

**PROTOCOL DEVIATIONS, VIOLATIONS AND ADVERSE EVENT REPORTING**

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| **Version** | **Date** | **Reason for Change** |
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1. **Background**

A protocol that has received ethics approval (and other regulatory approval as applicable) is a formal document defining what can and cannot be done as part of a research project and must be adhered to so that participant safety and research integrity can be maintained. Deviations from protocol can occur for a number of reasons and depending on the occurrence can be classed as a protocol deviation or a protocol violation.

A protocol deviation occurs when a process or criteria has not been actioned in line with the approved protocol. For example, a study visit outside defined visit schedule, or a variation in the management of a participant due to minor safety concerns. Deviations are occurrences which can be classed as minor and not affect participant safety or the integrity of the research. A protocol deviation may become a violation if it occurs on multiple occasions and/or affects multiple participants.

A protocol violation is a significant occurrence or event which may affect participant safety or the integrity of the research, or a consistent variation in practice from the defined protocol. Non-compliance with the inclusion and exclusion criteria is always classed as a significant protocol violation regardless of how minor the deviation appears to be, as these criteria define the participant group in relation to the scientific requirements of the protocol.

An adverse event [AE] is commonly defined as an untoward medical occurrence in a research participant who has been administered any research procedure. A Serious Adverse Event (SAE) is any untoward and unexpected medical occurrence or effect that:

* Results in death
* Is life-threatening – refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe
* Requires hospitalisation, or prolongation of existing inpatients’ hospitalisation
* Results in persistent or significant disability or incapacity
* Is a congenital anomaly or birth defect

Medical judgement should be exercised in deciding whether an AE is serious in other situations. Important AEs that are not immediately life-threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, should also be considered serious. To be compliant with the Research Governance Framework (RGF), and the Medical Devices Regulations 2002, sponsors of clinical studies have a responsibility to record and report SAEs.

1. **Purpose**

This Standard Operating Procedure (SOP) describes the processes for handling protocol deviations, protocol violations and Adverse Event reporting. It is applicable to all interventional research projects involving human participants.

1. **Procedure** 
   1. **Protocol Deviations**

The Chief Investigator (CI) of a research project is responsible for ensuring there appropriate oversight systems in place to monitor research activity and identify any deviations from the study protocol.

When a protocol deviation is identified, the CI must review it to assess whether participant safety or study integrity has been affected. If the deviation did not impact on safety or research integrity, a [File Note](http://www2.mmu.ac.uk/media/mmuacuk/content/documents/research/sop/linked-documents/File-Note-Template.docx) should be added to the Study Master File and/or CRF and patients medical notes (where applicable) explaining the action taken and its justification. If the CI is unsure whether an occurrence is a deviation or violation they should seek advice from the RKE office to ensure appropriate action is taken.

* 1. **Protocol Violations**

A [Protocol Violation Reporting Form](http://www2.mmu.ac.uk/media/mmuacuk/content/documents/research/sop/linked-documents/Protocol-Violation-Reporting-Form.docx) must be completed for any identified protocol violations. For single site studies this should be completed by the CI. For multi-site studies the form should be completed by the Principal Investigator (PI) at the site and then forwarded to the CI within 3 days of the event.

The CI must forward completed Protocol Violation Reporting Forms to the RKE office within 24 hours of receipt.

* 1. **Adverse Event Reporting**

All adverse events must be reported. Depending on the severity of the event the reporting procedures below should be followed.

Non-serious AEs

A [File Note](http://www2.mmu.ac.uk/media/mmuacuk/content/documents/research/sop/linked-documents/File-Note-Template.docx) should be completed by the CI and stored in the study master file.

Serious AEs

For single site studies the CI should complete an [SAE Form](http://www2.mmu.ac.uk/media/mmuacuk/content/documents/research/sop/linked-documents/SAE-Form.docx). For multi-site studies the PI should complete and SAE form and send this to the CI within 24 hours of the event. Unexpected events that are thought to be related to the research procedure (in the opinion of the CI) should be reported to the NHS REC (where applicable) within 15 days of the CI becoming aware of the event.

The CI must report all SAEs to the RKE Office within 24 hours of them becoming aware of the event.

1. **Related Documents**

[File Note](http://www2.mmu.ac.uk/media/mmuacuk/content/documents/research/sop/linked-documents/File-Note-Template.docx)

[Protocol Violation Reporting Form](http://www2.mmu.ac.uk/media/mmuacuk/content/documents/research/sop/linked-documents/Protocol-Violation-Reporting-Form.docx)

[SAE Form](http://www2.mmu.ac.uk/media/mmuacuk/content/documents/research/sop/linked-documents/SAE-Form.docx)

1. **References**

Research Governance Framework for Health and Social Care

<https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/139565/dh_4122427.pdf>

Medical Devices Regulations 2002

<http://www.legislation.gov.uk/uksi/2002/618/contents/made>