



Standard Operating Procedure

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DISCLAIMER

This generic R&D Standard Operating Procedure (SOP) must be followed unless a study specific SOP exists.

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| Full History | | | |
|--------------|----------------|---------------------------|---|
| Version | Date | Reviewed By | Reason |
| 1.0 | March 2011 | Assistant R&D Manager | First document |
| 2.0 | August 2011 | Assistant R&D Manager | Changes to layout Delegation of duties is more specific as are requirements for following up patients until the AE has resolved. Inclusion of e-SUSAR reporting. Appendix 3 was updated to include the comments from the MHRA Inspector. |
| 3.0 | September 2013 | Assistant R&D Manager | Change to annual reporting requirements updated from Annual Safety Report to Development Safety Update Report. Inclusion of reporting requirements for Comparators, Placebos and NIMPs. REC reporting requirements for SUSARs updated to include link to new form. Appendix 3 links to documents |
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| 5.0 | December 2017 | Assistant R&D Manager | Minor errors corrected and inclusion of reporting on unexpected pregnancies |
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| 7 | 18/12/2023 | Quality Assurance Manager | Ensuring the SOP covers the procedure for Eastern and Northern Services. |

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| Associated Trust Policies/ Procedural documents: | R&D Policy R&D/Reporting Required for Sponsored CTIMPs - SOP S31 R&D/Urgent Safety Measures - SOP S52 R&D How to Enter a Safety Report on Q-Pulse - WI01 FRM24 SAE/SAR Report Form FRM58 AE/AR Report Form FRM62 Adverse Event Log Template |
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KEY POINTS OF THIS PROCEDURAL DOCUMENT:

- If the CI or PI delegates the management of safety reporting tasks to a member of the research team, this must be clearly documented on the Delegation Log and signed/dated by all parties concerned.
- If a Nominated Designee undertakes the Safety Reporting functions, this must be stated in the trial Protocol and clearly documented on the Delegation Log for the trial.
- Trial staff with responsibility for AE/AR reporting must be able to identify AEs/ARs and be able to distinguish different types of AEs/ARs.

1. INTRODUCTION

For Clinical Trials of Investigational Medicinal Products (CTIMPs) there is a legal requirement for the management and reporting of adverse events (AEs) in accordance with the Medicines for Human Use (Clinical Trials) Regulations 2004. The regulations set out the requirements for notification and reporting of AEs and adverse reactions (ARs) during a CTIMP.

This Standard Operating Procedure (SOP) aims to ensure that arrangements are in place to protect patient safety in all research involving human subjects, that investigators are aware of the safety implications of their research, and that the appropriate bodies are notified of safety information relating to medicines and interventions. Research-related adverse events are not uncommon and range from mild expected drug reactions i.e. Adverse Reactions (ARs) to fatal or life-threatening suspected unexpected serious adverse reactions (SUSARs). All adverse events need to be reported correctly and within strict timeframes, in accordance with the Medicines for Human Use (Clinical Trials) Regulations 2004. These state that a Sponsor shall ensure that all relevant information about a SUSAR is recorded and reported to the Medicine and Healthcare Regulatory Agency (MHRA) and the Health Research Authority (HRA).

2. PURPOSE

The objectives of this SOP are:

- To define and classify Adverse Events (AEs) and Adverse Reactions (ARs).
- To describe the Royal Devon University Healthcare NHS Foundation Trust (hereafter referred to as 'the Trust') research procedure for identifying safety events when developing/setting up research; discovering, recording, reporting during the research; and following up of all AEs, ARs, Serious Adverse Events (SAEs), Suspected Serious Adverse Reactions (SSARs) and SUSARs
- To describe the procedure for reporting pregnancies occurring during research studies.

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3. SCOPE

This SOP applies to:

- All researchers conducting research at the Trust. This includes CTIMPs, interventional research and other research where safety events are required to be reported.
- R&D personnel administering the Safety Reporting process on behalf of the Sponsor. In circumstances where the Trust has delegated the responsibilities to a third party such as an external Clinical Trials Unit (CTU), the safety reporting procedures will be outlined in a trial specific agreement between the Sponsor, the third party and the Chief Investigator.

4. DEFINITIONS & ABBREVIATIONS

| | |
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| AE | Adverse Event - any unfavourable and unintended signs, including abnormal laboratory results, symptoms or a disease associated with treatment. |
| AR | Adverse Reaction - adverse events but causally related to investigational medicinal products. |
| DSUR | Development Safety Update Report |
| CI | Chief Investigator |
| CIMD | Clinical Investigation of a Medical Device |
| CRF | Case Report Form |
| CTIMP | Clinical Trial of an Investigational Medicinal Product |
| CTU | Clinical Trials Unit |
| DMC | Data Monitoring Committee |
| Expedited Reporting | A term used by REC and MHRA to mean immediate/quick/efficient reporting |
| EPR | Electronic Patient Record |
| GCP | Good Clinical Practice |
| GOG | R&D Governance Oversight Group |
| HRA | Health Research Authority |
| IB | Investigator Brochure |
| IMP | Investigational Medicinal Product |
| ISF | Investigator Site File |
| MHRA | Medicines and Healthcare products Regulatory Agency |
| PI | Principal Investigator |
| R&D | Research & Development |
| Royal Devon | Royal Devon University Healthcare NHS Foundation Trust |
| REC | Research Ethics Committee |
| RSI | Reference Safety Information |
| SAE | Serious Adverse Event - any untoward medical occurrence(s) that at any dose results in death, hospitalisation or prolongation of existing hospitalisation, persistent or significant disability/incapacity or a congenital anomaly or birth defect |

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| SAR | Serious Adverse Reaction - an adverse reaction that at any dose results in death, hospitalisation or prolongation of existing hospitalisation, persistent or significant disability/incapacity or a congenital anomaly or birth defect |
| SmPC | Summary of Product Characteristics |
| SOP | Standard Operating Procedure |
| SSAR | Suspected Serious Adverse Procedure |
| SUSAR | Suspected Unexpected Serious Adverse Reaction - when a SAR (see above) is unexpected |
| TMF | Trial Master File |
| TMG | Trial Management Group |
| TSC | Trial Steering Committee |

5. DUTIES AND RESPONSIBILITIES OF STAFF

5.1 All Researchers

It is the responsibility of all researchers in contact with research participants to discover, record and notify the Principal Investigator (PI) and/or Chief Investigator (CI) of all AEs/ARs not stated in the Protocol or Reference Safety Information (RSI) as being exempt from the recording process

5.2 Royal Devon Sponsored Trials

5.2.1 Staff and Sponsor Responsibilities

In respect of Trust sponsored trials, the safety reporting functions of the Sponsor will be delegated to the CI or Nominated Designee. All delegation from the Sponsor to the CI will be clearly documented and acknowledged by all parties concerned.

Only the reporting of Suspected Unexpected Serious Adverse Reactions (SUSARs) to the MHRA will be retained by the Sponsor.

5.2.2 Chief Investigator (CI)

As Sponsor, the Trust delegates the following duties to the CI:

- On-going safety evaluation of the Investigational Medicinal Product (IMP) or intervention, to include annual reviews and where necessary, updating the RSI (typically either an Investigator Brochure (IB) and/or Summary of Product Characteristics (SmPC)).
- Keeping records of all AEs/ARs occurring at the Trust and, if multi-centre, at participating sites. These records must be stored in the Trial Master File/Investigator Site File (TMF/ISF).
- Reporting Serious Adverse Reactions (SARs) and Serious Adverse Events (SAEs) which are listed in the Protocol as requiring expedited reporting to the Competent Authority(ies), and the Sponsor, within the required timeframes.
- Reporting all incidents whereby a trial participant unexpectedly becomes pregnant to the Sponsor, see Section 6.1.12 (sponsored) or 6.2.4 (hosted) below for further guidance.
- Ensuring the recording and prompt reporting of SUSARs to the Sponsor.

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- Providing an annual list of SUSARs and a Development Safety Update Report (DSUR) to the MHRA (CTIMPs only), see SOP [S31 - \(Reporting required for sponsored CTIMPS\)](#) for details of DSUR reporting requirements.
- Providing an Annual Report to REC (CTIMPS and non-CTIMPs).
- For multi-centre studies, promptly notifying all participating investigators of findings that could adversely affect the safety of the Trial participants, impact adversely on the conduct of the Trial or alter the REC's favourable opinion to continue the Trial.

N.B. The R&D Office (as Sponsor's representative) must be copied into all correspondence concerning safety reporting with Regulatory Authority(ies) and REC.

Where the CI further delegates any of these tasks to a member of the research team, this must be clearly documented on the Delegation Log and signed/dated by all parties concerned.

5.2.3 Principal Investigator (PI)

For all Trust sponsored and hosted studies, it is a legal requirement for the PI to:

- a) Report all SAEs/SARs immediately to the CI/Trial Sponsor unless specified in the Protocol or IB as not requiring expedited reporting.
- b) Report all AEs/ARs identified in the Protocol as being critical to the evaluation of trial safety to the CI/Trial Sponsor.
- c) Report all incidents whereby a trial participant unexpectedly becomes pregnant, to the CI and Sponsor see Section 6.1.12 (sponsored studies) or 6.2.4 (hosted studies) below for further guidance.
- d) Supply the CI, Sponsor and the REC with any additional requested information.

Where the PI further delegates any of these tasks to a member of the research team, this must be clearly documented on the Delegation Log and signed/dated by all parties concerned.

N.B. If a Nominated Designee undertakes the Safety Reporting functions (which may be necessary for blinded trials), this must be stated in the trial Protocol and clearly documented on the Delegation Log for the trial. The person(s) to whom the reporting functions have been delegated must be suitably qualified to assess the relatedness and expectedness of the adverse event and to understand the reporting requirements.

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6. PROCEDURES

6.1 Safety Reporting in Royal Devon Sponsored Studies

6.1.1 Study Set-up and Safety Considerations

Before initiating a clinical trial and finalising the protocol, a study assessment must be conducted by the CI and the Sponsor. Careful consideration must be given to the following points:

- 1) Whether a Data Monitoring Committee (DMC) and/or a Trial Steering Committee (TSC) is required;
- 2) Which AEs/ARs need to be recorded and reported;
- 3) How often SAEs need to be reviewed.

Depending on what is known about the safety profile of the IMP or the intervention (particularly in the population to be studied), it may be decided not to record or report any non-serious AEs and/or disease-related SAEs. In addition, it may be decided to exclude 'expected' SARs from expedited reporting to the trial Sponsor. Importantly, all AEs (serious and non-serious) to be excluded from the recording and/or expedited reporting process must be clearly defined in the Study Protocol (and/or the RSI in the case of a CTIMP).

Specific requirements/procedures for assessing, recording, notifying and reporting AEs must be clearly defined in the Study Protocol, including the specific timelines to be followed. This includes details of delegated responsibilities where appropriate.

6.1.2 Reference Safety Information (CTIMPs)

The RSI is the list of known adverse reactions for the IMP/IMPs under study and must be approved by the Medicines and Healthcare products Regulatory Agency (MHRA) as part of the original Clinical Trial Authorisation or through a substantial amendment in the event of an update to the RSI. Only the approved RSI can be used to assess the expectedness of any SAR that occurs during the trial. It is the Sponsor's responsibility to determine the RSI for the trial however this task may be delegated to the CI.

In general, the RSI may be a section within the Investigator Brochure (for IMP without a Marketing Authorisation) or the Summary of Product Characteristics (SmPC) (for IMP with a Marketing Authorisation and being used within the licensed indication). There can only be one RSI for each IMP under study.

6.1.3 Highlighting Reporting Adverse Events (AEs) at Enrolment

Upon enrolment into a study, the Research Team must flag the patient's participation onto the electronic patient record (EPR, also known as EPIC), along with entering the lead contact, PI and brief summary of the study. The team can then run daily reports to identify hospitalisations or illnesses occurring whilst in the trial.

Upon enrolment, the participant must also be given a trial participant card/leaflet. This will instruct the participant to inform a member of the trial team of any hospitalisation or illness occurring whilst in the trial. It is important that each participant be given a completed card (i.e. with participant's name, trial name and contact details for the Research Team) when enrolling in a trial.

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6.1.4 Discovering AEs/ARs

Trial staff with responsibility for AE/AR reporting i.e. the CI/PI or delegated individual (as identified on the Delegation Log) must be able to identify AEs/ARs and be able to distinguish different types of AEs/ARs from one another. Timely identification and defining of AEs/ARs is very important since each type of AE/AR is governed by its own particular reporting timescales.

Training around safety reporting is available through the NIHR Good Clinical Practice courses.

In the event of perceived immediate harm to a participant, the SOP [S52 \(Urgent Safety Measures\)](#) must be consulted.

Information regarding the occurrence of Serious and Non-Serious AEs/ARs must be sought from medical notes and followed up with the clinical teams, as well as asking all study participants at each trial visit. Participants must be asked about hospitalisations, disabilities or whether any other AEs have occurred.

6.1.5 Evaluating different types of AEs/ARs

It is expected that the CI/PI is responsible for making an informed judgement with regards to classifying AEs/ARs as they occur. When analysing AEs/ARs the CI/PI will assess for:

A. Seriousness

An AE/AR is classified as Serious if it:

- Results in death;
- Is life threatening;
- Requires hospitalisation or prolongation of existing hospitalisation;
- Results in persistent or significant disability or incapacity;
- Consists of a congenital anomaly or birth defect

B. Expectedness

Whether the nature and severity of the AE/AR are consistent (expected) or not consistent (unexpected) with information about the IMP set out in the IB or SmPC. In the case of non-CTIMPs, judgement must be made by the CI or PI about the expectedness of an event/reaction in relation to the intervention.

C. Causality

A causal association is suspected between the Investigational IMP and the AE if the relationship is classified as 'possibly', 'probably' or 'definitely' using the definitions below:

1. Not related

Temporal relationship of the onset of the AE, relative to the administration of the IMP, is not reasonable or another cause can itself explain the occurrence of the event.

2. Unlikely

Temporal relationship of the onset of the AE, relative to the administration of the IMP is unlikely but cannot be ruled out.

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3. Possibly

Temporal relationship of the onset of the AE, relative to the administration of the IMP, is reasonable and the event could have been due to another, equally likely cause.

4. Probably

Temporal relationship of the onset of the AE, relative to the administration of the IMP, is reasonable and the event is more likely explained by the drug than by any other cause.

5. Definitely

Temporal relationship of the onset of the AE, relative to the administration of the IMP, is reasonable and there is no other cause to explain the event or a re-challenge is positive.

Note these causal associations can be extended to relationship to an intervention in the case of non-CTIMP studies.

D. Severity (intensity)

The clinical severity of an AE/AR is classified as mild, moderate or severe. It must be noted that the clinical severity and seriousness of an AE/AR are not the same thing. For example, a patient may have a severe headache, which is not classified as serious unless it meets any of the outcome criteria in Section 6.1.5a).

6.1.6 Recording and Reporting AEs/ARs

Unless the Protocol/RSI states otherwise, all AEs/ARs (serious and non-serious) must be recorded. The person responsible for recording AEs/ARs must record the AE/AR in the:

- a) Source document (i.e. in the patient notes if applicable)
- b) Relevant participant's Case Report Form (CRF)
- c) Trial Master File/Investigator Site File (TMF/ISF)

An initial assessment of the AE/AR must be made on an [Adverse Event Form](#) (displayed on the Royal Devon website under [Templates and Forms](#)). The record must include a description of the AE, its start date, duration/end date; outcome and assessment of its seriousness, relatedness, expectedness and severity.

For SAEs a [Serious Adverse Event Form](#) (same location as above) must be completed unless it is disease-related and has been specified in the Protocol as not requiring recording.

A copy of the SAE must only be saved in the corresponding section within the TMF/ISF

For SUSARs see section 6.1.10.

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6.1.7 Reporting Requirements – Research Team

6.1.7.1 Single-Centre (Royal Devon only)

All safety events which occur within Trust single centre sponsored studies, must be reported to R&D (or delegated third party if applicable e.g. CTU supported study) within 24 hours of knowledge of the event.

- AEs, SAEs and SUSARs for both CTIMPs and non-CTIMPs must be sent by the CI or Nominated Designee(s) to the R&D Department (rduh.randdsafetyreporting@nhs.net) in the timeframe specified above.
- For some studies it will be appropriate instead to send a record of all AEs/ARs occurring during the life of the trial to be sent to the Sponsor (via the R&D office) on a periodic basis and this will be agreed and documented prior to the trial commencing. Any changes to reporting during the trial must be agreed by the Sponsor.
- The CI or Nominated Designee must in turn forward a copy of the SAE to the REC and MHRA if required.
- Non-CTIMPs: the [Trust AE or SAE report form](#) must be scanned and emailed to the R&D generic email inbox as shown below; a CI/PI (or delegated individual) must assess causality/severity/expectedness and countersign the Trust form
- CTIMPs: the [Trust AE or SAE report form](#) must be scanned and emailed to the R&D generic email inbox as shown below; a CI/PI (or delegated individual) must assess causality/severity/expectedness and countersign the Trust form.
- The above AE and SAE Trust reporting forms must be used unless prior agreement is made with the Sponsor that study specific or third party (in the case of CTU supported studies) safety reporting forms containing all the required information can be used.

In order to meet the prescribed 24-hour timeline for reporting SAEs to the Sponsor (or delegated party), it may not always be possible for the CI/PI (or delegated individual's) signature to be included on the SAE form. Where this is the case the form must be re-sent in due course with the CI/PI's signature included.

The generic email inbox address for ALL types of safety reporting is as follows: rduh.randdsafetyreporting@nhs.net. The correct versions of the report forms are available on the [Royal Devon website within Research & Development Useful documents](#).

Copies of all safety reports and logs must be kept in the site ISF and the TMF.

All safety events must be routinely reviewed by the CI & study team both individually and for trends.

6.1.7.2 Multi-Centre Sponsored Studies

All safety events which occur within Trust multi centre sponsored studies must be reported to the delegated central coordinating site e.g. CTU or Trial Manager and the CI within 24 hours of knowledge of the event as laid out either in the protocol or a study specific SOP. These will be reported periodically (as agreed

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with Sponsor at the outset) to the Sponsor (typically via the Trial Management Group/TMG) for Sponsor oversight. In small multicentre studies with no trial manager, all safety events must be reported to the CI and also the Sponsor directly by sites emailing the generic safety inbox, rdh.randdsafetyreporting@nhs.net.

In the case of any SUSAR, the Sponsor must be informed within the 24-hr period in addition to the central coordinating site. For further details see section 6.1.9 and 6.1.10.

It is expected that the Royal Devon safety reporting forms will be used unless prior agreement has been made for an alternative form containing all the relevant information to be employed.

Copies of all safety reports and Adverse Event logs must be kept in the site ISF and the TMF.

All safety events must be routinely reviewed by the CI & study team both individually and for trends.

6.1.8 Reporting Requirements - R&D Department

Upon receipt of the safety report form by the R&D designee (QA Coordinator or R&D Facilitator), the completeness of the form will be checked and any queries relayed back to the study team for corrections to be made as necessary before being entered onto the Q-Pulse Quality Management system as per [R&D Work Instruction WI01](#).

The safety report form must be sent to the Sponsor Manager for assessment and follow-up. When a DTX reference number is available from Q-Pulse this must be recorded on the safety report form.

A copy of the safety report form (with DTX reference number displayed) must be saved in the R&D study folder within section 2 'Safety Reporting' [P:\RESEARCH DEVELOP\Studies\Folders](#). This applies for initial reports, follow ups and final reports.

If the CI/PI has confirmed their causality assessment over email a copy of the email trail must also be saved in the R&D study folder with a reference to the relevant DTX number.

If an event is marked as 'Continuing' the R&D designee will liaise with the Research Team and Sponsor Manager or Research Governance and Quality Manager until the Outcome is 'Recovered/Resolved'/'Resolved with Sequelae'/'Fatal' and the Sponsor Manager or Research Governance and Quality Manager has signed off the DTX report on Q-Pulse.

When the safety reporting function has been delegated to a third party e.g. CTU or Trial Manager, the safety reports will not come direct to the Sponsor and will not be added to Q pulse as outlined above. The Sponsor Manager (or Research Governance and Quality Manager in their absence) will receive periodic safety event listings from the delegated party for sponsor oversight. These listings will be reviewed to ensure they are correctly assessed, timely and followed up. The listings will be saved in the R&D study folder and a summary plus any highlighted

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events reported to GOG every month. In studies where a Sponsor Oversight Group is established (in CTIMPs), full safety event listings will also be supplied.

6.1.9 Expedited Reporting

“Expedited Reporting” is a term used by REC and MHRA to mean immediate/quick/efficient reporting. The Regulations set time limits for expedited reporting:

Fatal or life-threatening SUSARs – not later than 7 calendar days after the Sponsor has information that the case reported fulfils the criteria for a fatal or life threatening SUSAR, with any follow up information to be reported within a further 8 calendar days.

All other SUSARs – Not later than 15 calendar days after the Sponsor has information that the case fulfilled the criteria for a SUSAR.

6.1.10 SUSAR Reporting in Royal Devon Sponsored Studies

All Expedited Reports of SUSARs for Trust sponsored studies must be completed by the CI or Nominated Designee and must be reported to the Sponsor within 24hrs via the generic safety reporting inbox:

rduh.randdsafetyreporting@nhs.net

This will enable the Sponsor, in the case of a CTIMP, to report to the MHRA electronically via their [Individual Case Safety Reports \(ICSR\) Submissions portal](#), within the appropriate timescales (as per above). Once the eSUSAR form is submitted, a PDF copy of the form must be saved for the Trial Master File/Site File (TMF/ISF) and for the R&D File as evidence of submission. A copy must also be sent to REC.

N.B. All SUSARs must be reported to the MHRA in an unblinded state. Upon discovery of the SUSAR and initial report to the Sponsor, the CI must provide the unblinded information to the Sponsor within 3 days in order to enable the Sponsor to meet the reporting requirements of the MHRA.

All SUSARs, both in CTIMP and non-CTIMP research, must be reported to the REC by the Sponsor in collaboration with the CI using the [CTIMP safety form and non-CTIMP safety form](#) respectively. There is no need for the form to be signed prior to submission. It must be sent by email to the REC. The REC co-ordinator will acknowledge receipt of the safety report within 30 days. The email address for the REC can be found on their initial approval letter for the trial. Refer also to [SOP S31 \(CTIMP Reporting\)](#).

In addition to following the expedited reporting process and entering the event onto Q-Pulse, details of the SUSAR will be entered onto the Trust Incident Reporting System (Datix) by the Sponsor Manager (or Research Governance and Quality Manager in their absence). SUSARs will be escalated by the Sponsor Manager to the Sponsor Oversight Group (in CTIMPs) for their immediate review and highlighted to the Governance Oversight Group (GOG) at their routine meetings. For non-CTIMPS, GOG will be informed at the next scheduled meeting.

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6.1.11 Managing Safety Events to Conclusion

All safety events must be followed through until they are resolved or resolved with sequelae, unless determined otherwise by the Sponsor Manager, even if the participant(s) affected has/have been withdrawn from the trial.

In the case of SUSARs, the CI/PI is required to inform R&D in writing that they are happy to continue with that trial and the study drug/intervention in question. This information will be relayed at the next R&D GOG, where the Sponsor Manager routinely reports on all safety events and SUSARs occurring in each study.

The risk of an AE or AR re-occurring will be reduced if the reasons why the AE or AR occurred in the first place are recognised and the lessons shared with all staff involved in the trial and, if possible, more widely.

6.1.12 Pregnancy Reporting in Trust Sponsored Studies

Pregnancy is not considered an AE or SAE; however, an abnormal outcome would be. For this reason, the Investigator must collect pregnancy information for female trial participants or female partners of male trial participants who become pregnant while participating in a CTIMP or trial where pregnancy is relevant to the intervention. This should be outlined in the protocol.

For female partners of male trial participants who become pregnant while participating in a study, consent should be obtained to follow up the pregnancy.

The Investigator must record the information on a [Pregnancy Notification Form \(FRM46\)](#) and to Sponsor within 14 days of being made aware of the pregnancy.

Any pregnancy that occurs in a trial participant or a trial participant's partner during a trial should be followed to outcome unless the trial participant or partner did not provide consent to follow the pregnancy to outcome. In some circumstances, it may be necessary to monitor the development of the new-born for an appropriate period post-delivery. Follow up information must be recorded on the [Pregnancy Follow Up Form \(FRM47\)](#) and sent to the Sponsor.

6.2 Safety Reporting in Hosted Studies

6.2.1 Highlighting Reporting Adverse Events (AEs) at Enrolment

Upon enrolment into a study, the research team must flag the patient's participation onto the electronic patient record (EPR, also known as EPIC), along with entering the lead contact, PI and brief summary of the study. The team then can run daily reports to identify hospitalisations or illnesses occurring whilst in the trial.

6.2.2 Recording and Reporting AEs/ARs

Safety reporting requirements for Hosted studies are defined by the Sponsor in the study Protocol. The Sponsor's instructions/guidance must be followed. This may include saving copies of SAE reports in the site file. Where the Sponsor has agreed to use Edge as the site file, SAE reports may be added to Edge in line with Sponsor requirements around site file maintenance. It is not necessary to

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report hosted safety events to R&D with the exception of SUSARs, see section 6.2.3.

6.2.3 SUSAR Reporting in Hosted Studies

SUSAR reporting requirements for Hosted studies are defined by the Sponsor in the study Protocol. The Sponsor's instructions/guidance must be followed.

All Expedited Reports of SUSARs which occur at the Trust must be completed by the PI or Nominated Designee and must be reported as follows:

- 1) To the Sponsor as outlined in the protocol within 24hrs to enable the Sponsor to report to the MHRA & REC
- 2) To the Trust R&D department via the generic safety reporting inbox: rduh.randdsafetyreporting@nhs.net, again within 24hrs of the Investigator being aware.

In addition to following the expedited reporting process and entering the event onto Q-Pulse, details of any SUSARs which occur at the Trust will be entered onto the Trust Incident Reporting System (Datix) by the Sponsor Manager (or Research Governance and Quality Manager in their absence).

The Sponsor Manager will escalate these to the R&D Governance Manager in the first instance who will bring to the attention of GOG.

6.2.4 Pregnancy Reporting in Hosted Studies

Pregnancy is not considered an AE or SAE; however, an abnormal outcome would be. For this reason, the Investigator must collect pregnancy information for female trial participants or female partners of male trial participants who become pregnant while participating in a CTIMP or trial where pregnancy is relevant to the intervention. This should be outlined in the protocol.

For female partners of male trial participants who become pregnant while participating in a hosted study, follow the study Protocol.

Pregnancy reporting requirements for Hosted studies should be defined by the Sponsor in the study Protocol. The Sponsor's instructions/guidance must be followed.

If the Sponsor does not provide any study pregnancy report forms, the Trust R&D department's pregnancy notification form ([FRM46](#)) and pregnancy follow up form ([FRM47](#)) can be used to record the required information.

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7. DISSEMINATION AND TRAINING

- 7.1 This SOP and associated templates and forms will be uploaded to the [Royal Devon Research and Development website](#) shortly after having been released.
- 7.2 All staff whose activities are subject to this SOP must ensure that they take time to read and understand the content of this SOP.
- 7.3 If applicable, a training log within the Investigator Site File/Trial Master File must be completed to document that members of staff have read and understood the contents of this SOP.

8. MONITORING COMPLIANCE AND EFFECTIVENESS OF THIS SOP

- 8.1 In order to monitor compliance with this SOP, the auditable standards will be monitored as follows:

| | | |
|----|--|--|
| 1. | Ensure reportable safety events are recorded by the research team | EPR, logs and forms in TMF/ISF |
| 2. | Ensure SAEs are reported to the sponsor (or delegated party) within 24hrs of awareness | SAE reporting form in TMF/ISF, Q-pulse |
| 3. | Ensure SUSARS are expediated to the regulatory bodies in a timely fashion | TMF/ISF, R&D study file |
| 4. | All safety events are followed up to completion | SAE reporting form in TMF/ISF, Q-pulse |
| 5. | Sponsor oversight of all reportable safety events | R&D file, Q-pulse, minutes of oversight committees (e.g. Trial Management Group/TMG, Trial Steering Committee/TSC) |

- 8.2 Outcomes from audit will be presented to the R&D Governance Oversight Group (GOG) which will monitor any resulting action plans until all issues have been addressed to satisfaction.
- 8.3 Issues identified via the audit process which require escalation will be referred to GOG.

9. ARCHIVING ARRANGEMENTS

- 9.1 The original of this document will remain with the R&D Quality Assurance Coordinator. An electronic copy will be maintained on the R&D section of the Q-Pulse document management system and a pdf copy on the [Royal Devon Research and Development website](#).
- 9.2 Archive copies must be maintained for any documents which have been superseded. Archive copies in electronic format must be retained indefinitely.

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10. REFERENCES

[Commission Directive \(2005/28/EC\) on Good Clinical Practice](#)

[EU Clinical Trials Directive 2001 \(2001/20/EC\)](#)

[Medicines for Human Use \(Clinical Trials\) Regulations 2004 \(S.I.2004/1031\)](#)

[Medicines for Human Use \(Clinical Trials\) Amendment Regulations 2006 \(S.I.2006/1928\)](#)