# Standard Operating Procedure CCTU/SOP053

# Paper-Based Randomisation

## 1. Scope

This Standard Operating Procedure applies to staff of the Cambridge Clinical Trials Unit, Chief Investigators and their trial teams working on Cambridge Sponsored CTIMPs or clinical studies coordinated by the CCTU.

## 2. Purpose

To describe the general steps required when setting up paper based randomisation for a study that is a simple small-scale study that does not require an electronic system

## 3. Definitions and Abbreviations

The headings below contain the definitions of terms and meaning of abbreviations used within the document.

### 3.1. Definitions

| Term | Definition |
|---|---|
| Cambridge Sponsored | Sponsored by Cambridge University Hospitals NHS Foundation Trust (CUH); or the University of Cambridge (UoC); or jointly by CUH and UoC<br>OR<br>Sponsored by: Cambridge University Hospitals NHS Foundation Trust (CUH) or CUH jointly with the University of Cambridge<br>or Cambridgeshire & Peterborough NHS Foundation Trust (CPFT) or CPFT jointly with the University of Cambridge |
| Open Label | When the treatment to be received is revealed to all with no attempt to blind |
| Blinded | When steps are taken to ensure all treatments appear identical and steps are taken so that patients or clinicians are unaware which treatment has been allocated |
| TENALEA | A specific IWRS system |

### 3.2. Abbreviations

| Abbreviation | Meaning |
|---|---|
| IWRS | Interactive Web-based Randomisation System |
| CCTU | Cambridge Clinical Trials Unit |
| CRF | Case Report Form |
| PI | Principal Investigator |
| DoB | Date of Birth |
| CI | Chief Investigator |

# 4. Undertaken by

Statisticians, Coordinators, Chief Investigator or delegate

# 5. Items Required

CCTU/TPL040 Paper-Based Randomisation Specification Template
CCTU/FRM091 Randomisation Specifications Overview Approval Form
CCTU/FRM045 Randomisation Closure Form
CCTU/SOP033 Database Locking
CCTU/GD038 Storage and Access to Confidential Materials

# 6. Summary of Significant Changes

Adding reference to CCTU/GD038

# 7. Method

The following sections provide a description of the processes to be followed when implementing this document's procedures.

## 7.1. Overview

The key components and principles of randomisation are described in CCTU/SOP036 Open Label Randomisation and CCTU/SOP046 Blinded Randomisation.

Critical deliverables that are required include:

- Randomisation Specification
- Randomisation list
- Concealment list in the case of blinded randomisation

The paper based equivalent to the TENALEA IWRS is described in the Randomisation Specification Document for assigning patients a treatment, or kit number.

Typically this might involve opening envelopes to reveal the required information.

In general a study using a paper-based randomisation system must not:

- Be large or complex
- Stratify on information other than site
- Use techniques other than blocked randomisation
- Have more than 30 patients

The above criteria might be considered too complex for a paper based system.

All the steps taken in setting up the system should be reproducible:

- Generation of randomisation and concealment lists must be documented and date-stamped
- Subsequent storage and access to unblinding information must be documented and dated

- The process of opening individual envelopes must have an audit trail with measures in place to prevent and detect any premature opening of envelopes or accessing of information

## 7.2. Specification Document

This document describes the steps taken in setting up and running a paper based randomisation system when open to recruitment. The Specification Template CCTU/TPL040 supplies the comprehensive details required.

The following elements of this specification must be documented in full before the system can be used to randomise subjects:

- Details of the data collected at the point of randomisation. Typically these should be written on the envelopes directly at the point of randomisation or sufficient information recorded (Subject ID, DOB, Initials) to link to a relevant page on the CRF
- Date, name and signature of PI or delegate that opened an envelope
- Method of randomisation: block size or range of block size if random block size; stratification
- Details of which roles and permissions are assigned to access information, randomise new subjects or record data for the randomisation process
- Description of which documents will be prepared in advance and where they will stored
- Details of an emergency unblinding procedure in the case of a blinded study e.g. who would be contacted to provide the required information
- Details of how opened envelopes will be stored until study close. Envelopes must not be discarded
- Details of how sets of envelopes will be distributed across multiple sites, if relevant, and the process of requesting and performing randomisation

## 7.3. Specification Approval

- The specification document (Randomisation Specification CCTU/TPL040) must be approved by the Coordinator, Study Statistician, and Chief Investigator or Delegate use CCTU/FRM091 Randomisation Specifications Overview Approval Form
- File the specification document and the approval forms in the TMF

## 7.4. Randomisation and Concealment Lists

- An independent statistician should prepare a randomisation and concealment list by writing a script or code for a statistical package with a recorded randomisation seed to allow reproducibility
- A randomisation list for each combination of strata levels will need to be produced. This will typically be produced using blocked randomisation
- The end product is a sequence of treatments
- These lists should be stored in a password protected system along with any other code/script needed to allow their reproduction. The processes outlined in CCTU/GD038 Storage and Access to Confidential Materials may need to be followed

- If a study is blinded then a concealment list will also be needed to produce kit numbers in an agreed format (number of digits, prefixes and suffixes) that are linked in a random fashion to treatment
- The randomisation list is augmented with a specific kit number for each patient
- An open-label study does not require any concealment lists or kit numbers. Only the explicit name of the treatment is placed in the envelope

## 7.5. Preparation of Envelopes

- A member of the wider coordination team ideally not involved in the trial should take the randomisation list and concealment list to prepare envelopes
- If stratification is required then individual sets of randomisation/concealment lists and envelopes need to be prepared for each combination of strata levels
- One per patient that gives sufficient detail to assign treatment
- The envelopes should be sealed with tamper-proof tape and be completely opaque
- The envelopes must be enumerated in the order in which they will be opened
- Ink should be used directly onto the envelope rather than pre-printed adhesive labels, style and content to be decided on a study-specific basis
- As minimum record the date/time and signature of the PI, or delegate, who opens the envelope
- A means to link the patient to the main body of study data. (A possible option is to pre-print the subject ID numbers on the envelopes)
- Only the kit number is placed in the envelopes for a blinded study, and the concealment list is given to the pharmacist or equivalent role to ensure the kit numbers match up to the treatments

## 7.6. Initiation

Sites should not be provided with the actual randomisation envelopes until the site initiation meeting has occurred and training related to the randomisation process has been undertaken.

## 7.7. Study Close

- The specification document describes the steps taken at the point of closing recruitment and study closure
- Upon the receipt of CCTU/FRM045 Randomisation Closure Form from the CI any unopened envelopes must be removed from all study sites
- A process to query and resolve any inconsistencies between the data recorded on the envelopes and other trial data, e.g. the details of randomisation recorded in the CRF should be undertaken
- The subsequent release of the unblinded randomisation and concealment lists should be integrated into the data locking plan (CCTU/SOP033 Database Locking) and generally not undertaken until the final hard lock of the data

# 8. Monitoring Compliance with and the Effectiveness of this Document

### a. Process for Monitoring Compliance and Effectiveness

As part of routine monitoring visits, audit and inspection

### b. Standards/Key Performance Indicators

This process forms part of a quality management system and is reviewed according to CCTU procedures. Standard Operating Procedures are reviewed every two years.

# 9. References

The Institute of Clinical Research, Abbreviations used in Clinical Trials.

MHRA, Good Clinical Practice "Grey Guide"

# 10. Associated Documents

CCTU/SOP036 Open Label Randomisation

CCTU/SOP046 Blinded Randomisation

# 11. Equality and Diversity Statement

This document complies with the Cambridge University Hospitals NHS Foundation Trust service equality and diversity statement.

# 12. Disclaimer

It is the user's responsibility to check against the electronic library that this printed out copy is the most recent issue of this document.

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