STANDARD OPERATING PROCEDURE (SOP)

TITLE: PROTOCOL DEVIATIONS AND VIOLATIONS

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 protocol deviations and violations 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 is responsible for reporting and documenting any deviations/violations to the CRA/Sponsor as soon as the deviation/violation is identified using the Protocol Deviation/Violation Report Form. In addition, if these are deemed a potential serious breach or an urgent safety measure, the Principal Investigator is to report the deviations/violations to the approving Ethics Committee (Institutional Review Board, IRB).

5.1 Protocol Deviation

A protocol deviation is usually an unintended departure from the expected conduct of the trial (with regards to the protocol and/or SOPs). These events may be identified by the trial team during trial conduct and must be continually monitored by the Principal Investigator/Clinical Research Associate for repeated occurrences.

- All such cases must be documented in the appropriate Case Report Form (CRF) or Study File Note and appropriate corrective and preventative action must be taken to ensure they do not reoccur.
- Examples of deviations may include, but are not limited to:

- ✓ A case where a potential participant does not meet, or only partially meets, one of the eligibility criteria, and the issue has been discussed with the Lead Investigator/CRA/Sponsor and it has been agreed that the participant can proceed.
- ✓ A protocol visit date deviation outside the study visit window, or not conducted.
- ✓ Isolated incident of a missed or incomplete study procedure (e.g. laboratory test or completion of a questionnaire);
- ✓ Isolated incident of a missed or incomplete study evaluation (e.g. exam).

5.2 Protocol Violation

A protocol violation is any departure from the approved protocol, trial documents, or any other information relating to the conduct of the study which may affect the safety of trial participants or the study outcomes.

- Any violations that may impact on the participants' safety or affect the integrity of the study data must be reported to the Sponsor and the approving Ethics Committee (HREC) within an agreed period of time usually 48hrs.
- Examples of violations may include, but are not limited to:
  - ✓ Failure to obtain informed consent (i.e. there is no documentation of this in source data or a signed Informed Consent form)
  - ✓ Enrolment of participants that do not meet the inclusion/exclusion criteria
  - ✓ Undertaking a trial procedure not approved by the Ethics Committee (HREC) (unless for immediate safety reasons), or HREC approval not obtained or incomplete
  - ✓ Failure to report adverse events, serious adverse events or suspected unexpected serious adverse reactions (SUSARs) in accordance with the legislation and sponsor and protocol requirements
  - ✓ Investigational product dispensing/dosing error

5.3 Corrective and Preventive Action (CAPA)

- The Trial Sub-Committee must agree on the appropriate corrective and preventative action to be taken and this should be documented and detailed within the body of the initial notification report.
- Follow-up reports should be made in writing (the Protocol Deviation/Violation Form can also be used for this) and should:
  - ✓ Be clearly identified as a follow-up report
  - ✓ Identify the unique ID allocated when the initial report was generated
  - ✓ Document the outcome of the decision

- ✓ Detail any follow-up to the discussion (e.g., further site or Principal Investigator training, removal of the participant data, protocol amendment)
- ✓ Be placed in the central record of the participant file.

6. VERSION CONTROL:

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

7. APPENDIX:

Management of Project Escalation SOP