Royal Papworth Hospital
NHS Foundation Trust

Document Title: Adverse Event Reporting Process for Non-Papworth Sponsored Studies.

Document Number: SOP132

Staff involved in development: *Job titles only*	Senior R&D Manager, R&D Operational Manager, Clinical Project Managers, QA Manager
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Key Related Documents	DN070 Trust policy for reporting accidents, adverse events, incidents and defects SOP012: Adverse Event Reporting SOP069: Code breaking/un-blinding of Clinical Trials. SOP071 Urgent Safety Measures SOP079 Reference Safety Information SOP087 Adverse Event Reporting for Device Trials SOP088 Clinical Trial Participants and Pregnancy

Key Points of this Document

- This document sets out the adverse event reporting procedures to be followed by all Royal Papworth Staff who are involved in setting up and running externally sponsored research studies.
- For non-Royal Papworth sponsored studies, the adverse event reporting process in the study protocol must be followed.
- For adverse event reporting procedures for a Royal Papworth sponsored study, please refer to SOP012.

1 Purpose and Content

a. All clinical trials of investigational medicinal products (CTIMPs) must be conducted in accordance with Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 and any subsequent amendments. This SOP serves to clarify the process for externally sponsored CTIMPs /Device studies. The safety reporting processes will also be detailed within the protocol and sponsor SOPs.

b. For CTIMPs and Device Trials, the sponsor is required to ensure that adverse events are appropriately recorded, reviewed and reported.

c. For non-CTIMP studies, it is the Sponsor's responsibility to decide what level of safety event recording is required before the study starts.

d. The reporting requirements in this SOP are mandatory in addition to the Trust's policy for the reporting of accidents / adverse events / incidents and defects (DN070) and non-compliance (where applicable).

2 Roles and Responsibilities

a. All staff are responsible for ensuring that all adverse events, whether or not related to research, are reported in accordance with the Royal Papworth Hospital NHS Trust's policy for the reporting of accidents / adverse events / incidents and defects (DN070), where applicable.

b. This SOP applies to all personnel that are conducting research at the Trust.

c. Staff involved in the conduct of non-Papworth sponsored research studies must comply with the requirements set out in this SOP.

Event Definitions:

For event definitions in relation to CTIMPS see SOP012.

For event definitions in relation to Device Trials see SOP087.

Assessment Definitions:

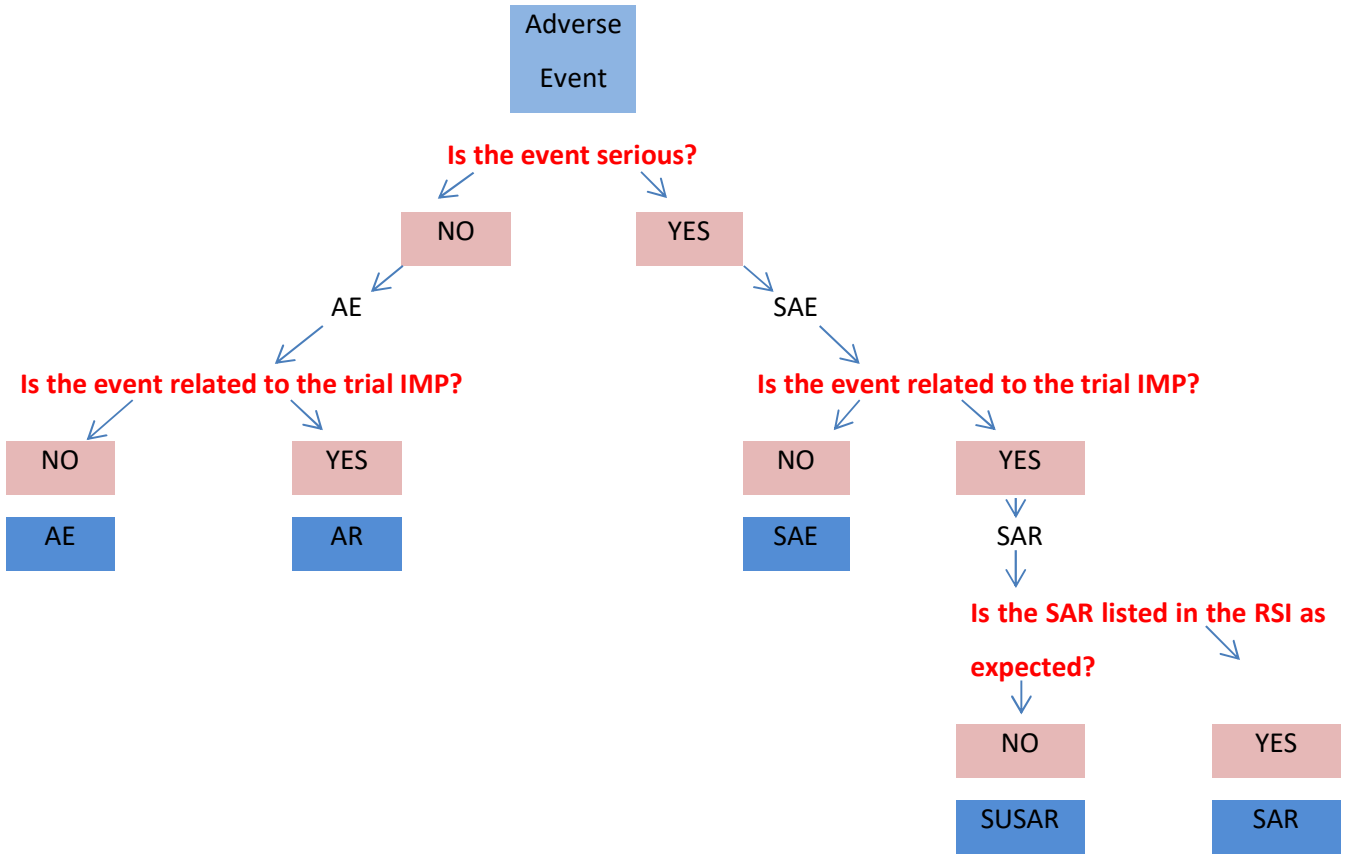
Assessment type:	**Person responsible for undertaking assessment:**	**Explanation of assessment:**
Seriousness	Member of the research team	An event is defined as being serious if it results in any of the following: • Death • Is life threatening • Results inpatient hospitalisation • Hospitalisation is prolonged • Results in disability or incapacity • Consist of a congenital anomaly or birth defect • Is an important medical event
Severity	PI/Medically qualified research team member	Assessment based on clinical judgement or use of specific scales as stipulated in the protocol e.g. Common Terminology Criteria for Adverse Events (CTCAE) Grading: • Mild • Moderate • Severe
Causality	PI/Medically qualified research team member	Assessment of whether or not the event is in any way related to the trial IMP/comparator or placebo or device are categorised as per the sponsor protocol Further information on causality can be found in the study Investigator Brochure, summary of product characteristics or specific reference safety information.
Expectedness	PI and/or sponsor	If an event becomes a SAR, it must undergo expectedness assessment to determine whether or not the SAR is expected in line with its RSI. • All CTIMPs must have clearly documented Reference Safety Information for all investigational medicinal products (IMPs) being used within the trial.

		• Comparator drugs and placebos used as a reference in a clinical trial should also have Reference Safety Information /Safety Data Sheet or equivalent available should it be required. • For IMPs that have a marketing authorisation, the RSI will usually be listed within the Summary of Product Characteristics (SPC). • For those IMPs without a marketing authorisation, the RSI will be listed in the Investigator Brochure (IB) for that trial. • Please refer to SOP079: Reference Safety Information. For SARs that are cited in the RSI – the event is deemed to be expected and, as such, no further expedited reporting is required. For SARs that that are not cited in the RSI – the event is deemed to be unexpected and expedited reporting is required (see section 3.3).

Other Terms

Term	Description
Investigational Medicinal Product	An Investigational Medicinal Product (IMP) is a pharmaceutical form of an active substance or placebo being tested or used in a reference product in a clinical trial.
Comparator	A comparator is a reference standard used to compare the effectiveness of a new drug or treatment against an existing one. This comparator can be either an investigational or marketed product (active control) or a placebo (inactive control). All drugs used in clinical trials as comparators, even those with market authorisation, are considered IMPs. Comparators are therefore subject to the same reporting requirements as the trial drug, and it is the responsibility of the Sponsor to report adverse events in relation to comparators.
Placebo	'Placebo' is defined as an inactive substance or preparation used as a control in an experiment or test to determine the efficacy of a medicine or treatment.

Decision making flow chart



	SOP section:	Requirements:
AE	3.1	No requirement for expedited reporting
AR	3.1	No requirement for expedited reporting
SAE	3.2	Investigator must immediately report to the sponsor followed up by a written report the following business day
SAR	3.2	Investigator must immediately report to the sponsor followed up by a written report the following business day
SUSAR	3.3	Investigator must immediately report to the sponsor and complete all required expedited reporting detailed as section 3.3

3 Safety Reporting Mailbox.

a. All SUSARs must be reported to QA Safety Team via this mailbox: papworth.safety-reporting@nhs.net.

b. The safety reporting mailbox will be monitored daily for incoming notification of events by the QA Manager and QA team. Where periods of extended leave occur, this will be delegated to a rota of Clinical Project Managers and Senior R&D management.

3.1 Adverse Events (AEs) and Adverse Reactions (ARs)

a. Recording and reporting of AEs must be defined in the trial protocol and timelines dictated within this must be adhered to.

b. Anyone can report a suspected adverse event. This must be reported to the Principal Investigator (or other delegated member of the Research team).

c. It is the responsibility of the Principal Investigator (or suitable delegate) to review the reported suspected adverse events and follow the procedures for recording and onward reporting outlined in the protocol. The Principal Investigator (or suitable delegate) is required to report to the sponsor any AEs that are identified in the protocol as critical to evaluations of the safety of the trial.

d. All AEs must also be recorded within the patient's electronic health record, for full details on how to access this for Royal Papworth Hospital patients refer to the Trust intranet.

e. All AEs must be assessed for seriousness, severity and causality and outcome as per protocol. Severity and causality must be completed by a medically qualified individual who has been delegated this task.

f. For CTIMPs, the assessment of causality must be performed against the IMP which includes the comparator (if applicable). For Interventional studies (excluding CTIMPs), the causality assessment must be performed against the intervention or as directed in the protocol.

g. The sponsor cannot downgrade the PIs causality assessment but, if a disagreement exists, both opinions should be provided.

h. For CTIMPS, it is the responsibility of the sponsor to assess if an increase of ARs merits an urgent safety measure or SUSAR/expediated reporting.

3.2 Serious adverse events (SAEs) or serious adverse reactions (SARs)

a. The process for recording and reporting of SAE/SARs must be documented in the trial protocol.

b. All SAEs/SARs must also be recorded within the patient's electronic health record, for full details on how to access this for Royal Papworth Hospital patients refer to the Trust intranet.

Process for reporting:

c. ***Immediate***: the Principal Investigator or their delegated representative must report the SAE to the Trial Sponsor as per specified instructions in the protocol. Where knowledge of an SAE necessitates further information being obtained e.g. from the patient's GP or the admitting hospital, then it is permissible for detail to be entered as soon as this becomes available. However, waiting for specific details should not delay the initial notification of the event to the sponsor.

d. For those events that are reported initially as "ongoing," follow-up of the event should be completed until resolution or as stipulated in the study protocol.

3.3 SUSARs

Identification of a SUSAR and Unblinding:

a. All procedures for recording of SARs must be followed as detailed in Section 3.2 above.

b. The assessment of expectedness of the SAR will be completed by the PI and sponsor with reference to the approved Reference Safety Information or Safety Data Sheet (for placebo). If the event is deemed unexpected following inspection of the RSI the event is a SUSAR.

c. If unblinding is required for patient care the blind should be broken in accordance with protocol specific guidelines on unblinding. SOP069: Code breaking/un-blinding of Clinical Trials may also provide guidance as necessary. The Sponsors unblinding procedure should be followed.

Method of reporting:

a. If required, refer to SOP012 for Sponsor responsibilities and timelines in relation to SUSAR reporting.

3.4 Special considerations:

Pregnancy:

a. Pregnancy does not meet the definition of an SAE, but a congenital abnormality or birth defect is classed as an SAE.

b. For all CTIMPs, if a pregnancy occurs either in a participant or the partner of a participant, the pregnancy should be followed up until at least the end of the pregnancy or as long as stipulated in the trial protocol.

c. The investigator is responsible for notifying the sponsor as soon as they become aware of a pregnancy. Complete documentation as per protocol.

d. A trial specific consent process regarding pregnancy of a trial participant or their partner will be detailed in the protocol and must be followed as per sponsor and protocol guidelines.

e. Following the end of the pregnancy an SAE form must be completed and reported appropriately if there is a congenital abnormality or birth defect.

f. Further guidance on the process for reporting pregnancy is documented in SOP088 Clinical Trial Participants and Pregnancy – this SOP is specific to Royal Papworth Sponsored studies.

Urgent safety measures:

a. Urgent safety measures may be identified as being necessary through safety reporting within a clinical trial. An urgent safety measure should be taken by the sponsor or investigator in order to protect the participants of a clinical trial against any immediate hazard to their health or safety.

   Should this be necessary please refer to SOP071: Urgent Safety Measures.

4 Risk Management / Liability / Monitoring & Audit

a. The R&D SOP Committee will ensure that this SOP and any future changes to this document are adequately disseminated.

b. The R&D Department will monitor adherence to this SOP via the routine audit and monitoring of individual clinical trials and the Trust's auditors will monitor this SOP as part of their audit of Research Governance. From time to time, the SOP may also be inspected by external regulatory agencies (e.g. Care Quality Commission, Medicines and Healthcare Regulatory Agency).

c. In exceptional circumstances it might be necessary to deviate from this SOP for which written approval of the Senior R&D Manager should be gained before any action is taken. SOP deviations should be recorded including details of alternative procedures followed and filed in the Site and Sponsor File.

d. The Research and Development Directorate is responsible for the ratification of this procedure.

Further Document Information

Approved by: *Management/Clinical Directorate Group*	Research and Development Directorate
Approval date: *(this version)*	Current active version approved date
Ratified by Board of Directors/ Committee of the Board of Directors:	STET
Date:	N/A
This document supports: *Standards and legislation*	Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 and any subsequent amendments UK Policy Framework for Health and Social Care Research (V3.3 dated 07/11/2017 and amendments thereafter)

Equality Impact Assessment: Does this document impact on any of the following groups? If YES, state positive or negative, complete Equality Impact Assessment Form available in Disability Equality Scheme document DN192 and attach.

Groups	Disability	Race	Gender	Age	Sexual orientation	Religious & belief	Other
Yes/No	No	No	No	No	No	No	No
Positive/Negative							

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