STANDARD OPERATING PROCEDURE (SOP)

TITLE: BLINDING AND UNBLINDING

DO NOT USE THIS SOP WITHOUT FIRST CHECKING IT IS THE LATEST VERSION

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Applicable Clinique Research Site(s):	All

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Signature:	
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1. PURPOSE:

The purpose of this SOP is to describe the measures for blinding and unblinding undertaken at Clinique Research and to ensure:

- All relevant parties (sponsors and sites) are consulted and can support the project.
- The proposed trials are a strategic fit and aligns with Clinique Research's core values.
- Research projects have the best possible outcome in terms of recruitment, patient safety, budget, and time frames.

2. SCOPE:

All clinical trials to be monitored and managed at Clinique Research.

3. APPLICABILITY:

This applies to all Clinique Research employees, contract staff and to all relevant external persons or parties proposing to engage in the clinical trial services at Clinique Research.

4. GLOSSARY OF TERMS:

Please refer to Clinique Research SOP Glossary of Terms (see Related Documents).

5. PROCEDURE:

The Principal Investigator and the Sponsor will determine what type of method will be used to reduce the chance of imbalance between treatment groups. The design and type should be detailed in the protocol.

- A 'blind' study is a clinical trial in which the subject or the Investigator (or both) are unaware of which trial product/drug the subject is taking.
- When only one is blinded to the treatment allocation this is a 'single blind' study. When both do not know the treatment, the study is 'double-blind'.
- Studies in which the participant takes part in three arms, such as placebo, active drug and comparative drug remain as double blind.
- Unblinding is the process by which the allocation code is broken so that the PI and/or a clinician managing the patient and/or trial statistician and/or Sponsor delegate becomes aware of the intervention.

5.1 Randomization

- Once the design and type of randomization has been established in the protocol, a randomization list with the details of the randomization codes should be produced in accordance with the protocol.
- The list should be generated by a person who has no direct contact with the trial subjects or involvement with the assessment for eligibility in the trial.
- For blinded trials, the Principal Investigator will need to provide details on the randomization codes to the sponsor to ensure the Investigational Products are packaged, coded and labelled in a manner that protects the blinding.

5.2 Blinding

- The protocol should define the level of blinding e.g., single-blind or double-blind and how the blinding will be implemented (e.g., through the use of an identical placebo).
- The Investigational Product should be packed, coded and labelled in a manner that protects the blinding.
- The study protocol should define all individuals involved in the study who will be blinded to treatment and those who will not.
- When carrying out interim analyses of blinded results, the integrity of the blinding of the study should not be compromised.
- Only personnel not directly involved in the running or conduct of the study should have access to the randomization list/code.
- Take adequate steps to ensure that the treatments are indistinguishable in placebo-controlled trials (for example, the smell, color and texture of the placebo should be identical to the Investigational Product).

5.3 Unblinding

If the trial or a single subject is accidentally unblinded or unblinded due to a serious adverse event (SAE), the Principal Investigator is responsible for promptly documenting the series of events and notifying the Sponsor and CRA. The details of all unblinding shall be included in the statistical report. It is a fundamental part of blinded trials to take measures to avoid accidental unblinding. However, unblinding will be necessary in certain circumstances such as:

- After the end of the trial: make sure a formal process to control the unblinding of the trial is agreed and documented. The Statistical Analysis Plan shall be provided in the protocol or be finalized prior to the release of the randomization codes. Any changes to the statistical

analysis plan shall be version controlled. A record shall be kept in the Investigator TMF to confirm when the randomization code was requested and when provided. Sponsor approval should be sought prior to unblinding. If approval is given, information should be provided to the requesting party and the unblinding template should be completed and forwarded to the CRA. All care shall be taken to ensure that the study team are kept blinded.

- Emergency and safety: ensure procedures are in place to instruct how unblinding can be dealt with for expedited reporting purposes without compromising the blinded members of the trial team. Details of any emergency unblinding shall be documented fully in the Sponsor file, Investigator Trial Master File (TMF), Pharmacy File and Site File(s).
- Interim analyses: all unblinded interim review of the data should be pre-planned, specified in the trial protocol and conducted by personnel who have no further involvement in the conduct of the trial or the final analysis (normally the Data Monitoring Committee)

Therefore, prior to initiating a blinded trial the PI should ensure that:

1) a robust unblinding process has been implemented and documented.
2) the code breaks are on site in a designated place.
3) all staff involved in the trial and process are aware of the arrangements.

Examples of code breaks include:

• A master randomization list held by the pharmacy
• Code break envelopes
• Scratch off panels on medication containers
• A sealed tear off portion on medication labels that would be filed in the pharmacy or with the participant's records
• An "on call" 24 hour-a-day process

- The PI should ensure the reasons and circumstances of any code break are documented appropriately.

6. VERSION CONTROL:

Document History	
Version	**Summary of Changes**
1.0	N/A – First Issue

7. APPENDIX: N/A