings

* Expected frequency of DMC meetings. It is recommended that the DMC meet at least yearly. There may be fixed points within the study design which require DMC oversight example e.g. review of interim clinical data for dose escalation recommendations or interim analysis.
* Whether meetings will be face-to-face or by teleconference. It is recommended that all meetings should be face-to-face if possible, with teleconference as a second option.
* How DMC meetings will be organised, especially regarding open and close sessions, including who will be present in each sessions. Commonly, only DMC members and others whom they specifically invite, e.g. the unblinded statistician, are present in closed sessions. In open sessions, all those attending the closed session are joined by the PI(s), and sometimes the Trial Manager, Trial Statistician, other trial staff and representatives of the Sponsor, funder, or regulator, as relevant. Illustrative example;

*Sessions involving only DMC membership (but often including the unblinded statistician as well, as a non-voting member) called Closed Sessions will be held to allow discussion of confidential data from the clinical trial, including information about the relative efficacy and safety of interventions. In order to ensure that the DMC will be fully informed in its primary mission of safeguarding the interest of participating patients, the DMC [will/will not] be [unblinded/partially unblinded] in its assessment of safety and efficacy data. Not all DMCs perform their reviews while fully unblinded. This will vary by trial. During these sessions, the DMC will develop a consensus on its list of recommendations, including that relating to whether the trial should continue.*

*DMC members and all other participants in the closed* session *of DMC meetings and the production of unblinded reports are expected to maintain confidentiality, and will refrain from revealing to the TSC, or any other party, information that would lead to compromising the integrity of the trial unless such release is required to protect patient safety.*

*In order to allow the DMC to have adequate access to information provided by the trial Investigators, or by members of the regulatory authorities, a joint session between these individuals and DMC members (called an Open Session) will be held before the Closed Session. If necessary, a further Open Session can be held, on request either in the middle or end of the Closed Session. Open sessions give the DMC an opportunity to query these individuals about issues that have arisen during their review in the initial Closed Session. With this format, important interactions are facilitated through which problems affecting trial integrity can be identified and resolved. These individuals will either be present at the DMC meeting or be provided a telephone link.*

# Trial Documentation and Procedures to Ensure Confidentiality and Proper Communication

* Intended content of material to be available in open sessions. Illustrative example;

*Open Reports, available to all who attend the DMC meeting, will include data on recruitment and baseline characteristics; pooled data on eligibility violations; completeness of follow-up and compliance. The trial statistician and/or the unblinded statistician will prepare/supervise preparation of these Open Reports.*

* Intended content of material to be available in closed sessions. Illustrative example;

*Closed Reports, available only to those attending the Closed Sessions of the DMC meeting, will include analyses of primary and secondary efficacy endpoints, subgroup and adjusted analyses; analyses of adverse events and symptom severity; and Open Report analyses that are displayed by intervention group. An unblinded statistician, not involved in any decisions relating to the trial, will prepare these Closed Reports.*

* Who will circulate the Open and Closed Reports to the DMC.
* Will the DMC be blinded to the treatment allocation
* Who will see the accumulating data and interim analysis
* Who will be responsible for identifying and circulating external evidence (e.g. from other trials/systematic reviews)
* To whom the DMC will communicate the decisions/recommendations that are reached and how i.e. a communication plan.
* Whether reports to the DMC be available before the meeting or only at/during the meeting. It is usually helpful for the DMC to receive reports at least 2 weeks before any meetings.
* What will happen to the confidential papers after the meeting.

# Decision Making

* What decisions/recommendations will be open to the DMC. Illustrative example;

*At each meeting of the DMC during the conduct of the trial, the DMC will make a recommendation to the TSC. Possible recommendations include:*

* + *Trial continues as planned*
	+ *Dose escalation*
	+ *Early termination of the trial*
	+ *Stopping recruitment within a subgroup*
	+ *Extending recruitment or extending follow-up*
	+ *Sanctioning or proposing protocol changes.*

*The recommendation(s) will be based primarily on safety and efficacy considerations and will be guided by statistical monitoring guidelines defined in this Charter. Should the DMC decide to recommend early termination of the trial, a full vote of the DMC will be required. In the event of a split vote, the decision will go with the majority vote, but a report should be provided to the TSC, written [anonymously] by the DMC members who are in the minority, for the purposes of officially stating their position on the issue. This report should not include unblinded data unless deemed necessary by the DMC. This information should be forwarded to the trial chief investigator as rapidly as possible.*

*The TSC is jointly responsible with the DMC 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 DMC will be considered and accepted or rejected by the TSC. The TSC will be responsible for deciding whether to continue or to stop the trial based on the DMC recommendations. The DMC will be notified of all changes to the protocol or to study conduct. The DMC concurrence will be sought on all substantive recommendations or changes to the protocol or study conduct prior to their implementation.*

* The role of formal statistical methods, specifically which methods will be used and whether they will be used as guideline or rules. This should include or provide reference to the planned interim analyses and statistical guidelines, i.e. the DMC should review and agree any interim analysis plan.
* How decisions or recommendations will be researched within the DMC. Issues to be specified include the process of decision making, including whether there will be voting or other formal methods of achieving consensus.
* When the DMC is quorate for decision-making. The minimum number of attendees should be specified before the DMC is quorate for decision making.
* Can DMC members who cannot attend the meeting input.
* What happens to members who do not attend meetings.
* Whether different weight will be given to different endpoints (e.g. safety/efficacy)
* Any specific issues relating to the trial design that might influence the proceedings, e.g. cluster trials, equivalence trials, multi-arm trials, phase I trials, Sponsor and Investigator(s) oversight of dose escalations.

# Reporting

* To whom will the DMC report their recommendations/decisions, and in what form i.e. a DMC letter of recommendation. A timescale should be specified.
* Whether minutes of the meeting be made and, if so, by whom, who and to whom they will be circulated, and where they will be kept. Illustrative example;

*The DMC Chair/other designated DMC member will prepare minutes of the DMC meetings. Two sets will be prepared: the Open Minutes and the Closed Minutes.*

*The Open Minutes will describe the proceedings in the Open Session of the DMC meeting and will summarize all recommendations by the DMC. Since these minutes will be circulated immediately to the trial CI and Sponsor, it is necessary that these minutes do not unblind the efficacy and safety data if the DMC is not recommending early termination.*

*The Closed Minutes will describe the proceedings from all sessions of the DMC meeting, including the listing of recommendations by the Committee. Because it is likely that these minutes will contain unblinded information, it is important that they are not made available to anyone outside the DMC. Rather, copies will be kept by [the DMC chair/other designated DMC member]. These will be sent to the trial manager and archived at the time of study closure.*

* What will be done if there is disagreement between the DMC and the body to which it reports.

# After the Trial

* Publication of results.
* The information about the DMC that will be included in published trial reports.
* Whether the DMC will have the opportunity to approve publications, especially with respect to reporting of any DMC recommendation regarding termination of a trial.
* Any constraints on DMC members divulging information about their deliberations after the trial has been published,