MEDICAL COLLEGE OF WISCONSIN CANCER CENTER

Cancer Center Clinical Trials Office

STANDARD OPERATING PROCEDURE STUDY SUBJECT RANDOMIZATION FOR INVESTIGATOR INITIATED STUDIES	
SOP#: 2.4	**Original Approval Date: 2/11/22**
Version#: 1.0	**Current Revision Date:**

1.0 PURPOSE/BACKGROUND

Randomization is an important tool in many fields of research. A randomized controlled trial is any research study that prospectively assigns human participants or groups of humans to one or more interventions to evaluate the effects on health or other research outcomes. Randomization is the process by which participants in a trial are allocated to intervention groups. Random allocation ensures that any differences between the groups at trial entry are due to chance alone. The aims of the randomization and blinding procedures are to avoid the introduction of bias into the conduct of the trial. The purpose of this SOP is to establish a quality standard for study subject Randomization for clinical trials managed by the Medical College of Wisconsin Cancer Center Clinical Trials Office (CCCTO).

2.0 SCOPE

This SOP applies to all randomized controlled trials sponsored or co-sponsored by the Medical College of Wisconsin Cancer. It applies to any personnel involved in the development or implementation of the randomization and/or blinding procedures.

3.0 RESPONSIBILITY

Individuals impacted by this SOP may include:

- Study Staff
- Investigational Drug Pharmacy
- Study Sponsors and their designees
- Others as required

4.0 DEFINITIONS

Refer to Glossary of Common Terms and Definitions.

Randomization: A method based on chance alone by which study participants are assigned to a treatment group.

Allocation Code: The code which identifies the intervention to which the subject is assigned.

Blinding: The procedure in which one or more parties in the study are kept unaware of the treatment assignment or allocation code (i.e. medication #1 vs. medication #2, investigational medication vs. placebo).

Double Blind: A blinded study design in which neither the study staff nor the study subjects know the treatment assignment or allocation code

5.0 ROLES AND PROCEDURES

Randomization:

An experienced statistician, or other appropriately qualified individual, should lead on the development of an appropriate randomization method for the trial and should have the responsibility of ensuring that the schedule is produced and documented.

Randomization Methodology:

5.1 The type of method used will be trial specific and must reduce the chance of imbalance between treatment groups (e.g. simple, block, stratified, minimization).

5.2 The randomization methods and parameters of the randomization process (e.g. stratification variables, inclusion and exclusion criteria) should be described fully in the protocol and may not change throughout the course of the study. Stratification factors must also be in the final publication.

Documentation of Design and Site Blinding Plan

5.3 Once the design and type of randomization has been established, a randomization list with details of the randomization codes should be produced.

5.4 The randomization schedule should be maintained electronically on a secure server.

5.5 Typically the production of the randomization schedule will be in collaboration with an appropriately qualified statistician.

5.6 In the process of producing the randomization schedule, all procedures should be documented with consideration given to the following details:

- 5.6.1 Method of generation of the randomized code list
- 5.6.2 Allocation of unique subject identifier (i.e. patient case number) and methods in place to prevent same subject being randomized more than once
- 5.6.3 Person/people (and job title) responsible for preparing and checking the randomized code list / schedule. The system should be tested to ensure it performs reliably and consistently as intended.
- 5.6.4 Distribution of electronic and paper copies of pharmacy records including approach used to conceal allocation (e.g. password protected electronic format)
- 5.6.5 Method of implementation (e.g. web-based system)
- 5.6.6 Computer software used to generate the randomization list and perform randomization and details on the validation of this system.
- 5.6.7 For blinded trials, consider the following:
  - 5.6.7.1 Method by which the emergency access to the unblinding code for individual subjects broken
  - 5.6.7.2 What reasons may allow unblinding
  - 5.6.7.3 Which individuals would have permission to unblind
  - 5.6.7.4 What documentation would be necessary from the study team for blind to be broken.
  - 5.6.7.5 Plan for “after hours” need for unblinding.

5.6.7.6 Documentation expectations of unblinding.

5.6.8 For blinded trials, details on how the randomization codes will be provided to investigational product (IP) manufacturer to ensure the IP is packaged, coded and labelled in a manner that protects the blinding at the site and at the coordinating center. (i.e. “Drug Name Strength/Placebo”)

5.6.9 For blinded trials, plan for interim analysis

5.6.10 How the treatment allocated will be compared with the treatment received at the end of the trial. Also how screen failures will be counted numerically and logistically (i.e. a subject that is randomized but not treated).

5.6.11 Any changes to the randomization schedule through the course of the trial, along with the date when the new scheme became active.

5.6.12 Details of the documentation needed to be completed prior to randomization (e.g. signed informed consent form, randomization checklist, eligibility criteria checklist)

5.6.13 Details on who will perform the randomization (if not blinded) and how pharmacy will be informed of the randomized treatment allocation (i.e. fax or email forwarded to pharmacy)

6.0 REFERENCES

Guidance for Industry E6: Good Clinical Practice, section 4.7 *Randomization Procedures & Unblinding*.

7.0 APPENDICES

Site Blinding Plan Template

Authorized by:

Signed Electronically by:
Betty Oleson - boleson@mcw.edu
11-Feb-2022 @ 04:03 PM CST Reason: Approval

CCCTO Administrative Director

Revision dates:

Review dates:

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SITE BLINDING PLAN

Drug Substance:
Version number:
Date:

Version	Section Change	Changes Made	Date
1.0	N/A	Initial issue of the document	TBD

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SCHEMA

[Insert Schema Here]

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Section 1: Randomization Methodology:	
Name of experienced statistician identified to assist with Site Blinding Plan:	
The type of method used will be trial specific and must reduce the chance of imbalance between treatment groups	
Describe randomization methods (e.g. simple, block, stratified, minimization) and parameters of the randomization process (e.g. stratification variables, inclusion and exclusion criteria): *These must not change throughout the life of the protocol.*	

Section 2: Documentation of Design and Site Blinding Plan:	
Provide randomization list with details of the randomization codes:	
Confirm secure server on which the randomization schedule will be maintained:	

Section 3: Randomization Schedule:	
Method of generation of the randomized code list:	
Allocation of unique subject identifier (i.e. patient case number) and methods in place to	

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prevent same subject being randomized more than once:	
Person/people (and job title) responsible for preparing and checking the randomized code list/schedule. The system should be tested to ensure it performs reliably and consistently as intended:	
Distribution of electronic and paper copies of pharmacy records including approach used to conceal allocation (e.g. password protected electronic format):	
Method of implementation (e.g. web-based system):	
Computer software used to generate the randomization list and perform randomization and details on the validation of this system:	

Section 4: Procedures:	
Unblinding:	
Method by which the emergency access to the unblinding code for individual subjects broken:	
Reasons that may allow unblinding:	
Individuals with permission to unblind:	

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Documentation from study team necessary for blind to be broken:	
Plan for “after hours” need for unblinding:	
Documentation expectations of unblinding:	
Other considerations:	
For blinded trials, details on how the randomization codes will be provided to investigational product (IP) manufacturer to ensure the IP is packaged, coded and labelled in a manner that protects the blinding at the site and at the coordinating center. (i.e. “Drug Name Strength/Placebo”):	
For blinded trials, detail plan for interim analysis:	
Detail how the treatment allocated will be compared with the treatment received at the end of the trial.	
Detail how screen failures will be counted numerically and logistically (i.e. a subject that is randomized but not treated):	
Confirm how changes to the randomization schedule through the	

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course of the trial, along with the date when the new scheme became active will be documented in the study file (i.e. updated version of site blinding plan):	
Detail of the documentation needed to be completed prior to randomization (e.g. signed informed consent form, randomization checklist, eligibility criteria checklist):	
Details on who will perform the randomization (if not blinded) and how pharmacy will be informed of the randomized treatment allocation (i.e. fax or email forwarded to pharmacy):	

Current Electronic Signatures (v.2):

Signed electronically by: Betty Oleson (boleson@mcw.edu)

Date: *11-Feb-2022 @ 04:03 PM CST*

Reason: *Approval*

Previous Electronic Signatures:

There are no signatures for any previous versions.