

# A proposed charter for clinical trial data monitoring committees: helping them to do their job well

DAMOCLES Study Group\*

*Lancet* 2005; 365: 711–22

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Formal monitoring of data from randomised controlled trials (RCTs) is becoming more common. Wide variation exists in the structure and organisation of data monitoring committees (DMCs), with little guidance on how they should operate. We used various strategies to consider the behavioural, procedural, and organisational aspects of data monitoring in RCTs: systematic reviews of DMCs and small group processes in decision making; surveys of reports of RCTs, recently completed and ongoing RCTs, and the policies of major organisations connected with RCTs; detailed case studies of four DMCs that faced difficult decisions; and interviews with experienced DMC members. The findings aided the development of a template for a charter for DMCs. We summarise the findings and outline the key considerations at every stage of the data monitoring process. Widespread use of a charter for the structure and organisation of DMCs would promote a systematic and transparent approach, and enable them to operate more effectively and efficiently.

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Randomised controlled trials (RCTs) are widely accepted as the principal research method for assessment of the effectiveness of health-care interventions, and monitoring of trial data by data monitoring committees (DMCs) has become common.<sup>1</sup> There are inherent difficulties in decision making when uncertainty exists. Occasionally, DMCs are faced with difficult decisions about the continuation of a major trial, which, in turn, will affect the future evidence base available to guide policy and practice for that clinical setting. Practices in such committees vary widely, however, and no standard approach exists. The UK NHS Health Technology Assessment Programme commissioned the DAMOCLES (DAta MOnitoring Committees: Lessons, Ethics, Statistics) Study Group to investigate the processes of monitoring accumulating trial data and to identify ways of increasing the likelihood that DMCs make good decisions. Several commentators have suggested that any DMC would benefit from the development of a standard operating procedure or charter outlining its mode of operation and the responsibilities of different parties.<sup>1–4</sup> Little explicit guidance has been published on what should be included in such a charter, with the exception of a book by Ellenberg and colleagues.<sup>1</sup> One main aim of the DAMOCLES study was, therefore, to develop a template for a charter to systematically describe the operating practices and procedures of a DMC.

## Research strategy

The DAMOCLES study used several complementary strategies to study behavioural and organisational aspects of DMCs and procedural issues of interim analyses. These are described fully elsewhere.<sup>5</sup> In brief, we used systematic reviews of published work on DMCs and on small group processes in decision-making; surveys of reports of RCTs, of recently completed and ongoing RCTs, and of the policies of major organisations connected with RCTs; detailed case studies of four DMCs in which difficult decisions were faced (including interviews); and interviews with experienced DMC members. At the beginning of the project, we developed a set of

23 questions relating to DMCs, around which the study was structured.<sup>5,6</sup> These questions fell into four main sections: (1) the roles of DMCs; (2) their structure and organisation; (3) what information should be available to DMCs; and (4) decision making and reporting in DMCs. On the basis of the results, we formulated a list of considerations that would be valuable for a DMC to address at the start of a trial. We developed these into a draft charter following the same broad lines as the 23 questions. The draft was piloted on a small number of trials by members of the group and revised in view of this experience.

## The charter

Full details of the systematic review, the results of the surveys, and the systematic review of small group processes in decision making have been reported elsewhere.<sup>5–9</sup> Here we present the proposed DMC charter (see end of article) with short summaries of the key points contributing to each of the charter's ten sections. From the review of published work and the cross-sectional surveys, we could see that various names and descriptors are used to describe the data monitoring process. We propose that groups responsible for data monitoring be given the standard name, Data Monitoring Committee (DMC).

## Section 1. Introduction

See *Panel 1*

The introduction should include the identifying details (eg, trial number) and objectives of the trial, and an outline of the scope of the charter to frame the charter for each specific DMC. A flow diagram of the trial design could also usefully be included (see additional figures and information at end of article).

## Section 2. Roles and responsibilities

See *Panel 2*

From the reviews and the interviews, there was consensus that all parties—DMC members, investigators, and sponsors or funders—can usefully agree in advance many

of the details of how a DMC will operate. The surveys of recently completed trials showed that these terms of reference were of two types: specific guidance about monitoring interim data; or a description of the aims of DMCs in more general terms, such as “consider outcome data from interim analyses”, “consider data about safety and adverse events”, and “report on continuation/stopping/amendment”. When experienced DMC members were interviewed, they commented on the importance of terms of reference when there are difficult decisions to be made. They expressed a desire that time be put aside to agree the aims, terms of reference, and specific roles of the DMC at the beginning of the trial. The charter shows ways to do this.

### Section 3. Before or early in the trial

See [Panel 3](#)

The potential roles for a DMC before trial recruitment starts have received little attention in published work. Issues include whether the DMC will have input into the trial protocol, whether the DMC should meet before data start to accrue, and whether specific issues relate to the trial in question—eg, any regulatory implications of their recommendations that need discussion. People invited to become members of a DMC should only do so on the basis that the trial protocol is acceptable to them, but the need for, and benefits of, a more direct role in the development of the protocol was less clear. The small group processes review and the interviews suggested that an early meeting of a DMC is beneficial, to allow the members to get to know one another, to consider the protocol in detail, and to discuss how the committee might respond to hypothetical situations. Several of these issues will need to be addressed at the first meeting of the DMC, irrespective of when it takes place.

### Section 4. Composition

See [Panel 4](#)

The sizes of DMCs reported in the published work varied considerably: the median number of participants identified in the survey of reports of trials was four members (range 1–8), and the review of published work identified DMCs ranging from three to more than 20 members (although these could include people attending who were not members). The conclusion of the review on small group processes was that size is not likely to change the actual decision made but might affect the quality of the decision-making process (larger committees are more likely to discuss a wider range of alternatives). Very small groups (three or four members) are less likely to represent the full range of opinions and individuals are more likely to dominate, hence poorer quality decisions are more likely. In larger groups (12 or more members), members might be reluctant to express views, conflicts can arise, and there might be a tendency to make riskier decisions. The DMC

members we interviewed thought that the size of the committee should not be more than six members. On balance, a group size of four to five might be appropriate for many DMCs. Choosing an odd number was seen as possibly helpful if voting was to be used in the decision-making process.

An appropriate range of membership was judged important, while keeping the size of the group manageable. Statistical and clinical inputs were deemed essential. Inclusion of more than one clinician could be appropriate; one of the case studies emphasised that over-dependence (or perceived over-dependence) on one clinician can unduly affect decision making. Although individuals with skills in key specialties are essential, the review of published work on small groups suggested that diversity is likely to improve decision making, provided that conflict is handled appropriately. No consensus was reached about ethicist or consumer or lay membership.

DMC members saw the appointment of the Chair of the DMC as crucial. They thought that the Chair should have previous experience of DMC meetings, an understanding of both clinical and statistical issues, experience of chairing meetings, and the ability to facilitate effective interaction in the group. Results from the small group processes review suggested that the Chair can have a big effect on decision outcome and the quality of decision making. Further, sound decision making was more likely if the Chair was facilitating (rather than directive) and impartial (being open to others' opinions and not expressing their own views until after a full discussion). The planned membership and size of the DMC should, therefore, be outlined together with a description of how the Chair is to be chosen.

The review of the published work identified three main models for DMCs. In the first model, all members (defined as those who take part in the decision-making process) are wholly independent of the trial and an independent statistician does the analyses. This model is favoured by the US Food and Drug Agency (FDA)<sup>10</sup> but has been less commonly used than other models, principally because of concerns about the ability of independent statisticians to do appropriate analyses when they are not intimately connected with a trial.

In the second model, one or more people involved in the trial attend some of the meetings, but decision making is limited to independent DMC members. Most typically, the trial's statistician prepares and presents interim analyses to the DMC. The statistician may sit in on the DMC's deliberations or be asked to leave once the report has been presented. If others associated with the trial attend, such as representatives of the investigators or the sponsor, the meeting is often split into open and closed sessions, with confidential information only discussed in closed sessions after these people have left the meeting.

In the third model, most attendees are independent DMC members, but people involved in the trial, especially

the study investigators, participate in decision making and hence, by definition, are members of the DMC. The claimed advantage of involving study investigators in the decision making was that the deeper knowledge of the trial that an investigator brings should increase a DMC's overall competence, while involvement of independent members should protect against biased decision making. The expected roles for the DMC statistician, the trial statistician, and the wider trial team should, therefore, be explicitly defined. Irrespective of the model used, to make an explicit record of any competing interests is advisable.

## Section 5. Relationships

See [Panel 5](#)

An advisory rather than executive function for DMCs was favoured in all parts of the project. A common approach described in the surveys and interviews with the experienced DMC members was for the Chair to report the recommendations of a DMC to the principal investigator(s), trial steering committee, or sponsor, on the basis that the trial organisers are ultimately responsible for the conduct of the trial. The planned relationships between the different trial committees and the sponsor should, therefore, be clearly defined.

## Section 6. Organisation of DMC meetings

See [Panel 6](#)

The most suitable timing for DMC meetings varies from trial to trial and so the frequency should be flexible and at the discretion of the DMC or its chair. Most DMCs have a specified minimum frequency. In the survey of ongoing trials, this period was generally every 6 months or annually, or after a specific number of outcome events. The review of small group processes suggested that face-to-face meetings are likely to be the most effective way for DMC members to communicate. This option was also preferred by the DMC members and respondents to the survey of ongoing trials, especially for the first meeting, for any meeting when a major decision might be made, or for members of multinational DMCs who do not share the same first language. Respondents judged that teleconferences were less satisfactory than face-to-face meetings because they might inhibit communication and hence decision making. However, they are helpful when getting a DMC together is difficult.

Our investigations suggested that, as a general rule, interim trial data should be kept confidential and restricted to the DMC and, if agreed by the DMC, the trial statistician. Emerging trends could well be attributable to chance, and could lead to premature or false conclusions or both. Trial participants or the clinicians involved in recruitment might then leave the trial, which would fail to provide a clear and reliable answer to the question being addressed. Also, others with a vested interest in the results, such as a sponsor, might withdraw support, leading to inappropriate early termination. However, open sessions with the trial investigators, sponsors, or both to

discuss general issues, such as recruitment rates, were deemed useful, and a combination of open and closed sessions is recommended. Plans for the frequency, format, and organisation of meetings, therefore, should be outlined.

## Section 7. Trial documentation and procedures to ensure confidentiality and proper communication

See [Panel 7](#)

Experienced DMC members emphasised the value of early discussions about the content of the reports to the DMC and the importance of being given the right information. The review of small group decision making suggested that too much detail could increase the likelihood of making a wrong decision—too much information might obscure the underlying theme(s) within the data. The small group processes review suggested that DMCs should be given all information about benefits and risks in a balanced and accessible way, since incomplete disclosure could affect decision making. Whether the treatment groups should be masked in DMC reports was a controversial issue. Although some argued in favour of masking on the basis that it might prevent inappropriate premature decisions, most commentators felt that masking hampers the DMC from doing its job properly, because knowledge of the allocation is needed for adequate monitoring of some aspects of data (eg, consideration of adverse events). The general conclusion from the published work was that the DMC should receive the report in advance because members then have a chance to read it thoroughly; DMC members endorsed this view. The planned content and distribution of DMC documentation should, therefore, be outlined to clarify who will have access to both the open and closed reports, and when.

## Section 8. Decision making

See [Panel 8](#)

From the review of published work, the main options available to a DMC are to recommend that the trial should: (1) stop wholly or partly (eg, stopping one arm of a multiarm trial); (2) continue with modification; or (3) continue without modification. The implications of a decision to stop a trial will differ depending on the stage of the trial—eg, during the recruitment phase, a decision to stop might mean accrual of patients being stopped and early release of trial data, whereas a decision to stop during the follow-up phase might only result in early release of trial data. At the outset, a DMC should understand the range of options open to it and the implications that these would have for the trial. There were few suggestions made in the published work as to how DMCs should reach their decisions and recommendations. The review of small group processes suggested that standards of proof should be explicit. Decisions should be achieved by consensus and be unanimous when possible, with voting encouraged only as a way of reaching consensus and after a full

discussion. This review also suggested that both informal and formal decision-making strategies (eg, devil's advocacy, Delphi technique, Nominal Group technique) might be useful for DMCs, especially when the information is complex, but further investigation is needed on this issue.

Statistical issues should be only one of several considerations that a DMC needs to take into account. Other considerations include the balance of primary risks and benefits, the internal consistency of results, the consistency with, and nature of, external evidence, and the likelihood that the results would affect clinical practice. Statistical criteria (often called stopping rules) should be agreed in advance and regarded as guidelines for recommending stopping rather than rules. Other procedural issues that can usefully be defined include when the DMC has sufficient members to make decisions, what input DMC members who cannot attend might have, and what action (if any) should be taken about members who regularly do not attend meetings.

### Section 9. Reporting

See [Panel 9](#)

The review of published work and the surveys suggested that DMCs usually report to the principal investigator, the trial steering committee, the sponsor, or the investigators (in the form of a representative executive committee). There was almost unanimous agreement that a formal record should be made of both closed and open sessions, and some funders (including the UK Health Technology Assessment Programme) now require this. The record should document the major points of discussion, any decisions and actions and their reasons, and any additional information needed for future meetings. The review of the published work suggested that names do not need to be attributed to all comments. Both international good clinical practice guidelines (ICH E9)<sup>11</sup> and the draft US FDA guidance<sup>10</sup> documents suggest that minutes of DMC meetings are expected and state that in regulatory trials all minutes should be submitted to the regulatory authorities.

A meeting between the DMC and the trial steering committee or sponsor usually takes place when a DMC recommends stopping recruitment, and this meeting usually leads to agreement (occasionally this is to continue the trial). Rare instances have arisen when the trial steering committee or the sponsor has disagreed with the DMC recommendation. In these situations, an alternative group might be convened to resolve any disagreement. This group could include members of the DMC, members of the trial steering committee, representatives of the sponsor, and independent members. Such independent resolution could prevent conflicts escalating, and could also protect the trial steering committee if a decision is taken to continue a trial despite an earlier DMC recommendation to close.

### Section 10. After the trial

See [Panel 10](#)

The possible involvement of the DMC in publication of the trial results has received little attention. Failure to report a trial can be judged a form of scientific misconduct,<sup>12</sup> and some commentators have suggested that it is the DMC's responsibility to ensure that reporting occurs. Because ultimate responsibility rests with the trial organisers or trial steering committee, the charter might specify what the DMC would do to encourage timely reporting. DMC members might also wish to see any statement describing the role of the DMC, and might wish to read and comment on reports. The role of the DMC after the trial should be explicit.

### Comment

The DAMOCLES study used a combination of research strategies to consider the behavioural, procedural, and organisational aspects of data monitoring in RCTs. The study drew on a wide range of work, from publications directly addressing the working of DMCs to psychological research on processes that aid small group decision making. The surveys provided empirical evidence of previous and current DMC practices, and the interviews and case studies provided valuable insights into the factors affecting decision making. The results of the DAMOCLES study showed that there was wide variation in the membership, composition, and practices of DMCs. The charter proposed in this paper aims to promote a systematic and transparent approach to the structure and operation of DMCs. We recommend that a detailed charter is prepared for every DMC before the start of the trial. Although there is nothing especially innovative in the charter itself, it sets out (in a structured manner) the issues that need to be considered, and issues that we believe are not considered systematically by most DMCs. A worked example of the charter is available on the internet.<sup>13</sup>

The discussion of DMC procedures has increased appreciably, especially after the publication in 2002 of the book by Ellenberg and colleagues,<sup>1</sup> which also includes a template for a charter. There is some degree of complementarity between the two charters as both address similar issues. The charter presented in this paper is, however, based on the results of a broad research project and generally provides more detailed discussion of each section. There are notable exceptions to this; for example, Ellenberg and colleagues<sup>1</sup> provide greater detail on what might be included in the report from the trial statistician than we do. The introduction of standardised procedures has proved beneficial in other specialties. The introduction of the CONSORT statement<sup>14,15</sup> has led to improved reporting quality.<sup>16-18</sup> We believe that the wide adoption of a charter such as the one we describe will lead to similar improvements in the practice of DMC decision making.

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**Contributors**

All authors contributed to the interpretation and reporting of all aspects of the project. M K Campbell, D G Altman, M R Sydes, and A M Grant led the development and reporting of the charter. M R Sydes, D G Altman, A G Babiker, M K B Parmar, and D J Spiegelhalter led the systematic review of the published work on DMCs and the cross-sectional study of reported use of DMCs in trial reports. A E Walker and S K McLeer led the overview of reviews of small group processes relevant to DMCs, the detailed case studies, and interviews with experienced DMC members. F Clemens, D R Elbourne, J H Darbyshire, and S J Pocock led the surveys of completed and ongoing RCTs, and of major organisations involved in RCTs. S A Wallace undertook the published work searches. A M Grant convened the group and is guarantor of the project.

**Conflict of interest statement**

We declare that we have no conflict of interest.

**Acknowledgments**

We thank members of the DMCs of the Medical Research Council RE04 and the CESAR trials for comments on earlier drafts of the charter. The DAMOCLES study was funded by the UK NHS Health Technology Assessment Programme. The Health Services Research Unit is funded by the Chief Scientist Office of the Scottish Executive Health Department. The views expressed are not necessarily those of the funding bodies. The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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**Panel 1: Introduction****Content**

Name (and sponsor's ID) of trial plus ISRCTN and/or EUDRACT number

Objectives of trial, including interventions being investigated

Outline of scope of charter

**Comments from DAMOCLES and illustrative examples**

Insert name (and sponsor's ID) of trial and registration number (eg ISRCTN and/or EUDRACT number)

Insert objectives of trial, including interventions being investigated from protocol. Suggest including a flow chart of the trial design (insert as figure 1).

Summary of the purpose and content of this document.

*Illustrative example:*

*The purpose of this document is to describe the roles and responsibilities of the independent DMC for the [--give name--] trial, including the timing of meetings, methods of providing information to and from the DMC, frequency and format of meetings, statistical issues and relationships with other committees.*



### Panel 2: Roles and responsibilities

#### Content

A broad statement of the aims of the committee

#### Comments from DAMOCLES and illustrative examples

*Illustrative example:\**

*"To protect and serve [trial] patients (especially re: safety) and to assist and advise Principal Investigators so as to protect the validity and credibility of the trial."*

*"To safeguard the interests of trial participants, assess the safety and efficacy of the interventions during the trial, and monitor the overall conduct of the clinical trial."*

#### Terms of reference

*Illustrative example:\**

*The DMC should receive and review the progress and accruing data of this trial and provide advice on the conduct of the trial to the Trial Steering Committee.*

*The DMC should inform the Chair of the steering committee if, in their view:*

*(i) the results are likely to convince a broad range of clinicians, including those supporting the trial and the general clinical community, that on balance one trial arm is clearly indicated or contraindicated for all participants or a particular category of participants, and there was a reasonable expectation that this new evidence would materially influence patient management; or (ii) it becomes evident that no clear outcome would be obtained."*

#### Specific roles of DMC

Interim review of the trial's progress including updated figures on recruitment, data quality, and main outcomes and safety data.

A selection of specific aspects could be compiled from the following list:-

- assess data quality, including completeness (and by so doing encourage collection of high quality data)

- monitor recruitment figures and losses to follow-up

- monitor compliance with the protocol by participants and investigators

- monitor organisation and implementation of trial protocol (the DMC should only perform this role in the absence of other trial oversight committees)

- monitor evidence for treatment differences in the main efficacy outcome measures

- monitor evidence for treatment harm (eg, toxicity data, SAEs, deaths)

- decide whether to recommend that the trial continues to recruit participants or whether recruitment should be terminated either for everyone or for some treatment groups and/or some participant subgroups

- suggest additional data analyses

- advise on protocol modifications suggested by investigators or sponsors (eg, to inclusion criteria, trial endpoints, or sample size)

- monitor planned sample size assumptions

- monitor continuing appropriateness of patient information

- monitor compliance with previous DMC recommendations

- consider the ethical implications of any recommendations made by the DMC

- assess the impact and relevance of external evidence

\*Based on real trial protocols.

### Panel 3: Before or early in the trial

#### Content

Whether the DMC will have input into the protocol

#### Comments from DAMOCLES and illustrative examples

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 (eg, 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 (eg, 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.

**Panel 3: (continued)**

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, the trial, any analysis plan, future meetings, and to have the opportunity to clarify any aspects with the principal investigators. The DMC should meet within one year of recruitment commencing.
Any issues specific to the disease under study	Consideration should be given to an initial "dummy" report, including the use of shell (empty) tables, to familiarise the DMC members with the format that will be used in the reports. Issues specific to the disease under study should be described.
Any specific regulatory issues	The DMC should be aware of any regulatory implications of their recommendations.
Any other issues specific to the treatment under study	Issues specific to the treatment under study should be described.
Whether members of the DMC will have a contract	Members of a DMC, particularly for a commercially sponsored trial, 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.

**Panel 4: Composition**

<b>Content</b>	<b>Comments from DAMOCLES and illustrative examples</b>
Membership and size of the DMC	Membership should consist of a small number of members (perhaps four to five), who include at least one clinician experienced in the clinical area and at least one statistician. Additional members experienced in clinical trials should reflect the other specialties involved in the trial. Consideration may be given to consumer representation. In the case of inter-group trials or trials with international collaboration consideration should be given to a broad representation. The members should be independent of the trial (eg, should not be involved with the trial in any other way or have some competing interest that could impact on the trial). Any competing interests, both real and potential, should be declared. A short competing interest form should be completed and returned by the DMC members to the trial coordinating centre (Annex 1).  The members of the DMC for this trial are: (1) [---give name---] (2) [---give name---] (3) [---give name---]  It may be helpful to provide the trial coordinating centre with brief personal details (say, one paragraph) of all DMC members especially relating to experience relevant to the trial and to the operation of DMCs (such information need not be contained within the Charter).
The Chair, how they are chosen and the Chair's role. (Likewise, if relevant, the vice-Chair)	The Chair should have previous experience of serving on DMCs and experience of chairing meetings, and should be able to facilitate and summarise discussions. The Chair is sometimes chosen by the sponsor or the investigators running the trial and sometimes by the DMC members themselves. The Chair is expected to facilitate and summarise discussions.
The responsibilities of the DMC statistician	The DMC membership will include a statistician to provide independent statistical expertise.
The responsibilities of the trial statistician	The trial statistician, [---give name---] will produce (or oversee the production of) the report to the DMC and will participate in DMC meetings, guiding the DMC through the report, participating in DMC discussions and, on some occasions, taking notes.
The responsibilities of the trial office team	The trial office team (eg, Trial Manager, etc) usually only inputs to the production of the non-confidential sections of the DMC report.
The responsibilities of the PI and other members of the Trial Management Group (TMG)	The PI may be asked, and should be available, to attend open sessions of the DMC meeting. The other TMG members will not usually be expected to attend but can attend open sessions when necessary (See Organisation of DMC Meetings).

### Panel 5: Relationships

#### Content

Relationships with Principal Investigators, other trial committees (eg, Trial Steering Committee (TSC) or Executive Committee), sponsor and regulatory bodies

Clarification of whether the DMC is advisory (makes recommendations) or executive (makes decisions)

Payments to DMC members

The need for DMC members to disclose information about any competing interests

#### Comments from DAMOCLES and illustrative examples

A diagram can help to clarify relationships when there are several inter-related committees. A short statement of the responsibilities of the other committees should be given if these are not provided in the protocol.

It is customary that the DMC does not make decisions about the trial, but rather makes recommendations to an appropriate executive committee or its Chair.

Members should be reimbursed for travel and accommodation. Any other payments or rewards should be specified.

Competing interests should be disclosed. 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. (See Annex 1)

DMC members should not use interim results to inform trading in pharmaceutical shares, and careful consideration should be given to trading in stock of companies with competing products.

### Panel 6: Organisation of DMC meetings

#### Content

Expected frequency of DMC meetings

Whether meetings will be face-to-face or by teleconference

How DMC meetings will be organised, especially regarding open and closed sessions, including who will be present in each session

#### Comments from DAMOCLES and illustrative examples

The exact frequency of meetings will depend upon any statistical plans specified, and otherwise on trial events. The wishes of the DMC and needs of the trial office will be considered when planning each meeting. It is recommended that the DMC meet at least yearly.

The first meeting should ideally be face-to-face to facilitate full discussion and allow members to get to know each other. It is recommended that all subsequent meetings should be face-to-face if possible, with teleconference as a second option.

A mixture of open and closed sessions is recommended. Closed and open sessions should be defined. Commonly, only DMC members and others whom they specifically invite, eg, the trial statistician, are present in closed sessions. In open sessions all those attending the closed session are joined by the PI(s), and/or the head of the trials office, and sometimes also representatives of the sponsor, funder, or regulator, as relevant.

The format of the meetings should be described.

*Illustrative example:*

1. Open session: Introduction and any "open" parts of the report
2. Closed session: DMC discussion of "closed" parts of the report and, if necessary,
3. Open session: Discussion with other attendees on any matters arising from the previous session(s)
4. Closed session: extra closed session

### Panel 7: Trial documentation and procedures to ensure confidentiality and proper communication

#### Content

Intended content of material to be available in open sessions

#### Comments from DAMOCLES and illustrative examples

*Illustrative example:*

Open sessions: Accumulating information relating to recruitment and data quality (eg, data return rates, treatment compliance) will be presented. Toxicity details based on pooled data will be presented and total numbers of events for the primary outcome measure and other outcome measures may be presented, at the discretion of the DMC.



**Panel 7: (continued)**

Intended content of material to be available in closed sessions	<p><i>Illustrative example:</i>  <i>Closed sessions: In addition to all the material available in the open session, the closed session material will include efficacy and safety data by treatment group.</i></p>
Whether or not the DMC will be blinded to the treatment allocation	Blinding is generally not recommended for DMC members, although opinions vary.
The people who will see the accumulating data and interim analysis	<p>These should be specified.</p> <p>DMC members do not have the right to share confidential information with anyone outside the DMC, including the PI.</p>
Responsibility for identifying and circulating external evidence (eg, from other trials/systematic reviews)	Identification and circulation of external evidence (eg, from other trials/systematic reviews) is not the responsibility of the DMC members. The PI or the trials office team will usually collate any such information.
To whom the DMC will communicate the decisions/recommendations that are reached	The DMC usually reports its recommendations in writing to the Trial Steering Committee or sponsor's representative. This should be copied to the trial statistician (or trial manager) and if possible should be sent via the trials office in time for consideration at a TSC meeting. If the trial is to continue largely unchanged then it is often useful for the report from the DMC to include a summary paragraph suitable for trial promotion purposes. (See Annex 2.)
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 the report at least 2 weeks before any meetings. Depending on the trial, it may sometimes be preferable for all papers to be brought to face-to-face meetings by the trial statistician; time would then be needed for DMC members to assimilate the report.
What will happen to the confidential papers after the meeting	<p><i>Illustrative examples:</i></p> <ol style="list-style-type: none"> <li>1. <i>The DMC members should destroy their reports after each meeting. Fresh copies of previous reports will be circulated with the newest report before each meeting.</i></li> <li>2. <i>The DMC members should store the papers safely after each meeting so they may check the next report against them. After the trial is reported, the DMC members should destroy all interim reports.</i></li> </ol>

**Panel 8: Decision making**

Content	Comments from DAMOCLES and illustrative examples
What decisions/recommendations will be open to the DMC	<p>Possible recommendations could include:-</p> <ul style="list-style-type: none"> <li>No action needed, trial continues as planned.</li> <li>Early stopping due, for example, to clear benefit or harm of a treatment, futility, or external evidence.</li> <li>Stopping recruitment within a subgroup.</li> <li>Extending recruitment (based on actual control arm response rates being different to predicted rather than on emerging differences) or extending follow-up.</li> <li>Stopping a single arm of a multi-arm trial.</li> <li>Sanctioning and/or proposing protocol changes.</li> </ul>
The role of formal statistical methods, specifically which methods will be used and whether they will be used as guidelines or rules	<p>This Charter should include or provide reference to the planned interim analyses and statistical guidelines, ie, the DMC should review and agree any interim analysis plan.</p> <p>Formal statistical methods are more generally used as guidelines rather than absolute rules. This is because they generally only consider one dimension of the trial. Reasons should be recorded for disregarding a stopping guideline.</p>
How decisions or recommendations will be reached within the DMC	<p>Issues to be specified can include:</p> <ul style="list-style-type: none"> <li>The decision making methods and criteria that will be adopted for guiding deliberations.</li> <li>The process of decision making, including whether there will be voting or other formal methods of achieving consensus. The method of deliberation should not be revealed to the overseeing committee as this may reveal information about the status of the trial's data.</li> <li>The role of the Chair - to summarise discussions and encourage consensus; it may be best for the Chair to give their own opinion last.</li> </ul>

**Panel 8: (continued)**

	<p>It is recommended that every effort should be made for the DMC to reach a unanimous decision. If the DMC cannot achieve this, a vote may be taken, although details of the vote should not be routinely included in the report to the TSC as these may inappropriately convey information about the state of the trial data.</p> <p>It is important that the implications (eg, ethical, statistical, practical, financial) for the trial be considered before any recommendation is made.</p>
When the DMC is quorate for decision-making	<p>There should be a minimum number of attendees before the DMC is quorate for decision making; this should be specified.</p> <p><i>Illustrative example*:</i></p> <p><i>"Effort should be made for all members to attend. The trials office team will try to ensure that a date is chosen to enable this. Members who cannot attend in person should be encouraged to attend by teleconference. If, at short notice, any DMC members cannot attend at all then the DMC may still meet if at least one statistician and one clinician, including the Chair (unless otherwise agreed), will be present. If the DMC is considering recommending major action after such a meeting the DMC 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 DMC."</i></p>
Can DMC members who cannot attend the meeting input	<p>If the report is circulated before the meeting, DMC members who will not be able to attend the meeting may pass comments to the DMC Chair for consideration during the discussions.</p>
What happens to members who do not attend meetings	<p><i>Illustrative example:</i></p> <p><i>If a member does not attend a meeting, it should be ensured that the member is available for the next meeting. If a member does not attend a second meeting, they should be asked if they wish to remain part of the DMC. If a member does not attend a third meeting, they should be replaced.</i></p>
Whether different weight will be given to different endpoints (eg, safety/efficacy)	<p>This should be specified and will depend on the trial.</p>
Any specific issues relating to the trial design that might influence the proceedings, eg, cluster trials, equivalence trials, multi-arm trials	<p>These should be specified and will depend on the trial.</p>

**Panel 9: Reporting**

<b>Content</b>	<b>Comments from DAMOCLES and illustrative examples</b>
To whom will the DMC report their recommendations/decisions, and in what form	<p>Usually, this will be a letter to the Trial Steering Committee or Sponsor's representative. A timescale should be specified, eg, usually within 3 weeks. It is helpful if a copy of this is lodged with the trial office.</p>
Whether minutes of the meeting be made and, if so, by whom and where they will be kept	<p>These details should be specified (separate records may be required for open and closed sessions). The DMC Chair should sign off any minutes or notes.</p>
What will be done if there is disagreement between the DMC and the body to which it reports	<p>Specify which committee has primacy or how disagreement will be resolved, eg, a further committee may be convened to adjudicate.</p> <p><i>Illustrative example:</i></p> <p><i>"If the DMC has serious problems or concerns with the TSC decision a meeting of these groups should be held. The information to be shown would depend upon the action proposed and the DMC's concerns. Depending on the reason for the disagreement confidential data will often have to be revealed to all those attending such a meeting. The meeting should be chaired by a senior member of the trials office staff or an external expert who is not directly involved with the trial."</i></p>

**Panel 10: After the trial****Content**

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

**Comments from DAMOCLES and illustrative examples**

At the end of the trial there may be a meeting to allow the DMC to discuss the final data with principal trial investigators/sponsors and give advice about data interpretation. The DMC may wish to see a statement that the trial results will be published in a correct and timely manner.

DMC members should be named and their affiliations listed in the main report, unless they explicitly request otherwise. A brief summary of the timings and conclusions of DMC meetings should be included in the body of this paper.

The DMC may wish to be given the opportunity to read and comment on any publications before submission.

It should be specific when the DMC may discuss issues from their involvement in the trial, eg, 12 months after the primary trial results have been published, or when permission is agreed with the overseeing committee.

**Annex 1: Suggested competing interests form****Potential competing interests of Data Monitoring Committee members for [Insert trial name (and sponsor's ID)]**

The avoidance of any perception that members of a DMC may be biased in some fashion is important for the credibility of the decisions made by the DMC 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) DMC member should remove the conflict or stop participating in the DMC. Table 1 lists potential competing interests.

Table 1: Potential competing interests

- Stock ownership in any commercial companies involved
- Stock transaction in any commercial company involved (if previously holding stock)
- Consulting arrangements with the sponsor
- 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, eg, 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
- Involvement in the publication

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Please complete the following section and return to the trials office.

- ☐ No, I have no competing interests to declare  
☐ Yes, I have competing interests to declare (please detail below)

Please provide details of any competing interests:

\_\_\_\_\_

Name: \_\_\_\_\_

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

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

**Additional figures and information**

Figure summarising trial

Figure showing relationship of trial committees, including DMC

List of abbreviations, and glossary

Annex 1: Competing interest form (see Annex 1)

Annex 2: Suggested letter from DMC to TSC (see Annex 2)

Annex 3: Details of interim analysis plan (if not in protocol).

Annex 2: Illustrative report from DMC to TSC where recommendation is to continue the trial according to the protocol

[Insert date]

To:

