Back-Up Emergency Un-blinding Guidance

Scope
This Guidance applies to staff of the Cambridge Clinical Trials Unit and Chief Investigators and their trial teams working on CTIMPs or clinical studies coordinated by the CCTU.

Purpose
To describe the process for breaking the statistical blind during a “Double Blind” clinical research study where the process described in the protocol cannot be followed.

Definitions and Abbreviations

<table>
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<tr>
<th>Term</th>
<th>Definition</th>
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<tr>
<td>Un-blinding</td>
<td>Reveal the treatment that the participant is receiving</td>
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<td>Double blind</td>
<td>Neither the study team or the participant know which treatment is being given</td>
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<td>Authorised Study Team member</td>
<td>Any member of a study team from whom the TENALEA support team may take instruction</td>
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<td>TENALEA Support</td>
<td>Responsible for emergency un-blinding</td>
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Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Meaning</th>
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<tr>
<td>TENALEA</td>
<td>Trans European Network ALEA</td>
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<tr>
<td>ALEA</td>
<td>ALEA® software suite for randomisation in clinical trials</td>
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<td>DMC</td>
<td>Data Monitoring Committee or similar: committee providing oversight of the trial</td>
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<td>GCP</td>
<td>Good Clinical Practice</td>
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<td>IWRS</td>
<td>Interactive Web Response System</td>
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Undertaken by

Principal Investigator
- Must follow the blind and un-blinding requirements as defined in the protocol
- Should consider in advance the conditions where a blind may be broken: For example as a response to a serious adverse event, in compliance with GCP
- Collect, manage, and retain documentation in support of the trial

Study Statistician
- Log and track all analysis related documentation and activities that occur after the clinical database is suspended or closed and data are exported or extracted from the clinical trials database for analysis and reporting
Pharmacist
- Principle responsibility for managing drug supply and the concealment list

Items Required
- Emergency Un-blinding Request Form CCTU/FRM055
- Trial Protocol

Summary of Significant Changes
Added reference to CCTU/GD038

When to Break the Statistical Blind
- How and why to break the statistical blind should be outlined in the study protocol; this procedure should cover both emergency and planned un-blinding
- All measures taken during the un-blinding process should be reported to the Clinical Study Team and thoroughly documented
- Breaking the statistical blind should be considered only when knowledge of the treatment assignment is deemed essential for the subject’s care by the subject’s physician or a regulatory body

Procedure
- DMC or Subject’s physician requests un-blinded clinical research data in writing when knowledge of the treatment is deemed essential for the subject’s care
- DMC requests clinical trial research data for review for safety issues.
- If applicable, DMC will request from the statistician / pharmacist ‘un-blinding’ of the patient allocation
- After receiving a request from the DMC for data to be un-blinded the Statistician or Pharmacist un-blinds according to the protocol
- The Statistician / Pharmacist sends un-blinded data to the DMC for review
- If possible, the clinical study team will remain blinded according to the clinical processes or protocol
- The processes outlined in CCTU/GD038 Storage and Access to Confidential Materials may need to be consulted to establish if the required information has been stored as per the guidance; the log of documents stored thus may need to be consulted

Back-up Emergency Un-blinding
- Processes to cope with the possibility that the relevant personnel are not available for an emergency unblinding or TENALEA and/or IWRS is not working must be made on an individual study basis using risk assessment
- Hard copies of the concealment and randomisation list may be kept by the local or central pharmacies or CCTU. A 24-hour telephone service may be put in place in extreme cases to deal with this possibility
- In any cases where emergency unblinding was not performed using the desired process File Notes should be kept
- Complete CCTU/FRM055 Emergency Unblinding Request Form
Audit Trail

- An audit trail of any emergency unblinding must be maintained. Copies of all forms submitted to CCTU must be provided for inclusion in the Trial Master File.

Associated Documents

CCTU/SOP036 Open Label Randomisation
CCTU/SOP046 Blinded Randomisation
CCTU/GD038 Storage and Access to Confidential Materials