# Standard Operating Procedure

## 4.7.1 Randomisation and Allocation

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| Author/s | C Strauss |
| Approved | M Agar |
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## Introduction / Background

Rigorous methodology for randomisation and for the allocation of people to study interventions is a critical element of randomised studies.

Correct documentation of the randomisation and allocation process ensures that the study results can be verified and are able to withstand external examination. Errors in the randomisation procedure itself, or shortcomings in documentation of the randomisation and allocation procedures, expose the study results to criticism, which could render the results dubious. This situation must be avoided at all costs.

The ITCC aims to conduct rigorous and quality clinical studies. All stages (design, execution and reporting) are conducted to the highest possible standard. An established mechanism for assessing the quality of a study via its report is the Jadad score, which allows a score to be allocated to the study by external review. A maximum score of 5 indicates high quality randomisation and masking of allocation (Jadad 1996).

## Objective

This SOP details the procedures by which participants are allocated to an intervention, and the roles and responsibilities of each party involved in these procedures.

This SOP does not describe the randomisation process by which the allocation codes are generated prior to distribution to each site. This process is described in the study protocol and is recorded by the Central Randomisation Service.

## Scope

This SOP applies to all staff involved in clinical studies conducted by the ITCC irrespective of individual organisational employment, role, or position.

This SOP also encompasses new procedures related to a ‘Direct to Patient’ delivery, of study investigational product, using a ‘Just In Time’ model, operating from a third-party pharmacy.

## Ownership and Responsibility

*Responsibilities of the Study Site*

- To recruit participants for clinical studies
- To ensure informed consent and confirmation of eligibility are provided for each participant prior to randomisation
- To ensure randomisation and all study procedures are performed according to the study protocol
- To liaise with the site or third-party pharmacy regarding investigational product prescriptions

*Responsibilities of the Pharmacist (at the Site or Third-Party Pharmacy)*

- To undertake the randomisation of enrolled participants at the Study Site in accordance with the study protocol
- To maintain the intervention allocation logs
- To supply the investigational product as per the study protocol

*Responsibilities of the IMPACCT Trials Coordination Centre*

- To manage the operationalisation of the study

*Responsibilities of the Central Randomisation Service*

- To develop the randomisation schedules for each site for each study
- To design and implement a methodology for providing the intervention allocation
- To provide a mechanism by which the code can be broken

## Procedure

This SOP is organised in sections corresponding to each of the parties actively involved in the study's randomisation and allocation procedures.

### 1. Study Site

- Following provision of informed consent and confirmation of eligibility, the participant is randomised.
- A member of the study team determines the day the participant will commence the study (Day 1) to ensure that all study procedures, such as supply of investigational product, pathology results and medical review, are undertaken at the times specified within the study protocol.
- A formal request for randomisation is recorded and sent to the site or third-party pharmacy. The formal request is a prescription (signed by the Principal Investigator). Most ITCC studies involve investigational product that require a medical order (*refer* SOP 5.14.1 Investigational Product Handling).
- After confirmation of the randomisation from the site or third-party pharmacy, a member of the study team is provided with the randomisation number (*refer* SOP 5.5.5 Allocation of Identification Number). This number is referred to as the PID number and is recorded in the Patient Master Index (Template 12), and on all subsequent data collection worksheets and Case Report Forms (CRFs) for that participant.
- A participant cannot be randomised to the same study more than once, regardless of the circumstances of the first enrolment or outcome. In the unlikely event that re-randomisation of a participant occurs, the first data set is maintained, and the second data set is deleted from the data base.

### 2. Study Pharmacy

- Procedures for randomisation and allocation are kept in the pharmacy Randomisation/Study folder at each site pharmacy or at the third-party pharmacy; all documents related to the procedure are filed within that folder.
- The site pharmacy or at the third-party pharmacy receives the Randomisation/Study Folder (provided by the ITCC) containing allocation code schedules (sealed), instruction manual, study protocols, investigational product accountability logs, and documents relating to the recording and reporting of randomisation for each study. This folder is maintained by the clinical trials pharmacist in keeping with Good Clinical Practice.
- At the time a participant is randomised and allocated to an intervention, site pharmacy or at the third-party pharmacy receives a prescription (which also confirms the stratum assignment, if applicable) (refer to Guidance 6: Prescription of Study Drug). This serves as confirmation of the person's eligibility for the study and specifies Day 1 of the intervention (the day the participant commences the study).
- The pharmacist at the site or third-party pharmacy checks the prescription for completeness and legibility. The study site is notified if the prescription does not meet requirements.

- The site or third-party pharmacist follows the study specific procedures described within the pharmacy instruction manual. In most cases, this procedure involves a telephone call or email to the Central Randomisation Service to request the intervention allocation and the randomization number. This is then followed by an email confirmation. Alternatively, the randomisation may be via the facility within REDCap, in which case the instructions for access and recording are to be followed, these are study specific and provided at the time of site initiation.
- Pharmacy staff at the site or third-party pharmacy locate the appropriate study drug and dispense it in accordance with the protocol and instructions.
- Should the site or the third-party pharmacist receive more than one request in one day, the pharmacist:
    - undertakes the randomisation procedure **in the order that the prescriptions are received**
    - records each randomisation according to the prescription and completes the dispensing of investigational product before undertaking the next randomisation.
- If the site or third-party pharmacist makes an error in recording data within any documents related to the intervention allocation and logging, the pharmacist takes the following actions:
    - Strike out the error with a single line, then sign and date the randomisation log next to the error.
        - Use pen and ink, but never liquid paper.
        - Do not obliterate the original error; the original writing must remain intact and visible.
- If the process involves site generated randomisation tables, the study specific instructions and other guidance documents provided at site initiation are to be followed.
- The site or third-party pharmacist completes a Randomisation Registration Notification (Template 17) and emails this to the ITCC on the day of the randomisation.
- The pharmacist at the site or third-party pharmacy prepares the study medicine according to the allocation code for each individual person.
- The site pharmacist delivers the study medicine to the person participating in the study (or the ward if inpatient, or the relevant study team member if the study drug is to be delivered to the participant at home) on the day specified within the study protocol (this might be the previous day in the case of people at home for the morning intervention doses) and as per the arrangements already confirmed with the study team member. The third-party pharmacist may use an appropriate courier service with the level of licence and security in line with the medication schedule to deliver the study medicine to the participant at home (or to the hospital pharmacy for internal delivery to the ward or relevant study team member if inpatient).
- The site and/or third-party pharmacist performs internal checks and maintains records that make it possible to verify that the participant received the intervention as determined by the allocation code.

- At the end of the study and after the close-out monitoring visit, the Randomisation/Study folder containing all the randomisation records, pharmacy instructions, logs and related correspondence are sealed and provided to the Site Principal Investigator for inclusion in the Investigator Site File.

## 3. IMPACCT Trials Coordination Centre

The role of the ITCC is operational management of the study. The ITCC:

- receives automatic notification when the Study Site has entered eligibility and baseline data (including any stratum data) into the Research Data Management Software (RDMS).
- upon automated email notification of data entry from the RDMS, checks:
  - the randomisation data against the expected stratum assignment based upon the predetermined characteristics (if applicable)
  - all eligibility criteria have been confirmed prior to the randomisation process
- maintains a log of those enrolled in the study as per the data entry and compares the participant registration emails received from the site or third-party pharmacy.
- if discrepancies are identified, the ITCC contacts the Study Site.

## 4. Central Randomisation Service

The primary responsibility of the Central Randomisation Service is to develop the randomisation schedules for each site for each study, and to provide a mechanism by which the code can be broken (unblinding envelopes).

## 5. Contact details

Any problems during the study are to be directed to the company or service as per the contact listing provided within the Randomisation/Study Folder.

Any problems with materials, procedures, timeframes or other questions are directed to:

Ms Belinda Fazekas
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University of Technology Sydney
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## Related SOPs

5.14.1 Investigational Product Handling
4.7.2 Unblinding
5.5.1 Electronic Data Handling
5.5.5 Allocation of Identification Numbers

## Related documents

Template 9: File Notes
Template 12: Patient Master Index
Template 17: Randomisation Registration Notification
Guidance 6: Prescription for Study Drug (example)

## References

Jadad AR, Moore RA, Carroll D et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Controlled Clinical Trials 1996; 17:1-12.

Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95). Annotated with TGA comments 2000 (accessed 17/10/2017)
https://www.tga.gov.au/sites/default/files/ich13595an.pdf

## Acknowledgments

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

| History | | | |
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| Version | Date | Author | Reason |
| 1.1 | 21/08/2007 | B Fazekas | New procedure adapted from Oxygen study SOP V4.2.6 |
| 1.2 | 14/12/2007 | B Fazekas | Update after MAB review |
| 1.3 | 19/02/2008 | B Fazekas | Update after David Currow review |
| 1.4 | 7/06/2010 | B Fazekas | Periodic review |
| 2.0 | 23/02/2011 | B Fazekas | Changes ratified by MAB |
| 2.1 | 13/05/2015 | C Hope | Periodic review |
| 2.2 | 28/02/2018 | B Fazekas,<br>S Kochovska | Periodic review<br>Publication of the ICH GCP E6 (R2) |
| 2.3 | 16/03/2020 | C Strauss | Periodic review |
| 2.4 | 17/01/2022 | C Strauss | Periodic review<br>Include third-party pharmacy and incorporate new direct to patient delivery and Just in Time dispensing model |

| Approval | | |
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| Version | Approval Name | Approval Signature |
| 2.4 | Meera Agar |  |