

1. PURPOSE

- 1.1 The purpose of this policy is to describe the requirements for reporting of protocol deviations, unanticipated problems, and serious breaches to the Division of Microbiology and Infectious Diseases (DMID).

2. SCOPE

- 2.1 This policy applies to:
- 2.1.1 Clinical trials where DMID is the Investigational New Drug (IND)/ Investigational Device Exemption (IDE) or equivalent sponsor (regardless of funding type).
 - 2.1.2 Non-IND clinical trials funded under contract.
 - 2.1.3 For non-IND clinical trials funded under cooperative agreement, the Program Officer (PO) may require adherence to this policy.
- 2.2 For clinical studies (that are not clinical trials) funded under contract, the Contracting Officer's Representative (COR) may require adherence to this policy.

3. DEFINITIONS

- 3.1 Protocol Deviation: Any change, divergence, or departure from the study design or procedures defined in the current and IRB-approved protocol.
- 3.1.1 Major deviation – A deviation from the protocol that has or has the potential to negatively impact the rights, safety, or welfare of safety of the participant, or integrity or validity of the study data.
 - 3.1.2 Minor deviation – A deviation that has no potential to negatively impact the rights, safety, or welfare of participants, or the integrity or validity of the study data.
- 3.2 Unanticipated Problem (UP): Any incident, experience, or outcome that meets all of the following criteria:
- 3.2.1 Unexpected (in terms of nature, severity, or frequency) given
 - (a) the research procedures that are described in the protocol and related documents, and
 - (b) the characteristics of the subject population being studied
 - 3.2.2 related or possibly related to participation in the research; and
 - 3.2.3 suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.
- 3.3 Serious Breach: Any deviation of the approved protocol version or the clinical trial regulation that is likely to affect the safety, rights of trial participants and/or data reliability and robustness to a significant degree in a clinical trial.

For other definitions, see [DMID glossary](#).

4. RESPONSIBILITIES

- 4.1 Principal Investigator or designated clinical research staff is responsible for ensuring the reportable events identified in this policy are reported to DMID in accordance with this policy, contract requirements, and applicable regulations.
- 4.2 DMID staff are responsible for determining whether a reported major deviation, unanticipated problem, or Serious Breach requires additional reporting to regulatory authorities.

5. POLICY

- 5.1 For DMID sponsored studies protocol deviations, UPs, and Serious Breaches must be documented, effectively tracked by the Principal Investigator or designated clinical research staff in a system that is compliant with all applicable regulations and must be reported to the IRB/IEC of record according to institutional policies.
- 5.2 For clinical studies in scope of this policy, a major deviation, UP, or Serious Breach must be reported to DMID within 5 business days of identification of the issue, or within 5 business days of the scheduled protocol-required activity.
 - 5.2.1 For clinical studies utilizing the DMID Statistical and Data Coordinating Center (SDCC) contractor, protocol deviations, serious breaches, and unanticipated problems are submitted via the Internet Data Entry System are automatically reported to DMID, no other reporting is required.
 - 5.2.2 For clinical studies utilizing other DCCs to capture study data, issues must be reported directly to DMID via a [web-based report form](#) or email at protocoldeviations@dmidcroms.com or DMIDUP@mail.nih.gov.
- 5.3 DMID staff will make the determination of whether the reported event qualifies as a Serious Breach and requires additional reporting to regulatory authorities

6. REFERENCES

- 6.1 [FDA Code of Federal Regulations \(CFR\) Title 21](#):
 - 6.1.1 21 CFR Part 312: Investigational New Drug Application
 - 6.1.2 21 CFR Part 812: Investigational Device Exemptions
- 6.2 [MHRA Guidance for industry and organizations to follow from 01 January 2021](#)
- 6.3 [International Council for Harmonisation ICH E6 \(R2\): Good Clinical Practice](#)
 - 6.3.1 Section 4.5: Compliance with Protocol
 - 6.3.2 Section 5.1: Quality Assurance and Quality Control
- 6.4 [Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events: OHRP Guidance \(2007\)](#)
- 6.5 [Guideline for the notification of serious breaches of Regulation \(EU\) No 536/2014 or the clinical trial protocol](#)

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6.6 [EMA Guidelines: Notification of Serious Breaches](#)

7. APPENDICES

7.1 Enter Quality Record Name/Number (Update if applicable. If not enter "Not applicable" on this row)

8. REVISION HISTORY

8.1 DMID-SM-POL-00006- DMID Reportable Events Policy is the original version of this procedure within the eQMS. It replaces Guidance & Tools- Protocol Deviation Reporting and Form.

9. ADDITIONAL INFORMATION

9.1 Document Lead: Office of Clinical Research Affairs (OCRA)

9.2 Posting externally: Yes