



1. Purpose

The purpose of this SOP is to clearly outline the development, implementation, maintenance and backup of the randomization system for a research study.

2. Responsibilities

Methods Centre: Responsible for overseeing the setup, testing, maintenance, verification and backup of the central randomization system.

Biostatistician: Responsible for preparation of the randomization list and to keep a backup copy of the original randomization list.

Data Developer: Responsible for electronic implementation, validation and ongoing maintenance and verification of randomization system. They should also keep a backup copy of the list and treatment codes.

3. Procedures

Randomization System Setup

- 3.1 Unless otherwise stated, the methods centre (MC) will employ a central randomization system with a randomization scheme as defined in the study protocol
- 3.2 The randomization list is prepared by the study biostatistician. This process will be documented by the biostatistician.
- 3.3 The central randomization system is the preferred method of randomization because it ensures randomization is concealed (and when appropriate double-blinded) and does not rely on the sites' correct implementation of the randomization schedule. Automated (web or telephone) randomization systems are preferred because they provide 24-hour access without requiring manual intervention regardless of the site's location.
- 3.4 A randomization script or screening specifications document will be written by the MC to be incorporated into the central randomization system.
- 3.5 The data developers incorporate the randomization script into the electronic data capture system.
- 3.6 The randomization system should be fully tested prior to the commencement of patient recruitment. All testing should be documented.
- 3.7 If deemed appropriate by the Sponsor, a randomization system backup plan should be established.
 - 3.7.1 The need for a randomization system backup plan is to be determined by the Sponsor prior to the initiation of the clinical trial. This assessment is based on the following, but is not limited to:
 - 3.7.1.1 Compatibility with central randomization system
 - 3.7.1.2 Anticipated loss of recruitment in the absence of the central randomization system
- 3.8 A master randomization list is kept by the study biostatistician in a secure location.



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- 3.9 Any changes to the central randomization system should be documented. The system should be re-tested as appropriate to ensure the integrity of the system is maintained.

Randomization System Maintenance

- 3.10 The MC will perform regular checks of the randomization data. These checks will be performed at intervals specified for the particular study.
- 3.11 Patients which have been randomized in error should never be removed from the study database or the randomization system. These patients will be coded in the database to distinguish them from correctly randomized patients. Refer to study specific procedures for details concerning the coding of randomization errors. The reason for the randomization error should be documented.

Randomization System Backup

- 3.12 Applicable when the Sponsor has determined that a backup randomization system is necessary.
- 3.13 In the event of a randomization system failure the following steps are to be followed to ensure research sites have uninterrupted access to the randomization system:
- 3.13.1 The research site will contact the study specific unblinded designee, to report the problem they are having with the randomization system (e.g. busy signal, no answer, website unavailable).
 - 3.13.2 The unblinded individual will have the research site caller confirm eligibility by asking if the patient has provided informed consent and the inclusion/exclusion criteria has been reviewed.
 - 3.13.3 If the above is fulfilled, the unblinded individual will refer to a treatment allocation list reserved for manual randomizations and provide the research site caller with (1) the next randomization code in the sequence and (2) the corresponding treatment allocation.
 - 3.13.4 The unblinded individual will document the manual randomization discussions including the randomization ID and treatment allocation.
 - 3.13.5 The unblinded individual will report the randomization system failure to the Project Leader.

4. References

- 4.1 Friedman L, Furberg C and DeMets D. Fundamentals of Clinical Trials Third Edition, Springer Publishing: chapter 5 pgs 61-81.
- 4.2 Prokscha, S. (2007). CRF Design Considerations. In: Practical Guide to Clinical Data Management. FL: Taylor & Francis Group. 9-18.