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Standard Operating Procedure
Protocol Deviation

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REVISION HISTORY

Rev #	**Section**	**Revision Date**	**Reason for Revision**	**Signature of MREC Secretary**
0	All	04/07/2016	Version 2.0, new format with additional information	
1	All	14/05/2018	Version 2.1, New flow chart for PD review using the new platform with added abbreviations	
2	8.5.5, References	20/01/2022	Version 2.1, updated references and clarification on wording in 8.5.5	
3	All	08/04/2026	Version 3.0, updated PD reporting flowchart as per latest MGCP	

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1. PURPOSE

To establish a standardized process for the identification, reporting, documentation, review, and management of Protocol Deviations (PD) in research studies approved by the Medical Research and Ethics Committee (MREC), including both:

- Important Protocol Deviations
- Non-Important Protocol Deviations

This procedure ensures:

- protection of research participants,
- integrity of research data,
- compliance with approved study protocols,
- adherence to national and international research ethics standards.

2. SCOPE

This standard operating procedure describes the management, documentation and submission of protocol deviation and incidents of non-compliance and scientific misconduct.

3. ABBREVIATIONS

MREC	Medical Research and Ethics Committee
NMRR	National Medical Research Register
PD	Protocol Deviation
PDRP	Protocol Deviation Reporting Platform
PDSC	Protocol Deviation Sub-Committee

4. GLOSSARY

Term	Definition
Protocol Deviation	Protocol deviations are generally unintentional departures from the IRB-approved protocol and are commonly not discovered until after they occur (e.g., an investigator's failure to perform a protocol-required test is discovered by the study monitor during a routine monitoring visit). Protocol deviations may also include an intentional departure from the IRB-approved protocol for a single participant (e.g., investigator seeks and receives sponsor and IRB approval to enroll a participant above the maximum age criteria); such intentional departures should be rare because the protocol should include appropriate flexibility regarding trial conduct (e.g., eligibility criteria, reasonable visit windows).
Important Protocol Deviation	Important protocol deviations are a subset of protocol deviations that may significantly impact the completeness, accuracy, and/or reliability of the trial data or that may significantly affect a participant's rights, safety or well-being

Non-Important Protocol Deviation	Non-Important protocol deviations are a subset of protocol deviations that may not impact the completeness, accuracy, and/or reliability of the trial data or that may significantly affect a participant's rights, safety or well-being

5. REQUIRED AND RELATED DOCUMENTS

#	**Document Title**
1.	SOP 5-1: Maintenance, Archival and Disposal of Study and Non-Study Files
2.	TP5-1-1 Template for reminder letter

6. PROCEDURE

6.1 Important Protocol Deviation

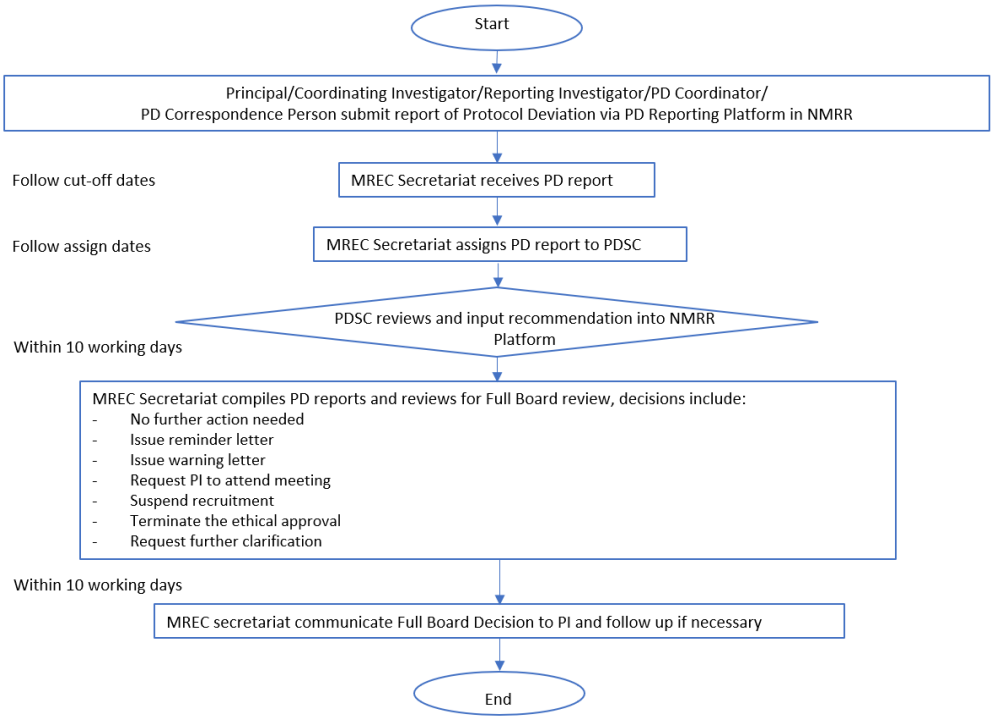
Step #	Process	Responsibility
1	Principal / Coordinating Investigator//PD Coordinator/ PD Correspondence Person submit report of Important Protocol Deviation via PD reporting platform in NMRR system	Principal / Coordinating Investigator//PD Coordinator/ PD Correspondence Person
2.	MREC Secretary receives report of Important Protocol Deviation via PD reporting platform in NMRR system	Secretary
3.	MREC secretariat assign Important PD report for PDSC review.	Secretariat
4.	PDSC review within 10 working days	PDSC
5.	MREC Secretariat receives recommendation from PDSC - No further action needed - Issue reminder letter - Issue warning letter - Request PI to attend meeting - Suspend recruitment - Terminate the ethical approval - Request further clarification	Secretariat/ PDSC
6	MREC Secretariat tables the Important PD reports along with PDSC recommendations to full board following cut off date of Full Board Meeting.	Secretariat/Chairperson
7	MREC Secretariat communicates decision from MREC Full Board via the PD-Reporting Platform on NMRR and feedback is sent to (when required). a. Principal / Coordinating Investigator c. PD Coordinator, PD Correspondence Person d. Person who created or submitted the PD Report Follow-up on action to be taken by investigator (where applicable).	Secretariat/Secretary
8	End	

6.2 Non-Important Protocol Deviation

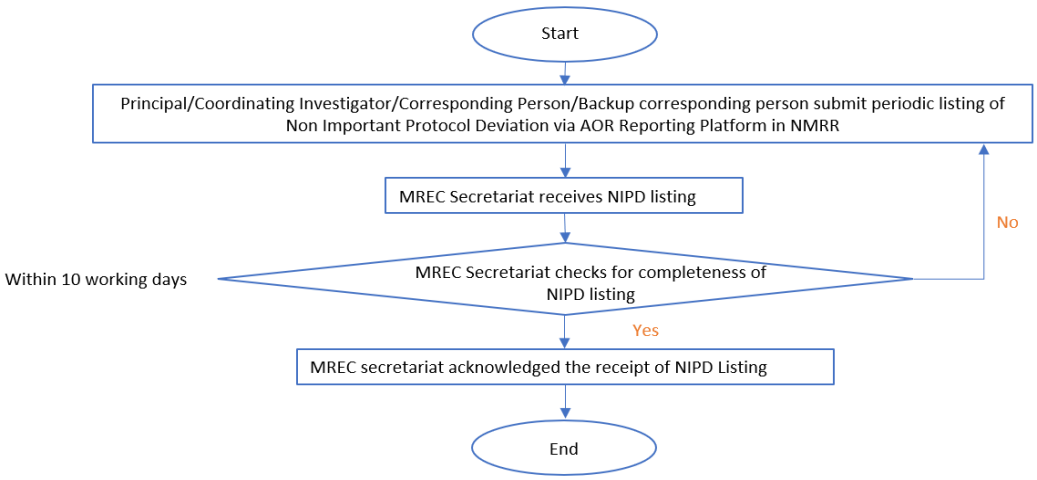
Step #	Process	Responsibility
1	Principal / Coordinating Investigator/ Corresponding Person/Backup Corresponding Person submit periodic listing of Non-Important Protocol Deviation via AOR reporting platform in NMRR system	Principal / Coordinating Investigator/ Corresponding Person/ Backup Corresponding Person
2.	MREC Secretariat receives periodic listing of Non-Important Protocol Deviation via AOR reporting platform in NMRR system	Secretariat
3.	MREC secretariat checks through Non-Important Protocol Deviation for the completeness of the report If incomplete, MREC secretariat will revert and request for revision via NMRR system -> Step 1	Secretariat
4.	MREC secretariat acknowledges the receipt of periodic listing of Non-Important Protocol Deviation	Secretariat
7	End	

7. FLOWCHART

PD FLOWCHART (IMPORTANT PROTOCOL DEVIATION)



PD FLOWCHART (NON-IMPORTANT PROTOCOL DEVIATION)



8. DETAILED INSTRUCTION

8.1 Principal Investigator (PI) shall identify and document protocol deviations, communicates the deviations with the sponsor to classify deviations as Important or Non-Important. The following are considered important protocol deviations as they may compromise participant safety, rights, or data integrity, and therefore should be promptly reported to MREC:

a) Failure to perform protocol-required procedures for participant safety monitoring, or inadequate monitoring of participants.
b) Failure to collect essential laboratory investigations required for safety assessment
c) Failure to administer the investigational product in accordance with protocol specifications
d) Use of prohibited concomitant medication or treatment, which may:
e) Increase risk to participants (e.g., drug–drug interactions), and/or
f) Affect the evaluation of safety and efficacy outcomes
g) Failure to obtain valid informed consent, or non-compliance with ethical and regulatory requirements for the protection of human subjects
h) Failure to ensure confidentiality and protection of participants' identifiable personal or health information
i) Failure to discontinue investigational product in participants who meet withdrawal or stopping criteria
j) Administration of incorrect treatment, incorrect dosage, or incorrect device to participants
k) Failure to adhere to the protocol-defined randomization procedures, potentially affecting study validity

8.2 The investigator submits the Important PD report through the NMRR PD Reporting Platform

8.3 The MREC Secretariat receives the PD report via NMRR, conducts completeness screening.

a) If incomplete, the report will be returned to investigator for revision.
b) If complete, the report will be assigned to the Protocol Deviation Subcommittee (PDSC).

8.4 Establishment of Protocol Deviation Sub Committee (PDSC)

8.4.1 The PDSC is established to assist the MREC in the post approval monitoring of Protocol Deviations/ Violations reports received from the investigators.

8.4.2 Members of the PDSC are appointed by the MREC Chairperson, as and when the need arises. The membership of this committee may comprise of medical members/ any suitably qualified personnel

8.5 Review of Protocol Deviation/ Violation

8.5.1 PDSC conducts a review of the PD reports and provide recommendation to Full board for further actions within 10 working days, includes:
a) No further action needed
b) Issue reminder letter
c) Issue warning letter
d) Request PI to attend meeting
e) Suspend recruitment
f) Terminate the ethical approval
g) Request further clarification

8.5.2 MREC Secretariat will table the PD reports with recommendation from PDSC to the Full Board meeting according to the cut off dates for further discussion and decision. Possible decisions include:
a) No further action required
b) Reminder letter
c) Warning letter
d) Request PI to attend meeting
e) Suspend recruitment
f) Terminate ethical approval
g) Request additional clarification.

8.5.3 The MREC Secretariat communicates the decision to the investigator **within 10 working days** after the Full Board meeting.

8.5.4 The PI will be communicated with where relevant and the PI may be requested to provide additional information, submit additional documents, or implement corrective action(s).

8.5.5 In the case of when the recruitment has been suspended, the suspension may be revoked once all noncompliance issues are addressed

8.6 Management of Non-Important Protocol Deviations

8.6.1 Principal / Coordinating Investigator/ Corresponding Person/Backup Corresponding Person submit periodic listing of Non-Important Protocol Deviation via AOR reporting platform in NMRR system

8.6.2 MREC Secretariat receives periodic listing of Non-Important Protocol Deviation via AOR reporting platform in NMRR system

8.6.3 MREC secretariat checks through Non-Important Protocol Deviation for the completeness of the report within **10 working days**:
a) If incomplete, the report will be returned to investigator for revision.
b) If complete, the report will be acknowledged.

8.6.4 Non-important PDs must be escalated and reported as Important PDs if:
a) deviations occur repeatedly,
b) a pattern of non-compliance is identified,
c) participant safety may be affected.

8.7 All documentation related to Protocol Deviations shall be retained according to MOH record retention policies and stored within the NMRR electronic system.

9. REFERENCES

9.1 Ministry of Health Malaysia. Malaysian Guideline for Good Clinical Practice (5th Edition). National Pharmaceutical Regulatory Agency (NPRA), Ministry of Health Malaysia; 2026.

9.2 International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R3). ICH Harmonised Guideline; 2025.

9.3 World Medical Association. World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. Adopted June 1964, Helsinki, Finland; latest amendment 2024

10. APPENDIX

None