| Joint Research Management Office Standard Operating Procedure for: | | | |
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| **Pharmacovigilance and safety reporting for sponsored Interventional and Research studies** | | | |
| SOP Number: | **26b** | Version Number: | **4.0** |
| Effective Date: | **15th September 2021** | Review Date: | **15th September 2024** |

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**Purpose:**

The purpose of this standard operating procedure (SOP) is to describe the process for reporting adverse events (AEs) and adverse reactions (ARs), serious adverse events (SAEs), serious adverse reactions (SARs), and urgent safety measures (USMs) for all clinical research sponsored by Barts Health NHS Trust (Barts Health) or Queen Mary University of London (Queen Mary), excluding those regulated by the Medicines and Healthcare Products Regulatory Agency (MHRA).

This SOP is applicable to the safety reporting procedures for all sponsored Interventional and Research studies.

For guidance on safety reporting procedures for sponsored MHRA-regulated studies see SOP 26a Site level PV and safety reporting for Clinical Trial of an Investigational Medicinal Products (CTIMP) and Advanced Therapy Investigational Medicinal Products (ATIMP), *SOP 26c Pharmacovigilance (Process for the Sponsor & Chief Investigator (CI)* and *SOP 26d Safety reporting for clinical investigations of medical devices*.

This SOP will provide guidance to ensure that systems are in place for the management of AEs, and that Barts Health and Queen Mary meet the sponsor safety reporting requirements of Good Clinical Practice (GCP) and the UK Policy Framework for Health and Social Care Research.

**Scope:**

This SOP defines the standard procedure for Interventional and Research studies. In some cases, the procedure may be adapted to meet the requirements of a specific study. Any such adaptation must be agreed with the Joint Research management Office (JRMO) during study set up and documented in the protocol.

For all studies sponsored by external organisations i.e., NHS Trusts other than Barts Health, universities other than Queen Mary, or commercial companies, the sponsor's pharmacovigilance procedure must be followed.

**Delegation of Responsibilities**

The CI has overall responsibility safety reporting for sponsored studies at all the sites and if medically qualified is deemed the medical assessor. If the CI is not medially qualified a medical assessor should be delegated.

Each Principal Investigator (PI) is delegated responsibilities for safety reporting for studies at their site.

**Abbreviations:**

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| AE | Adverse Events |
| AR | Adverse Reactions |
| ATIMP | Advanced Therapy Investigational Medicinal Products |
| Barts Health | Barts Health NHS Trust |
| CI | Chief Investigator |
| CTIMP | Clinical Trial of an Investigational Medicinal Product |
| GCP | Good Clinical Practice |
| HRA | Health Research Authority |
| JRMO | Joint Research Management Office |
| MHRA | Medicines and Healthcare Regulatory Agency |
| PI | Principal Investigator |
| Queen Mary | Queen Mary University of London |
| REC | Research Ethics Committee |
| SAE | Serious Adverse Event |
| SAR | Serious Adverse Reaction |
| SOP | Standard Operating Procedure |
| USM | Urgent Safety Measures |

**Definitions:**

- Interventional studies: Research involving a change in treatment, care or other services defined by a research protocol, which are not regulated by the MHRA
- Research Studies: Any study related to human research where no physical intervention is occurring.

**Relevant SOPs:**

- SOP 26a Site level PV and safety reporting CTIMPs and ATIMPs

- SOP 26b Pharmacovigilance (Process for the Sponsor & CI)
- SOP 26d Safety reporting for clinical investigations of medical devices.

| SOP Text: | | |
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| | **Responsibility** | **Activity** |
| **1.** | **CI** | **Define safety reporting requirements in the clinical trial protocol.**<br><br>The level of safety reporting required will vary depending on the nature of the study. For high-risk interventions, consider following the full safety reporting procedure described in this SOP. For observational studies and low risk interventions, consider reducing the safety reporting requirements. For example, the requirement to record and report non-serious AEs and unrelated SAEs can be omitted. Unexpected serious adverse reactions (SAR) must always be reported to the sponsor and Research Ethics Committee (REC) (see section 7), this cannot be omitted.<br><br>Any changes to the standard safety reporting procedures should be described in the study protocol, or it will be assumed that the full procedure will be followed.<br><br>The protocol should also describe the reporting procedure for SAEs. |
| **2.** | **All** | **Identify and document all AEs and AR.**<br><br>An AE is an untoward medical occurrence in a clinical trial participant who has undergone any research procedure.<br><br>An AR is an AE that may have a causal relationship with the research procedure that the patient has undergone.<br><br>The research team must identify all AEs and ARs experienced by research participants. The AEs must be recorded in the participant's medical records and case report forms, and should include a description of the event, the date and time that the event started and stopped, the severity of the event and any action taken in response to the event.<br><br>The study protocol will define the exact reporting period for each study. |
| **3.** | **PI/medically qualified delegated team member** | **Assess the seriousness of all AEs.**<br><br>The PI or a medically qualified research team member must assess each identified AE and AR to establish if it should be classified as an SAE.<br>An AE is classed as an SAE if it meets at least one of the following criteria:<br>• Results in death.<br>• Is life threatening.<br>• Requires hospitalisation or prolongation of hospitalisation.<br>• Results in persistent or significant disability or incapacity.<br>• Is a congenital anomaly or birth defect.<br>• Deemed by the PI to be medically significant.<br><br>The seriousness assessment must be documented in the participant's medical records. For volunteer studies without medical records, the seriousness assessment must be documented in the agreed source document. |

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| **4.** | **PI/medically qualified delegated** research team member. | **Assess the relatedness and expectedness of each AE.**<br><br>**Relatedness**<br>The PI or delegate must use their medical specialist knowledge and experience to assess whether there is a reasonable possibility that the AE is related to a research procedure.<br><br>**Expectedness**<br>Each study protocol should include a list of expected reactions to the research procedures. The PI or delegate must use this list to determine whether the adverse event is an expected reaction to the research procedures.<br>Expectedness is not related to the disease or conditions being studied.<br><br>These assessments must be documented in the participant's medical records (or agreed source document for healthy volunteer studies) and case report forms. |
| **5.** | PI/delegated team member | **Report all required SAEs to the CI or delegate.**<br><br>A safety reporting form (associated document 1) must be completed for each SAE that requires reporting. Once completed the SAE form should be signed by the PI or appropriate delegated person and emailed to the CI, trial coordinator or study email address in accordance with the protocol.<br><br>Individual protocols will specify which events require reporting. |
| **6.** | CI / PI/ delegated team member | **Report related, unexpected SAEs to the sponsor and CI.**<br><br>SAEs which are both related and unexpected must be reported to the JRMO.<br><br>A scanned signed copy of the SAE form should be emailed to: research.safety@qmul.ac.uk. |
| **7.** | CI | **Assess reported SAEs.**<br><br>Assess the relatedness and expectedness of the SAE and document the assessment.<br><br>If the CI disagrees with the PIs assessment both should be recorded but the PI assessment should not be changed. If the CI 'upgrades' the event, i.e., changing the event the PIs has reported to become 'related' or 'unexpected' this is how the sponsor will class the event. If required, escalate to the Research Governance Operations Manager and then to the Sponsor Oversight Group if needed for review.<br><br>If the event is an unexpected serious adverse reaction, then the CI should forward the safety report form to research.safety@qmul.ac.uk and include their assessment of the event. |
| **8.** | Clinical Trial Monitor | **Process received events as per SOP 26c Pharmacovigilance (Process for the Sponsor and CI)** |
| **9.** | CI | **Report SAEs which are unexpected and related to the REC.**<br><br>See the Health Research Authority (HRA) website for details of submitting Interventional and Research studies SAE forms. |

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| | | http://www.hra.nhs.uk/research-community/during-your-research-project/safety-reporting/<br><br>If the SAE relates to any of the following it should also be submitted to REC:<br>• It is a new event, related to the conduct of the study or the development of an investigational medical device, that is likely to affect the safety of subjects.<br>• An SAE associated with the study procedures which could modify the conduct of the study.<br><br>When submitting to REC, assess whether the SAE impacts on study design i.e., whether there are new risks to be included in patient information sheet or whether the protocol needs to be an amendment. |
| **10.** | PI | **Follow-up all AEs to completion.**<br>Follow-up the participant until the event abates. Document all relevant information in the participant's medical records. Update the case report form or SAE form as appropriate and update the CI and sponsor if required. |
| **11.** | Site PI | **Ensure any incident that falls within the Barts Health incident policy is appropriately reported.**<br>Please see the Barts Health intranet for the adverse incident policy for details of events to be reported. |

## Change control

This section outlines changes from version **3.0** to version **4.0**

| Section changed | Summary and description of changes |
|---|---|
| All | Formatting changes throughout |
| All | Removal of Annual Progress Reports and reference to SOP 19 |
| Section 1 | Definition of the safety reporting requirements |

## List of appendices

There are no appendices for this SOP.

## List of associated documents

| Document ref. | Document name |
|---|---|
| Associated document 1 | JRMO Interventional and Research SAE reporting form |