ECTU Central Office WPD ECTU_ST_W3: DMC Reporting

Version No: 3.0
Effective Date: 27th April 2020

Authorship and Approval

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<td>8th April 2020</td>
<td>See retained approval email dated 8th April 2020</td>
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Document Revision History

<table>
<thead>
<tr>
<th>Version No</th>
<th>Date</th>
<th>Summary of Revisions</th>
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<tbody>
<tr>
<td>1.0</td>
<td>13th March 2017</td>
<td>Initial creation</td>
</tr>
<tr>
<td>2.0</td>
<td>12th March 2018</td>
<td>Addition of instructions regarding centre split in section 2.3.4 and 2.3.5</td>
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<tr>
<td>3.0</td>
<td>27th April 2020</td>
<td>Updated at scheduled review. Document moved to new WPD template. N/A has been amended to Version 1.0 in the Document Revision History – N/A was included in error. Minor revisions throughout document.</td>
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1. INTRODUCTION

This Working Practice Document provides guidance on preparing statistical analysis reports for Data Monitoring Committees (DMC) as referred to in ECTU Central Office SOP ECTU_SOP_ST_03 DMC.

2. INSTRUCTIONS and GUIDANCE

2.1 Planning and executing analyses for DMC

2.1.1 Ensure that there is oversight of the DMC Charter and the wording appropriately reflects the trial design.

2.1.2 There should be documentation of the analyses that the DMC require to see at their first meeting where data are available. This might be detailed in the DMC Charter or there could be a separate SAP for DMC analyses. A dummy report could be provided to the DMC at the first meeting without data for their review.

2.1.3 Unless the DMC specifically ask for a lot of data to be presented, keep the report reasonably brief and to the point.

2.1.4 Obtain list of protocol deviations and violations, serious adverse events and pregnancy information from the sponsor (e.g. ACCORD) if not recorded on the trial database. Check with trial manager the appropriate person to contact for the study.

2.1.5 It should be stated clearly throughout the report exactly how many participants should have data in each table and how many have missing values.

2.1.6 ECTU Central Office WPD ECTU_ST_W5 Statistical Analysis and Reporting should be referred to for general guidance on analysis processes.

2.1.7 Run the DMC report and send to DMC members, ideally two weeks before the date of the DMC, via a secure method, such as the University of Edinburgh DataSync service. Instructions on how to do this are available (see section 3 for details).

2.1.8 Ensure that the unblinded (closed) report is NOT copied to the Chief Investigator, Trial Manager or anyone else who should remain blind to results split by treatment allocation. Produce a blinded (open) report and send to those who are to remain blind to results split by treatment allocation.

2.1.9 Record the date of each DMC meeting, making sure to also note if it was a meeting with no data in the ECTU stats and funding document on the shared drive (see Section 3 for location details).

2.1.10 Record the date, version no and location of each DMC report in the ECTU Statistical Master File Essential Document Checklist.

2.2 Recommended Content for DMC Reports

2.2.1 Title Page

- Name of trial and logo (if available)
- Name and number of report and version no. The report name should be clear and unambiguous and it should also be clearly specified whether the version is a final or draft version
- Date that report was produced and who produced the report
- Current protocol version
• Date of trial database analysis

2.2.2 Introduction
• Trial summary - this may be useful as a reminder to the DMC members without having to refer to the protocol. The trial summary may include information on: trial design, interventions, participants, eligibility criteria, primary research question, primary outcome measure, secondary outcome measures, trial start and end date, target sample size, interim analyses and stopping rules. The content of this section should be carefully reviewed for each report as certain aspects (e.g. eligibility criteria, trial end date etc.) may change throughout the trial.
• Trial Flow Chart - a simple overall summary of patient status in the study by treatment group, including the number of withdrawals from treatment and/or follow-up (including reasons for withdrawal).

2.3 Suggested Analyses for unblinded (closed) report
2.3.1 Dates of randomised patients
Include the dates of the first and last randomised patient included in the current report

2.3.2 Recruitment – generally not split by randomised treatment
A summary of recruitment and whether it is on target. Depending on how responsibilities are divided between the TSC and the DMC, this could include numbers screened and screening failure reasons in addition to numbers randomised and could include recruitment by centre.

2.3.3 Baseline Balance – split by randomised treatment
A summary of key baseline variables to show balance with a clear indication of what minimisation/stratification variables there are.

2.3.4 Data Completeness – split by treatment
A more complex summary of expected number of participants at each visit and number of patients with data at each visit (to show which data/forms are missing) along with details of how many are long overdue or are missed completely.

2.3.5 Adherence – split by randomised treatment
Whether any ineligible participants are in the trial or whether any have become ineligible (violate inclusion/exclusion criteria); number not receiving any study treatment or crossing over to a different treatment arm (including reasons for this), whether treatment has been received as planned (dose, number of tablets, number of therapy sessions etc.); whether treatment given at the right time and/or assessments made at the right time; whether blinding has been broken for any participants (in the case of blinded trials); if there is adjudication of outcomes, whether this is happening in a timely manner.
If the data allows, adherence should be split by centre, particularly to assess whether there are too many crossovers/non-compliers at any centre i.e. people getting the opposite treatment to that allocated.

2.3.6 Primary Outcome – split by randomised treatment
A suitable summary of the primary outcome.
If formal analyses are planned in a group sequential design then could include a chart showing the analyses over time.
For trials without pre-specified analyses, no formal tests of hypotheses will be performed for the DMC unless they specifically request it. An appropriate method needs to be used to avoid inflation of the type I error rate and should be stated in the DMC charter e.g. at least 3 standard errors between groups in an interim analysis of the primary outcome is needed to justify halting, or modifying, a study before the planned completed recruitment. This criterion has the practical advantage that the exact number of interim analyses would be of little importance, and so no fixed schedule is proposed.
If there is sufficient data and the DMC request it, some subgroup analyses could be provided. Similarly, primary outcomes could be split by centre to look for centre-outliers e.g. too few or too many primary outcome events.

2.3.7 Secondary Outcome – split by randomised treatment
To be provided where relevant. If there is sufficient data, centres could be presented individually to check for too few or too many secondary outcome events.

2.3.8 Safety – generally split by treatment received
A summary of any safety areas the DMC needs to consider – including pregnancies if relevant but more generally adverse events. If there are any serious unexpected suspected adverse reactions (SUSARs), these need to be listed. All adverse events could be listed if that is requested by the DMC.

2.3.9 Any other relevant information
For example, similar trials that have been recently published, updated systematic reviews (if requested by the DMC).

2.4 Suggested Analyses for blinded (open) report
2.4.1 Similar analyses will performed as for the closed report but analyses will NOT be split by randomised treatment. Careful consideration should be given as to the inclusion of data that has the potential to unblind e.g. patient visit schedules that reflect their treatment allocation.

3. RELEVANT DOCUMENTS AND REFERENCES

ECTU Central Office WPD ECTU_ST_W5 Statistical Analysis and Reporting (on shared drive):
ECT Unit/SOPs/Finalised SOP and WPD/ST/WPD/Current PDF version for use

University of Edinburgh DataSync Service
https://www.ed.ac.uk/information-services/computing/desktop-personal/datasync

ECTU stats and funding document (on shared drive):
ECT Unit/1. ECTU FILING SYSTEM – AMENDED 2010/ECTU Operational/Statistics/Project planning/ECTU stats and funding.docx

ECTU Central Office SOP ECTU_ST_03 DMC (on shared drive):
ECT Unit/SOPs/Finalised SOP and WPD/ST/SOP/Current PDF version for use

Example DMC Report (on shared drive):
ECTU Unit/SOPs/Finalised SOP and WPD/ST/SOP and WPD Related Documents