





Standard Operating Procedures

4.7.2 Unblinding ©2008

History			
Version	Date	Author	Reason
1.1	21 st August 2007	B Fazekas	New procedure
1.2	14 th December 2007	B Fazekas	Update after MAB review
1.3	19 th February 2008	B Fazekas	Update after review by D Currow

Approval				
Version	Author	Signature	Approval Name	Approval Signature
1.3	B Fazekas		D Currow	

Scheduled review

Date: August 2009

Responsible person: PaCCSC Project Officer

Purpose

Unblinding is the process by which the allocation code is broken so that the investigator, clinical staff and/or the trial statistician becomes aware of the intervention for a person participating in a trial.

Unblinding must be undertaken by a pre-determined process to ensure that participating people are not unblinded unnecessarily and the study results are not compromised. Equally, unblinding should occur in a responsive manner when it is clinically indicated.

Unblinding is required:

- To make clinical treatment decisions or when an unexpected serious adverse event occurs and the intervention must be made known. This is called emergency unblinding.
- During an unmasked analysis in accordance with the study analysis plan
- At the request of the Data Safety Monitoring Board
- At the conclusion of the study to determine the effect of the intervention.

This SOP describes the conditions under which unblinding occurs, and the process to ensure correct unblinding procedures are followed.

Other related SOPs

- 4.7.1 Randomisation
 - 5.5.1 Electronic Data Handling
 - 5.5.2 Electronic Data Transfer
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Attachments

Unblind request form
Unblind Report Fax

References

Notes for Guidance on Good Clinical Practice (GCMP/ICH/135/95) annotated with TGA comments. July 2000.

Acknowledgments

Trans-Tasman Radiation Oncology Group (TROG), for generous access to the Policy and Procedure Manual – the Red Book.

Definitions

Allocation code – The code which identifies the intervention to which the person is assigned; the code is the output from the randomisation process. This code (A=intervention 1, B=intervention 2, and C=intervention 3) does not change throughout the study or from one site to another.

Blinding – The procedure in which one or more parties in the study are kept unaware of the treatment assignment (i.e., medicine 1 vs medicine 2, study medicine vs placebo) or the allocation code (i.e., A or B). All studies in PaCCSC are double-blind, meaning that the person participating, investigators, and other study staff are unaware of the treatment assignment. This process is also called “masking”. The allocation code and person’s treatment assignment are known to:

- each Site Pharmacy involved in administration of blinded medicine as the study intervention; the site pharmacy holds the record of randomisation for that site;
- the Study Statistician who is responsible for reporting unblinded analyses to the Data Safety Monitoring Board (DSMB) and
- the Central Randomisation Centre where the schedules for each site were developed.

Central Randomisation Service – The service where the allocation codes for the whole study, across all sites, are generated. The schedule for each site is prepared and sent from this service to the coordinating site for provision to the site pharmacies.

Central Registry – The location that holds the allocation codes for each person participating in a trial in the form of unblinding envelopes. This will vary from one study to the next, and is specified within the study protocol. This location may include; the site pharmacy, a central pharmacy (a pharmacy nominated to hold the unblinding envelopes), the lead investigator or, the central randomisation service.

Site pharmacy – The location which collates and records the allocation codes for each study site and may provide out-of-hours access to the allocation codes (if acting as the central registry). The site pharmacy will maintain a register of people in the trial, and the allocation code for that site for the duration of the trial.

Randomisation – The process of assigning people to one treatment group or the other using an element of chance to determine the assignments in order to reduce bias.

Unblinding – Unblinding is the process by which the allocation code is broken so that the investigator, clinical staff and/or the trial statistician becomes

aware of the intervention for a person participating in a trial. The usual reason for unblinding in a study context is that a person participating in the study has encountered an urgent medical problem necessitating that the clinician know his/her intervention allocation. People are not unblinded at the end of their participation in the study.

Unblinding envelopes – A series of envelopes, each labelled with the randomisation number that contain the allocation for that person. These envelopes are sealed by the central randomisation service, and are only opened if emergency unblinding is required.

Procedure

1. For individual unblinding.

- Study site
 - The lead investigator, in consultation with the clinical team, assess the need for unblinding
 - Where a serious adverse event has occurred and the treatment or allocation code is required in order to enable clinical treatments to be planned.
 - Contact the
 - Site pharmacy, Central Randomisation Service, Lead investigator or as specified within the study protocol
 - Provide details,
 - Caller details (own name and position)
 - Study site
 - Site Investigator
 - Name of person participating
 - Study protocol number or identifier
 - Study Identification Number if known
 - Upon unblinding, the site personnel will record the participant withdrawal and allocation in the person's clinical and trial notes along with the appropriate clinical notations.

- Central Registry

In receipt of an unblinding request the Central Registry will;

- Complete an unblind Request Form and obtain the contact details
- Identify the unblinding envelope associated with the specific randomisation number provided by the study site
- Determine the allocation code according to the randomisation tables held within the envelope
- Call the study site back with the allocation
- Notify the site pharmacist when possible
- File the Unblind request form within their files for later audit
- Fax the unblind report form to the coordinating site for recording.

- Coordinating site

- Log the unblind reports and report the unblind rates to the Trial Sub-Committee and Trials Management Committee as part of routine reporting.

2. For unmasked analysis.

- The Data Safety Monitoring Board (DSMB)
 - o The DSMB will determine that an unmasked analysis is required.
 - o The decision will be minuted within the committee meeting minutes
 - o A DSMB designee or the study's Lead Statistician will make a written request to the lead investigator to instruct for study unblinding

- Lead investigator
 - o Will request the PaCCSC coordinating site to provide the randomisation schedules to the lead statistician or the DSMB

- Coordinating site
 - o Will provide a written request to each site pharmacy that the table of allocation schedules be copied and faxed to the lead statistician or DSMB designee

- Site pharmacy

On receipt of request from the coordinating site will;

 - Check the allocation log for completions to date
 - Sign and date the last entry with a note to indicate point of request
 - Provide the DSMB designee or the study's Lead Statistician with the Register of all study allocations by fax

- Lead Statistician

The Lead Statistician will;

 - Merge the main study data with the table of allocation codes as per the data transfer instructions within the Data Management SOP.
 - Undertake unmasked analysis as determined by the DSMB

3. For study unblinding on completion.

- Lead Investigator
 - o The lead Investigator will determine that the study recruitment is complete and unblinding is required for analysis.
 - o The lead Investigator or Lead Statistician will make a written request to the coordinating site to instruct for study unblinding

- Coordinating site

On receipt of an instruction to unblind the study will;

- Contact each site pharmacy for the schedules and request urgent postage
- Request return of all unblinding envelopes by registered mail
- Enter all Identification Numbers and allocations into an excel file
- Send via email to the Lead Statistician (refer to 5.5.2 Electronic Data Transfer)

- Site pharmacies

In receipt of an instruction for the coordinating site, the site pharmacy will;

- Check the allocation log for completion
- Sign and date the last entry
- Provide the Coordinating site with the schedule of all study allocations.
- Ensure all invoicing has been completed.

- Lead Statistician

The Lead Statistician will;

- Confirm receipt of the excel file containing the ID numbers and allocations
- Merge the main study data with the new excel file in preparation for analysis



Unblind Request Report Form

Request details:

Study Code or name _____ Site Code or name _____
Requesting person _____
Position of requesting person _____
Call back number _____ STD: _____
Date/Time of request _____ / _____ / _____ : _____
Request taken by (Name/position) _____

Details of person participating:

Surname:	
First Name:	
Study ID Number:	
Strata:	

Result of request:

Code: _____
Intervention: _____

Signature: _____

Date: _____

File this in the study files held on site along with the unblinding envelopes, and under locked supervision.



Unblind Report Fax

To: **National Project Officer** From: _____
Fax: **+61 8 8374 0350** Fax: _____
Phone: **+61 8 8275 1396** Phone: _____
Pages: **1** Date: _____

Dear Coordinating site

The following patient has been unblinded for a PaCCSC clinical study.

Study ID Number:	
Site Name	
Reason for unblinding	
Date of unblinding	
Method of confirmation of notification to site	

Yours sincerely

Lead Investigator