

Research and Development SOP035 – Recording, Managing and Reporting Adverse Events Standard Operating Procedure

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Data Protection Act 2018 (UK General Data Protection Regulation – GDPR) Legislation

The Trust has a duty under the Data Protection Act 2018 and UK General Data Protection Regulations 2016/679 to ensure that there is a valid legal basis to process personal and sensitive data. The legal basis for processing must be identified and documented before the processing begins. In many cases we may need consent; this must be explicit, informed, and documented. We cannot rely on opt out, it must be opt in.

Data Protection Act 2018 and UK General Data Protection Regulations 2016/679 is applicable to all staff; this includes those working as contractors and providers of services.

For more information about your obligations under the Data Protection Act 2018 and UK General Data Protection Regulations 2016/679 please see the Information Use Framework Policy or contact the Information Governance Team

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1 Introduction

- 1.1 The Medicines for Human Use (Clinical Trials) Regulations 2004 (“the Clinical Trials Regulations”) as amended by the Medicines in Human use (Clinical Trials) (Amendment) Regulations 2025 (referred to as the “amended Clinical Trials Regulations”), Directive 2001/20/EC and other associated EU guidance along with subsequent amendments apply to all clinical trials involving Investigational Medicinal Products (IMPs) and in some instances non-investigational medicinal products (NIMPS) and specify the reporting requirements for safety reporting. To breach these requirements constitutes a breach of criminal law and therefore the requirements to comply with this legislation are incorporated within this procedural document.
- 1.2 Medical devices, food supplements and other non-medicinal products are not covered by Directive 2001/20/EC. The UK Medical Devices Regulation 2002 associated EU guidance and MHRA guidance apply to clinical investigations involving medical devices.
- 1.3 In accordance with International Conference on Harmonisation Good Clinical Practice (ICH GCP) E6 (R3) and the UK Policy Framework for Health and Social Care Research (2017) and subsequent amendments, research sites are responsible for investigating, reporting and recording events and incidents that occur in relation to the conduct of a clinical trial and research study.
- 1.4 Adverse Events which occur during any clinical trial or research study should be recorded and monitored because they can indicate when things are going wrong; for example, when the safety profile of an investigational product has changed, or when a study protocol or procedure may be causing harm.
- 1.5 ICH GCP and UK Policy Framework for Health and Social Care Research (2017 and subsequent amendments), clarifies the responsibilities of research sponsors and investigators with regards to research related adverse events.
- 1.6 This version supersedes any previous versions of this document.
- 1.7 **Scope**
 - 1.7.1 This Standard Operating Procedure (SOP) applies to the processing and reporting of all adverse events for research activity being conducted for Royal Cornwall Hospitals NHS Trust (RCHT).
 - 1.7.2 This SOP applies to all staff involved in research activities being conducted for RCHT.
 - 1.7.3 This SOP does not include details of the reporting procedures for studies that are sponsored by RCHT. Please refer to SOP036 Reporting Adverse Events for Sponsored Studies.
- 1.8 **Definitions and Glossary**
 - 1.8.1 **International Conference on Harmonisation (ICH) Good Clinical Practice (GCP)** is an international ethical and scientific quality standard for the design, conduct, performance, monitoring, auditing, recording,

analysis, and reporting of clinical trials that provides assurance that the rights, safety and well-being of trial participants are protected and that the data and reported results are credible and accurate.

- 1.8.2 **Investigational Product** is defined in ICH GCP E6 (R3) as “a pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use. Investigational products should be considered synonymous with drugs, medicines, medicinal products, vaccines and biological products. [ICH E6\(R3\) Step4 FinalGuideline 2025 0106.pdf](#).
- 1.8.3 **Non-investigational Medical Product (NIMP)** is defined in the amended Clinical Trials Regulations 2025 as a medicinal product used or to be used in a clinical trial, as described in the protocol, but not as an investigational medicinal product. NIMPS are typically used in clinical trials to ensure participant safety and may include rescue medications, challenge agents, or background treatments. In most cases, they hold a marketing authorisation, but exceptions may apply if an authorised product is not available. Refer to [Clinical trials for medicines: non-investigational medicinal products - GOV.UK](#).
- 1.8.4 **Research Ethics Committee (REC)** is a group of people appointed to review research proposals to assess formally if the research is ethical. This means the research must conform to recognised ethical standards, which includes respecting the dignity, rights, safety and well-being of the people who take part.
- 1.8.5 **Medicines and Healthcare products Regulatory Agency (MHRA)** is the executive agency of the Department of Health and Social Care in the UK which is responsible for regulating the use of medicines, medical devices and blood components for transfusion in the UK.
- 1.8.6 **Sponsor** is an individual, company, institution or organisation which takes responsibility for the initiation, management and/or financing of a clinical trial. A group of individuals and/or organisations may take on Sponsorship responsibilities and distribute them by agreement among the members of the group, provided that, collectively, they make arrangements to allocate all the responsibilities that are relevant to the study in line with the UK Policy Framework for Health and Social Care Research.
- 1.8.7 **Chief Investigator (CI)** is the authorised health care professional who takes primary responsibility for the conduct of the study. The CI must be a senior individual, with appropriate experience, expertise and training to undertake the design, conduct and analysis of the study to meet the requirements set out in legislation.

They must also lead and manage others who have been delegated responsibilities as part of the research project.

- 1.8.8 **Principal Investigator (PI)** is the person who takes responsibility for the initiation and conduct of the study at site. There is one Principal Investigator at each site participating in a research study. For a single site study, the Chief Investigator (CI) may also take on the role of Principal Investigator (PI).
- 1.8.9 **The Research Team** is a group of people involved in the conduct of a research project at site. It may include care professionals, academics, patients and service users, members of the public, research professionals, students and/or scientists.
- 1.8.10 **Investigator Site File (ISF)** contains the essential documents which show that the investigator and the conduct of the study are following the regulatory requirements.
- 1.8.11 **Reference Safety Information (RSI)** - The RSI defines which reactions are expected for the Investigational Medical Product (IMP) being administered to participants in a clinical trial. The RSI can be found within an Investigators Brochure (IB), if the IMP does not have a marketing authorisation or Summary of Product Characteristics (SmPC), provided by the Sponsor.
- 1.8.12 **Summary of the Product Characteristics (SmPC)** is a document describing the properties and the officially approved conditions of use of a medicine. Summaries of product characteristics form the basis of information for healthcare professionals on how to use the medicine safely and effectively.
- 1.8.13 **Adverse Event (AE)** is defined as any unfavourable medical occurrence in a clinical trial participant administered the investigational product. The adverse event does not necessarily have a causal relationship with the treatment.
- 1.8.14 **Adverse Event of Special Interest (AESI)** is an Adverse Event which has additional reporting requirements defined by the Sponsor.
- 1.8.15 **Adverse Drug Reaction (ADR) or Adverse Reaction (AR)** is defined as any unfavourable and unintended responses, such as a sign (e.g., laboratory results), symptom or disease related to any dose of a medicinal product where a causal relationship between a medicinal product and an adverse event is a reasonable possibility. The level of certainty about the relatedness of the adverse drug reaction to an investigational product will vary. If the ADR or AR is suspected to be medicinal product-related with a high level of certainty, it should be included in the reference safety information (RSI) and/or the Investigator's Brochure (IB).
- 1.8.16 **Serious Adverse Event (SAE) or Serious Adverse Reaction (SAR)** is defined as any adverse event or adverse reaction or unexpected adverse reaction respectively that:

- Results in death.

- Is life threatening.
- Requires inpatient hospitalisation or prolongation of existing hospitalisation.
- Results in persistent or significant disability or incapacity. Or,
- Is a congenital anomaly or birth defect.

An important medical event that may or may not immediately be life-threatening or results in death or hospitalisation, that may jeopardise the participant or that may require intervention to prevent serious outcomes should generally be considered as serious.

1.8.17 **Suspected Unexpected Serious Adverse Reaction (SUSAR)** is when the nature and severity of an adverse reaction is not consistent with the information about the medicinal product in question set out:

- In the case of a product with a marketing authorisation, in the Summary of the Product Characteristics (SmPC).
- In the case of any investigational medicinal product, in the investigator's brochure relating to the trial in question.
- Reference Safety Information (RSI) is the information used for assessing whether an adverse reaction is expected. This is contained in either the investigator's brochure or the summary of the product characteristics.

1.8.18 **Adverse Device Effect (ADE)** - This includes any AE resulting from insufficiencies or inadequacies in the instructions for use, the deployment, implantation or operation of the medical device or any malfunction. This also includes any AE that is a result of an error in use or intentional misuse of the medical device.

1.8.19 **Serious Adverse Device Effect (SADE) or Unexpected Serious Adverse Device Effect (USADE)** - An Adverse Device Effect (ADE) that results in:

- Death.
- Life threatening illness or injury.
- Hospitalisation, or prolongation of existing hospitalisation.
- Persistent or significant disability or incapacity.
- Foetal distress, foetal death or congenital anomaly or birth defect.
- Is otherwise considered medically significant by the Investigator.

Expectedness of the event is based on the information contained in the Investigator Brochure and the Protocol.

- 1.8.20 **Device Deficiency** - Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. Device Deficiencies include malfunctions, misuse or use errors and inadequate labelling.
- 1.8.21 **Unanticipated Serious Adverse Device Effect (USADE)** is a Serious Adverse Device Effect which by its nature, incidence, severity or outcome has not been identified as an Anticipated Serious Adverse Device Effect (ASADE) and is previously undocumented.
- 1.8.22 **Development of Safety Update Reports (DSUR)** is the annual clinical trial safety report for adverse reactions which are observed during clinical studies, which is submitted to the MHRA and REC.
- 1.8.23 **EDGE** is a dedicated, web-based, research database which is used within, and managed by, the R and D department at RCHT.

Acronyms

ADE: Adverse Device Effect.

ADR: Adverse Drug Reaction.

AE: Adverse Event.

AESI: Adverse Event of Special Interest.

AR: Adverse Reaction.

CI: Chief Investigator.

CRF: Case Report Form.

CTIMP: Clinical Trial of an Investigational Medicinal Product.

DSUR: Development of Safety Update Reports.

eCRF: Electronic Case Report Form.

NIMP: Non-Investigational Medicinal Product.

CV: Curriculum Vitae.

GCP: Good Clinical Practice.

HRA: Health Research Authority.

IB: Investigator Brochure.

IMP: Investigational Medicinal Products.

ISF: Investigator Site File.

MHRA: Medicines and Healthcare products Regulatory Agency.

NIMP: Non-investigational Medicinal Products.

PI: Principal Investigator.

QMS: Quality Management System.

R and D: Research and Development.

RCHT: Royal Cornwall Hospitals NHS Trust.

REC: Research Ethics Committee.

RSI: Reference Safety Information.

SADE: Serious Adverse Device Effect.

SAE: Serious Adverse Event.

SAR: Serious Adverse Reaction.

SmPC: Summary of Product Characteristics.

SOP: Standard Operating Procedure.

SSAR Suspected Serious Adverse Reaction.

Sub-I: Sub Investigator.

SUSAR: Suspected Unexpected Serious Adverse Reaction.

TMF: Trial Master File.

USADE: Unanticipated Serious Adverse Device Effect.

2 Purpose of the Standard Operating Procedure

This Standard Operating Procedure (SOP) describes the procedures for recording, managing and reporting adverse events (AEs), ensuring that clinical trials and research studies being conducted for Royal Cornwall Hospitals NHS Trust (RCHT) are compliant with the UK Clinical Trial Regulations as well as the principles of ICH GCP and the UK Policy Framework for Health and Social Care Research.

3 Ownership and Responsibilities

3.1 Role of the R and D Clinical Director

The R and D Clinical Director is responsible for:

- Having oversight of the implementation of robust arrangements to ensure staff follow the processes described in [Section 4](#), Standards and Practice.
- Gaining assurance from the Senior Management Team (SMT) to ensure compliance with the processes outlined in [Section 4](#), Standards and Practice.

3.2 Role of the Senior Management Team (SMT)

The SMT is responsible for:

- Providing assurance to the R and D Clinical Director of the compliance with the processes outlined in [Section 4](#), Standards and Practice.
- Ensuring adequate provision of training for staff to perform their roles and responsibilities in association with the processes described in [Section 4](#), Standards and Practice.
- Supporting the Principal Investigator (PI) to fulfil the duties, responsibilities and obligations in executing the processes described in [Section 4](#), Standards and Practice.
- Arranging monitoring and auditing of the systems and processes associated with the standards and practice described in [Section 4](#).
- Ensuring any non-compliance associated with the standards and practice are processed in accordance with the R and D SOP004 Reporting and Managing Non-compliance and Serious Breaches (see Documents folder in EDGE).

3.3 Role of the Chief Investigator (CI)

The CI has overall responsibility for the conduct of the study. In a multi-site study, the CI has co-ordinating responsibility for reporting adverse events to the Medicines and Healthcare products Regulatory Agency (MHRA) and to the relevant Research Ethics Committee (REC). The CI is responsible for ensuring:

- All Serious Adverse Events (SAEs) are reported to the sponsor, MHRA, REC and R and D within the agreed timelines.
- The sponsor is provided with details of all AEs identified in the protocol as critical to the evaluation of safety within the agreed timeframes specified in the protocol.
- SAE reports from investigators are reviewed and evaluation performed with respect to seriousness, causality and expectedness.
- The sponsor, MHRA, REC and R and D departments are supplied with any supplementary information they request.

3.4 Role of the Principal Investigator (PI)

The Principal Investigator (PI) has overall responsibility for the conduct of the study at the site. The International Council for Harmonisation (ICH) Good Clinical Practice (GCP) E6 (R3) guidelines state the PI must be qualified by education, training and experience to assume responsibility for the proper conduct of the trial. The PI can delegate duties but cannot delegate overarching responsibilities.

The PI is responsible for:

- Ensuring the conduct of the study is compliant with the applicable regulatory requirements and adheres to the principles of GCP.
- Ensuring robust study specific systems and processes are in place for recording, managing and reporting adverse events.
- Ensuring that all staff carrying out delegated duties are qualified by education, training and experience.
- Ensuring that all staff carrying out delegated duties are familiar with all aspects of the clinical trial or study, described in the latest version of the protocol, and throughout the trial or study any protocol modifications, as approved by the sponsor, Health Research Authority (HRA), REC and where appropriate the MHRA.
- Ensuring episodes of non-compliance with the standards and practice described in [Section 4](#) are processed in accordance with R and D SOP004 Reporting and Managing Non-compliance and Serious Breaches (see Documents folder in EDGE).
- Supporting monitors, regulators and auditors with queries relating to the recording, management and reporting of safety events.

3.5 **Role of all investigators including the PI**

The PI and all other investigators with delegated investigator duties are responsible for:

- Carrying out causality assessments and making decisions which require medical and scientific judgement. If the investigator is not a medically qualified doctor, this task must be delegated to a medically qualified doctor who is a member of the research team with appropriate knowledge.
- Performing expectedness assessments in accordance with the Reference Safety Information (RSI), where this task has been delegated by the sponsor.
- Ensuring that Serious Adverse Events (SAEs), Suspected Unexpected Serious Adverse Reactions (SUSARs), Serious Adverse Device Effects (SADEs) and Unexpected Serious Adverse Device Effects (USADEs) are reported to the sponsor, in accordance with the sponsor and regulatory requirements.
- Having oversight of the safety escalation plan and the necessary arrangements for an out of hours process to be in place, as appropriate for the clinical trial or research study, to ensure that events are identified and processed in a timely manner.

- Processing episodes of non-compliance with the systems and process described in [Section 4](#), in accordance with R and D SOP004 Reporting and Managing Non-compliance and Serious Breaches (see Documents folder in EDGE).
- Supporting monitors, regulators and auditors with queries relating to the recording, management and reporting of safety events.
- Supporting monitors, regulators, auditors, investigators and other persons undertaking official duties, with queries relating to episodes of non-compliance.

3.6 Role of the Team Leader

The Team Leader is responsible for:

- Supporting the PI to fulfil the duties, responsibilities and obligations in executing the processes described in [Section 4](#), Standards and Practice.
- Ensuring fulfilment of the duties delegated by the PI regarding the standards and processes described in [Section 4](#).
- Ensuring that the out of hours process is in place, as appropriate to the study, to ensure that events are picked up and able to be processed in a timely manner.
- Identifying staff with the appropriate knowledge, skills and experience to support the PI to undertake delegated duties in respect of the standards and practices described in [Section 4](#), and in accordance with the principles of GCP.
- Identifying training needs for the research delivery team and other staff involved in the clinical trial or research study, and to provide support to help all staff to undertake their delegated duties.
- Ensuring that adverse events are reported and recorded in accordance with the requirements of the sponsor and regulatory requirements, described in [Section 4](#).
- Ensuring that the PI is informed of all SAEs, SUSARs, SADEs and USADEs on becoming aware of their occurrence.
- Ensuring all adverse events for participants of clinical trials of an investigational product are recorded in the participant's medical notes.
- Having oversight of the safety escalation plan and the necessary arrangements for an out of hours process to be in place, as appropriate for the clinical trial or research study, to ensure that events are identified and processed in a timely manner.

- Processing episodes of non-compliance with the systems and practices described in [Section 4](#) in accordance with R and D SOP004 Reporting and Managing Non-compliance and Serious Breaches (see Documents folder in EDGE).
- Providing monitors, auditors and regulators with access to the study files and documentation, relevant to the clinical trial or research study being reviewed.
- Supporting monitors, regulators and auditors with queries relating to the reporting of safety events.
- Supporting monitors, regulators, auditors, investigators and other persons undertaking official duties, with queries relating to episodes of non-compliance.

3.7 Role of the Research Nurse

The Research Nurse is responsible for:

- Putting in place a safety escalation plan and the necessary arrangements for an out of hours process, as appropriate for the clinical trial or research study, to ensure that safety events are identified and processed in a timely manner.
- Gathering, recording and reporting all relevant information in relation to adverse events in accordance with the requirements of the sponsor and regulatory requirements, described in [Section 4](#).
- Informing the PI of all SAEs, SUSARs, SADEs and USADEs on becoming aware of their occurrence.
- Ensuring all adverse events for participants in clinical trials of an investigational product are recorded in the participant's medical notes.
- Supporting data entry through ensuring that all adverse events and adverse reactions are entered in the Case Report Forms (CRF) and electronic CRF (eCRF) in a timely manner.
- Processing episodes of non-compliance with the systems and practices described in [Section 4](#) in accordance with R and D SOP004 Reporting and Managing Non-compliance and Serious Breaches (see Documents folder in EDGE).
- Supporting monitors, regulators and auditors with queries relating to the reporting of safety events.
- Supporting monitors, regulators, auditors, investigators and other persons undertaking official duties with queries relating to episodes of non-compliance.

3.8 Role of the Research Administration Team

The Research Administration Team is responsible for:

- Ensuring all SAE, Serious Adverse Reactions (SAR), SUSAR, SADEs and USADEs reports, and follow-up information are filed in the Investigator Site File (ISF) as required by the sponsor and in line with their processes.
- Supporting monitors, regulators and auditors with queries relating to the reporting of safety events.
- Supporting monitors, regulators, auditors, investigators and other persons undertaking official duties with queries relating to episodes of non-compliance.

3.9 Role of the Supporting Service

The Supporting Service is responsible for:

- Informing the PI of any adverse events.
- Supporting the PI in gathering information for the review and reporting of SAEs, SARs, SUSARs, SADEs and USADEs.
- Supporting the PI, Team Leader and Research Nurse to document all adverse events in the participant's medical notes.
- Supporting the Data Officers to ensure all adverse events are entered in the CRFs in a timely manner.

3.10 Role of the Data Personnel

The assigned data person is responsible for:

- Ensuring all adverse events are entered into the CRF in a timely manner, this could be an electronic or paper-based format.
- Supporting monitors, regulators and auditors with the coordination of queries relating to the reporting of adverse events.
- Supporting monitors, regulators, auditors, investigators and other persons undertaking official duties with queries relating to episodes of non-compliance.

4 Standards and Practice

4.1 Delegation of Duties

- 4.1.1 The Principal Investigator (PI) is responsible for the review and sign-off for all Serious Adverse Events (SAEs). It may be possible for additional medically qualified individuals to be delegated the responsibility for reviewing and signing off the SAE form.

- 4.1.2 In accordance with R and D SOP010 Investigator Responsibilities (see Documents folder in EDGE), adequate processes must be in place to ensure cover for review of SAEs, Suspected Unexpected Serious Adverse Reactions (SUSARs), Serious Adverse Device Effects (SADEs) and Unexpected Serious Adverse Device Effects (USADEs) by suitably qualified investigator, where either planned or unplanned leave is taken by the PI. This must be in place before trial or study commencement and updated as applicable throughout the study. This must be recorded on the Delegation Log which is stored in the Investigator Site File (ISF).
- 4.1.3 Refer to R and D SOP030 Delegation of Duties (see Documents folder in EDGE) for the processes and documentation required when delegating tasks.

4.2 Identifying and recording Adverse Events (AEs)

- 4.2.1 There is no legal requirement for investigators to record all non-serious adverse events for a clinical trial or research study. Sponsors will determine what adverse events require recording and reporting, in particular those relating to the safety of the participant, the integrity of the data and the outcome for clinical trial, these should be detailed in the protocol.
- 4.2.2 AEs should be captured from the time of a participant's consent into a clinical trial or research study, until the end of their participation (unless otherwise stated in the protocol).
- 4.2.3 AEs and Adverse Reactions (ARs) must be documented in accordance with the sponsor requirements. They should always be documented in the Case Report Form (CRF) and participants' medical notes and, reporting any escalation as a Serious Adverse Event (SAE). For some trials or studies, it may be necessary to use a log for capturing, reporting and tracking AEs and ARs for individual participants.
- 4.2.4 Participation in a study that requires AEs to be reported, should be clearly annotated in the participant's medical notes whether paper or electronic, to alert all RCHT staff as to the patient's inclusion and facilitate reporting of all AEs and ARs whilst participating in a study.
- 4.2.5 At each point of contact, research participants should be asked if they have experienced any AEs and/or ARs since the previous visit or assessment. Any events identified should be documented in accordance with the Sponsor terminology specifications.
- 4.2.6 AEs and ARs which are ongoing from previous visits should be reviewed and documented at each point of contact.
- 4.2.7 The dates of the beginning and end of the event should be recorded in the participant's medical notes, CRF and AE log. If the participant cannot remember, then approximate dates should be recorded. If the participant is unable to provide a timeframe, this will be recorded as unknown.

- 4.2.8 Adverse Events should be assessed for seriousness, expectedness, and causality against GCP standard definitions, see details for assessing causality in [Section 4.5](#).
- 4.2.9 Any adverse events that require clinical intervention to prevent an escalation should be documented as per protocol requirements.
- 4.2.10 A final sign off of participants' AEs and ARs should occur on completion of the trial or study as required by the protocol.
- 4.2.11 AEs and ARs on-going at completion of the study should be followed up as clinically indicated.

4.3 Reporting Serious Adverse Events (SAE)

- 4.3.1 All SAEs must be reported to the sponsor within 24 hours of the investigator becoming aware of the occurrence.
- 4.3.2 All sponsors should define the parameters of a SAE and how they are reported. Follow-up information should be sent as soon as the information is available after the initial report, using the sponsor's reporting format.
- 4.3.3 It is the Chief Investigator's (CI) responsibility to report SAE incidents relating to Clinical Trials of an Investigational Medicinal Product (CTIMP) to the MHRA as soon as possible.
- 4.3.4 The sponsor should assess the SAE and where necessary liaise with the Principal Investigator. The sponsor cannot downgrade causality but can upgrade, unless discussed and agreed by PI.
- 4.3.5 The sponsor should also consult the Reference Safety Information (RSI) (see definitions in [Section 1.8.11](#) above) to determine expectedness for all SARs. If the Sponsor suspects the information is not consistent with the RSI, and is therefore unexpected, the episode must be treated as a Suspected Unexpected Serious Adverse Reaction (SUSAR) (see definitions in [Section 1.8.17](#)).

4.4 Reporting medical device-related adverse incidents

- 4.4.1 Medical device trials are clinical investigations designed to evaluate the safety, performance, and effectiveness of medical devices, often required for regulatory approval and market access. Medical device research also includes medical devices already on the market that are being evaluated for new intended uses, new populations, new materials or design changes.
- 4.4.2 It is essential that all medical device-related adverse events are appropriately recorded, managed and reported, to ensure participants' continued safety.

- 4.4.3 It is the CI's responsibility to report all device-related adverse events to the MHRA as soon as possible, including incidents where user error is suspected. Even minor safety or quality problems should be reported as these can help to demonstrate trends or highlight inadequate manufacturing or supply systems.
- 4.4.4 The PI must inform the CI of all medical device-related adverse events. SAEs, Serious Adverse Device Effects (SADE) and Unexpected Serious Adverse Device Effects (USADEs) should be reported to the CI as soon as the investigator becomes aware that they have led to:
- Death or if it were to occur again, could lead to death.
 - Serious injury.
 - Medical or surgical intervention (including implant revision).
 - Hospitalisation.
 - Unreliable test results.
- 4.4.5 The sponsor will decide how adverse events should be recorded and reported. All device related AEs should be recorded in the participant's medical records and on the CRFs as necessary.
- 4.4.6 Where a device defect is identified, the device should be quarantined and should not be repaired, returned to the manufacturer or discarded until the MHRA has been given the opportunity to carry out an investigation. The MHRA will advise when it is necessary to submit a device for examination and how it should be sent to them.

4.5 Causality

- 4.5.1 Causality assessment is the process of determining the likelihood that a specific adverse event (AE) or outcome is directly related to a treatment, investigational medicinal product (IMP), non-investigational medicinal product (NIMP), medical device, or other intervention under clinical trial or research study.
- 4.5.2 If the investigator is not a medically qualified doctor, this task for assessing must be delegated to a medically qualified doctor who is a member of the research team, with the appropriate knowledge. Refer to R and D SOP030 Delegation of Duties (see Documents folder in EDGE) for the processes and documentation required when delegating tasks.
- 4.5.3 The investigator should assess and evaluate the relationship between the adverse event and the investigational product, considering alternative causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors.
- 4.5.4 When considering causality for adverse events related to medical devices, the investigator will make the assessment based on the knowledge of the event and any relevant product information, including the structure and functionality of the device.

4.5.5 Causality must be assessed by the PI or delegate, based upon their clinical judgement and categorised as below. The investigator should consult the protocol, Investigator Brochure, Summary of Product Characteristics (SmPC) and any other product information which has been approved by the MHRA before making a final judgement and categorise as follows:

- **Not related:** Temporal relationship of the onset of the event, relative to administration of the product or procedure, is not reasonable or another cause can by itself explain the occurrence of the event.
- **Unlikely to be related:** Temporal relationship of the onset of the event, relative to administration of the product or procedure, is likely to have another cause, which can by itself explain the occurrence of the event.
- **Possibly related:** Temporal relationship of the onset of the event, relative to administration of the product or procedure, is reasonable but the event could have been due to another, equally likely cause.
- **Probably related:** Temporal relationship of the onset of the event, relative to administration of the product or procedure, is reasonable and the event is more likely explained by the product/procedure than any other cause.
- **Definitely related:** Temporal relationship of the onset of the event, relative to administration of the product or procedure, is reasonable and there is no other cause to explain the event, or a re-challenge (if feasible) is positive.

Note: Where an event is assessed as possibly, probably, or definitely related, the event is classed as an adverse reaction.

4.6 Adverse Events of Special Interest

In addition to the expedited reporting of SAE and SAR's, investigators must also report Adverse Events of Special Interest (AESI), this is an adverse event which has additional reporting requirements as defined by the sponsor in the study protocol and is critical to the safety evaluation of the study.

4.7 Pregnancy Reporting in CTIMPs

- 4.7.1 Pregnancy in a study participant or their partner is not classified as an adverse event in itself; however, a congenital anomaly or birth defect is considered an SAE.
- 4.7.2 GCP guidance recommends that when a pregnancy occurs for a participant or their partner in a CTIMP study, this should be reported and followed up until at least the end of the pregnancy. The Sponsor should provide specific documentation for completion in the event of a pregnancy being reported.

- 4.7.3 Follow-up for the pregnancy, its outcome and appropriate follow-up of the infant will depend on obtaining informed consent for this from the participant or their partner.

4.8 Reporting SAEs

- 4.8.1 All Sponsors should define how SAEs are reported. An example of a research-related SAE Initial Report Form is available in the documents folder on EDGE (R and D AD 28b).
- 4.8.2 Follow-up information should be sent as soon as the information is available after the initial report using the Sponsor's reporting format. In most cases the follow-up information is submitted on the same SAE reporting form with it clearly marked as initial or follow up accordingly. An example of the research-related SAE Follow-up Report Form is available in the documents folder on EDGE (R and D AD 28c).

5 Dissemination and Implementation

- 5.1 Trust-wide Research and Development (R and D) procedural documents will be stored on the Trust's Document Library, and a working copy will be accessible through EDGE providing alternative access for research staff.
- 5.2 The Research Governance Manager or delegate will arrange for documents to be published on the Trust Documents Library and EDGE.
- 5.3 The Research Governance Manager or delegate will ensure that any previous versions of the document are made inaccessible to general EDGE users, in accordance with the EDGE document archiving procedure.
- 5.4 R and D SMT to define any training requirements prior to the implementation of any procedural documentation. There will be appropriate time allowed for such training prior to the publishing of the SOP or WI.
- 5.5. Relevant research staff registered on EDGE will be notified by email of the new or reviewed document. Relevant staff will be identified from the ownership and responsibilities ([Section 3](#)) of this procedural document and the R and D AD19 Training Matrix (see Documents folder in EDGE).
- 5.6. Details of how to access EDGE is available by contacting the Research Systems Officer via rch-tr.edge@nhs.net.
- 5.7. It is the responsibility of all staff to check the website regularly, in order to see if SOPs have been added or amended. R and D will endeavour to notify research staff of any SOP developments that may be relevant to them via staff communications, for example, R and D Newsletters, Leadership Huddle and Workstream Huddles. A list of any new or updated SOPs will be reviewed and ratified at the R and D Senior Management Team Governance and Performance monthly meetings.
- 5.8. Consideration must be given at study set up as to which SOPs will not apply to a specific study, with agreement from the R and D Senior Management Team (SMT). Full details must be included as a written statement in the study site file.

5.9. Whilst SOPs may be printed, the electronic version maintained on the R and D internet page is the controlled copy. Any printed copies are not controlled documents.

5.10. Chief and Principal Investigators will be notified as per the Trust's process for notifying all staff of new procedural documents.

5.11. Training and Development

5.11.1. When a new SOP is authorised, or when an existing SOP is revised, self-directed training as specified and detailed by the SMT must be carried out by all staff to which the SOP is relevant, and this training documented on EDGE.

5.11.2. Staff should take time to read and fully understand the SOP and relevant documents, ensuring that they are able to implement the SOP as required. If clarification is needed, the staff member should approach the Research Governance Manager, or another member of the SMT, who will arrange additional training. All staff are responsible for maintaining their own training logs and copies must be made available to study monitors on request.

5.12. SOP Deviations

5.12.1. If a process deviates from an approved SOP, a risk assessment will be undertaken to determine the consequences and identify any remedial action(s) that needs to be taken. It may also be appropriate to submit an incident report via the Datix system.

5.12.2. The author of the risk assessment must submit the risk assessment to SMT.

6 Monitoring compliance and effectiveness

Information Category	Detail of process and methodology for monitoring compliance
Element to be monitored	Successful implementation of the procedures described in this SOP ensures a clear understanding of the roles and responsibilities and associated training requirements for staff conducting research studies and clinical trials.
Lead	Research Governance Manager.
Tool	Internal and external monitoring of research studies and clinical trial will monitor implementation of this SOP and compliance with Good Clinical Practice (GCP).

Information Category	Detail of process and methodology for monitoring compliance
Frequency	Compliance with this procedural document will be monitored as part of the R and D risk-based, audit and monitoring process directed through the SMT Governance Meetings.
Reporting arrangements	The Research Governance Manager will provide monthly reports to the R and D Governance SMT.
Acting on recommendations and Lead(s)	The R and D Governance SMT will provide effective oversight and corrective actions.
Change in practice and lessons to be shared	The R and D Governance SMT will identify non-compliance and appoint a member of the SMT to provide support and advice to identify training needs and improve practice. Required changes to practice will be implemented as soon as practically possible.

7 Updating and Review

This R and D procedural document will be reviewed no less than every three years by the R and D SMT unless an earlier review is required and in accordance with Section 9 of the Trust Policy for the Development and Management of Knowledge, Procedural and Web Documents (The Policy on Policies).

8 Equality and Diversity

8.1 This document complies with the Royal Cornwall Hospitals NHS Trust service Equality and Diversity statement which can be found in the [‘Equality, Inclusion and Human Rights Policy’](#) or the [Equality and Diversity website](#).

8.2 Equality Impact Assessment

The Initial Equality Impact Assessment Screening Form is at Appendix 2.

Appendix 1. Governance Information

Information Category	Detailed Information
Document Title:	Research and Development SOP035 – Recording, Managing and Reporting Adverse Events Standard Operating Procedure V6.0
This document replaces (exact title of previous version):	Research and Development SOP035 – Recording, Managing and Reporting Adverse Events Standard Operating Procedure V5.0
Date Issued/Approved:	June 2026
Date Valid From:	July 2026
Date Valid To:	July 2029
Directorate / Department responsible (author/owner):	Caroline Phillips – Research Governance Manager.
Contact details:	rcht.researchqualityassurance@nhs.net
Brief summary of contents:	This SOP describes the procedures for recording, managing and reporting Adverse Events which occur during a clinical trial or research study.
Suggested Keywords:	Standard Operating Procedures (SOP). Good Clinical Practice (GCP). Research and Development (R and D).
Target Audience:	RCHT: Yes CFT: No CIOs ICB: No
Executive Director responsible for Policy:	Chief Strategy Officer.
Approval route for consultation and ratification:	R and D Senior Management Team (SMT).
General Manager confirming approval processes:	Bianca Mills, Head of Research and Development.
Name of Governance Lead confirming approval by specialty and care group management meetings:	Caroline Phillips, Research Governance Manager.
Links to key external standards:	Good Clinical Practice for Clinical Trials. https://www.gov.uk/guidance/good-clinical-

Information Category	Detailed Information
	practice-for-clinical-trials.
Related Documents:	The Medicines for Human Use (Clinical Trials) Regulations 2004 The Medicines for Human Use (Clinical Trials) Regulations 2004. The Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 The Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025. International Council for Harmonisation (ICH) Guideline for Good Clinical Practice E6 (R3), (06 January 2025). https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step4_FinalGuideline_2025_0106.pdf. Medical Device Regulations 2002 The Medical Devices Regulations 2002 [Accessed 04/06/2026]. Medical Device Directive 90/385/EEC EUR-Lex - 01990L0385-20071011 - EN - EUR-Lex [Accessed 04/06/2026]. Medical Device Directive 93/42/EEC EUR-Lex - 01993L0042-20071011 - EN - EUR-Lex [Accessed 04/06/2026]. Medical devices: post market surveillance Medical devices: guidance for manufacturers on vigilance - GOV.UK [Accessed 04/06/2026]. UK Policy Framework for Health and Social Care (2017) https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/ [Accessed 04/06/2026]. Directive 2001/20/EC of the European Parliament and of the Council (Article 2) https://www.legislation.gov.uk/eudr/2001/20/article/2 [Accessed 04/06/2026]. Directive 2001/83/EC of the European Parliament and of the Council Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (legislation.gov.uk) [Accessed 04/06/2026]. EC Guidelines on Good Clinical Practice (GCP) specific to Advanced Therapy Medicinal Products (2019).

Information Category	Detailed Information
	https://health.ec.europa.eu/system/files/2019-10/atmp_guidelines_en_0.pdf [Accessed 04/06/2026]. Good Clinical Practice for Clinical Trials (How to show MHRA you're meeting good clinical practice (GCP) standards and what to expect from an inspection) https://www.gov.uk/guidance/good-clinical-practice-for-clinical-trials [Accessed 04/06/2026]. HRA Guidance – Good Clinical Practice https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/good-clinical-practice/ [Accessed 04/06/2026]. The documents listed below are available via the Trust Documents Library and/or EDGE: R and D SOP001 - Preparation, Approval, Review and Issue of R and D Policies and Standard Operating Procedures. R and D SOP004 – Reporting and Managing Non-compliance and Serious Breaches. R and D SOP010 – Investigators Responsibilities. R and D SOP030 Delegation of Duties. R and D SOP036 Reporting Adverse Events for Sponsored Studies. R and D AD19 – Training Matrix. R and D AD28b SAE Initial Report Form. R and D AD28c SAE Follow-up Report Form.
Training Need Identified?	Staff may need help, support or training with obtaining access to the documents folder of EDGE.
Publication Location (refer to Policy on Policies – Approvals and Ratification):	Internet and Intranet.
Document Library Folder/Sub Folder:	Research and Development (R and D).

Version Control Table

Date	Version Number	Summary of Changes	Changes Made by
01/07/2014	V1.0	2 Year Review.	Dr N Morley,

Date	Version Number	Summary of Changes	Changes Made by
			R and D ARM.
01/07/2014	V2.0	Complete revision to reflect current practice.	Dr N Morley, R and D ARM.
27/04/2017	V3.0	'Policy Under review' label added.	Helen Holman, Data Quality and Project Monitoring Officer.
01/08/2017	V3.0	Complete rewrite to align with Trust policies.	Dr N Morley, R and D ARM.
01/06/2021	V4.0	Update and review to align to updates in laws and trust policies.	Dr N Morley, R and D ARM.
20/02/2025	V5.0	Change of the title of the SOP. Changes to the scope and purpose of the SOP to focus on the recording, managing and reporting of adverse events for hosted studies. Changes from RD and I to R and D. Review of SOP in line with GCP guidance, feedback from external monitoring and audits and changes to R and D procedures. Review and update in accordance with Trust policies.	Caroline Phillips, Research Governance Manager.
18/06/2026	V6.0	Review to reflect the changes to the Clinical Trials Regulations and ICH GCP guidance. Review of SOP in line with GCP guidance, feedback from external monitoring and audits and changes to R and D procedures. Review and update in accordance with Trust policies.	Caroline Phillips, Research Governance Manager.

All or part of this document can be released under the Freedom of Information Act 2000.

All Policies, Strategies and Operating Procedures, including Business Plans, are to be kept for the lifetime of the organisation plus 6 years.

This document is only valid on the day of printing.

Controlled Document.

This document has been created following the Royal Cornwall Hospitals NHS Trust [The Policy on Policies \(Development and Management of Knowledge Procedural and Web Documents Policy\)](#). It should not be altered in any way without the express permission of the author or their Line Manager.

Appendix 2. Quality and Equality Impact Assessment (QEIA) Form

The QEIA process allows RCHT to monitor the impact of changes to its policies and services, ensuring that nobody is unduly disadvantaged.

Please ensure you have completed a Quality and Equality Impact Assessment (QEIA) using this link to complete the form:

[E11 QEIA Policy](#).

For guidance, please see the [QEIA Essentials – Quick Reference Guide](#) or contact as required below:

Equality, Diversity and Inclusion guidance, please contact: rcht.inclusion@nhs.net.

Quality Governance guidance, please contact Jillian Tozer: jillian.tozer3@nhs.net.