CHARTER FOR DMCs

CONTENT	COMMENTS FROM DAMOCLES AND ILLUSTRATIVE EXAMPLES
1. INTRODUCTION	
Name (and sponsor's ID) of trial plus ISRCTN and/or EUDRACT number	Stop or Go? Tapering antidepressants in pregnancy: A pragmatic multicentre RCT to investigate risk and benefits for mother and child. ZonMw 836021011 / EudraCT 80-83600-98-20095
Objectives of trial, including interventions being investigated	The aim of this study is to investigate the effect of guided tapering in early pregnancy as compared to continuation of SSRIs during pregnancy. We will study effects on both mother and child with a pragmatic approach. After informed consent, women will be randomly allocated into two groups: I. Gradual, guided discontinuation of SSRI under clinical management and additional cognitive therapy (experimental group). II. Continuation of SSRI (control group).
Outline of scope of charter	The purpose of this document is to describe the roles and responsibilities of the independent DMC for the 'Stop or Go?' 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.
2. ROLES AND RESPONSIBILITIES	
A broad statement of the aims of the committee	The committee will be responsible for assignment, to the best of their knowledge, of the degree of causality between Sever Adverse Events and SSRI use/tapering.
Terms of reference	The DMC will receive regular updates on trial progress and incidence of treatment failures. Severe adverse events (SAE) will be reported immediately to the committee. The committee will be responsible for assignment, to the best of their knowledge, of the degree of causality between SAE and SSRI use/tapering. The study investigators will facilitate the committee, but has no formal position in their judgement. A stopping rule cannot be stated, but at any stage the safety board may request reconsideration of the trial.
Specific roles of DMC	• 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 • advise on protocol modifications suggested by investigators or sponsors (eg to inclusion criteria, trial endpoints, or sample size) • monitor compliance with previous DMC recommendations • considering the ethical implications of any recommendations made by the DMC

3. 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 medical ethical commission of the Erasmus MC. 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.

Whether the DMC will meet before the start of the trial	According to the preference of the DMC.
Any issues specific to the disease under study	We will study pregnant women who are treated for symptoms of depression and/or anxiety. Risk and benefits are therefore applicable for both mother and child.
Any specific regulatory issues	None.
Any other issues specific to the treatment under study	Usual care (continuation of SSRI) will be compared to tapering of SSRI with additional preventive cognitive therapy (proven efficient in non-pregnant participants).
Whether members of the DMC will have a contract	No contract will be signed. DMC members should formally state: (1) that they agree to be on the DMC and (2) that they agree with the contents of this Charter.
4. COMPOSITION	
Membership and size of the DMC	The members of the DMC for this trial are: 1. Dr. A.N. Schonewille-Rosman, midwife 2. Dr. R. van Westrhenen, psychiatrists/pharmacologist 3. Drs. E.G.J. Rijntjes-Jacobs, paediatrician 4. Dr. W. Ganzevoort, gynaecologist 5.
The Chair, how they are chosen and the Chair's role. (Likewise, if relevant, the vice-Chairman)	

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 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).
5. RELATIONSHIPS	
Clarification of whether the DMC are advisory (make recommendations) or executive (make decisions)	The role of the DMC will be advisory. They can, at any stage, request reconsideration of the trial.
Payments to DMC members	Members will be reimbursed for travel and accommodation.
The need for DMC members to	Competing interests should be disclosed. These are not restricted to

disclose information about any competing interests	financial matters – involvement in other trials or intellectual investment could be relevant.
6. ORGANISATION OF DMC MEETINGS	
Expected frequency of DMC meetings	The DMC will have a scheduled meeting at 6 months, 12 months, 24 months and 36 months. In case of a severe adverse event like the death of a participant, the committee will schedule a meeting within two weeks, either by teleconference or face-to-face.
Whether meetings will be face-to-face or by teleconference	The scheduled meetings at 6, 12, 24 and 36 months are preferably face-to-face. Second option is teleconference. A meeting on short notice, in case of a severe adverse event, may be by teleconference.
How DMC meetings will be organised, especially regarding open and closed sessions, including who will be present in each session	A mixture of open and closed sessions will be possible. The meeting at 6 months will be an open session. Al other meetings will be closed unless the DMC requests an open meeting. At least 3 members will have to be present during each session.
7. TRIAL DOCUMENTATION AND PROCEDURES TO ENSURE CONFIDENTIALITY AND PROPER COMMUNICATION	
Intended content of material to be available in 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.
Intended content of material to be available in closed sessions	In addition to all the material available in the open session, the closed session material will include safety data by treatment group.
Will the DMC be blinded to the treatment allocation	The DMC will not be blinded.
Who will see the accumulating data and interim analysis	All DMC members.
Who will be responsible 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 will collate any such information.
To whom the DMC will communicate the decisions/ recommendations that are reached	The DMC will communicate the recommendations directly to the principal investigator.
Whether reports to the DMC be available before the meeting or only at/during the meeting	Reports will be received by the members 2 weeks before the meeting is scheduled.
What will happen to the confidential papers after the meeting	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.
8. DECISION MAKING	
What decisions/recommendations will be open to the DMC	Possible recommendations could include: • No action needed, trial continues as planned • Early stopping due, for example, to clear benefit or harm of a

	treatment, futility, or external evidence • Proposing protocol changes

How decisions or recommendations will be reached within the DMC	Every effort should be made to reach a unanimous decision. If the DMC cannot achieve this, a vote will be taken. It is important that the implications for the trial are considered before any recommendation is made.
When the DMC is quorate for decision-making	Effort should be made for all members to attend. Members who cannot attend in person should be encouraged to attend by teleconference. If the DMC is considereing recommending major action after 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.
Can DMC members who cannot attend the meeting input	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.
What happens to members who do not attend meetings	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.
Whether different weight will be given to different endpoints (eg safety/efficacy)	The causality between tapering of SSRI and SAE will be the primary task of the DMC.

9. REPORTING	
To whom will the DMC report their recommendations/decisions, and in what form	They will report to the principal investigator within 3 weeks.
What will be done if there is disagreement between the DMC and the body to which it reports	If the DMC has serious problems or concerns a meeting with the principal investigator and other investigators involved should be held. An external expert who is not directly involved with the trial will chair the meeting.
10. AFTER THE TRIAL	
Publication of results	At the end of the trial a meeting is allowed to discuss the final data with the principal investigator. The DMC can give advice about data interpretation.
The information about the DMC that will be included in published trial reports	DMC members will be named and their affiliations listed in the main report, unless they explicitly request otherwise.
Whether the DMC will have the opportunity to approve publications, especially with respect to reporting of any DMC recommendation regarding termination of a trial	The DMC may wish to be given the opportunity to read and comment on any publications before submission.
Any constraints on DMC members divulging information about their deliberations after the trial has been published	The DMC may discuss issues from their involvement in the trial 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 *Stop or Go? Trial (ZonMw 836021011)*

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

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: _____