York and Scarborough Teaching Hospitals NHS Foundation Trust R&D Unit
Standard operating Procedure
R&D/S19

Research Related Adverse Event Reporting Procedure for Hosted Studies

IT IS THE RESPONSIBILITY OF ALL USERS OF THIS SOP TO ENSURE THAT THE CORRECT VERSION IS BEING USED

All staff should regularly check the R&D Unit's website and/or Q-Pulse for information relating to the implementation of new or revised versions. Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use unless notified otherwise by the SOP Controller.

The definitive versions of all R&D Unit SOPs appear online. If you are reading this in printed form check that the version number and date below is the most recent one as shown on the R&D Unit website: www.research.yorkhospitals.nhs.uk/sops-and-guidance-/ and/or Q-Pulse

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Author:	Deborah Phillips
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Approved by:	Name/Position:	Lydia Harris, Head of R&D
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	Name/Position:	Sarah Sheath, SOP Controller
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This SOP will normally be reviewed every 3 years unless changes to the legislation require otherwise

Version History Log

This area should detail the version history for this document. It should detail the key elements of the changes to the versions.

Version	Date implemented	Reviewers	Details of significant changes
1.0	22nd August 2017		
2.0	4th February 2021		Change of link to R&D website.
3.0	3rd January 2024	Monica Haritakis Jonathan Hawker Deborah Phillips	Change of author. Changed SOP to describe process for hosted studies.

Contents

1 Introduction, Background and Purpose

The purpose of this SOP is to describe and standardise the adverse event reporting procedure that should be followed for all studies Hosted by York and Scarborough Teaching Hospitals NHS Foundation Trust (the Trust). This SOP helps to safeguard that all systems are in place for the management of AEs for hosted studies to ensure that during the course of a study the participants' involvement in research is recorded and reported to ensure their continued safety.

To be compliant with GCP, Sponsors have a responsibility to record and report SAEs. The reporting requirements for each research project will differ, dependent on the nature of the study and the patient population. In all cases the individual study protocol will state clearly what events are expected to be reported and what exceptions there may be in safety reporting.

As well as research related adverse events, adverse incidents occur on research studies. It is important that research related adverse incidents are reported in the same way as non-research related adverse incidents (see Section 5.4).

2 Who Should Use This SOP

This SOP should be used by investigators involved in studies Hosted by the Trust.

In these circumstances, the Sponsor reporting procedure should be followed although there is an additional requirement to notify the R&D Unit in the event of a Serious Adverse Reactions (SARs) occurring in the Trust. This notification must be made in an expedited fashion to yhs-tr.research.governance@nhs.net.

3 When this SOP Should be Used

Recording and reporting of Adverse Events (AEs), including Adverse Reactions (ARs), Serious Adverse Events (SAEs), Serious Adverse Reactions (SARs), and Suspected Unexpected Serious Adverse Reactions (SUSARs) should be managed in line with the reporting procedure of the sponsor of the research study.

4 Procedure(s)

4.1 Abbreviations

AI	Adverse Incident
AE	Adverse Event
AR	Adverse Reaction
CTIMP	Clinical Trial of an Investigational Medicinal Product
GCP	Good Clinical Practice
IMP	Investigational Medicinal Product
ISF	Investigator Site File
NIMP	Non-investigational Medicinal Product
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File

4.2 Definitions

Non-Investigational Medicinal Product (NIMP)
Products that are not the object of investigation (for example drugs used as part of standard care) may be supplied to subjects participating in the study and used in accordance with the protocol. This might be, for example, medicinal products such as support/rescue medication for preventative, diagnostic or therapeutic reasons and/or to ensure that adequate medical care is provided for the subject. These medicinal products do not fall within the definition of investigational medicinal products (IMPs) in Directive 2001/20/EC and are called **non-investigational medicinal products** (NIMPs).

Investigational Medicinal Product
An ***Investigational Medicinal Product*** (IMP) is a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial including a medicinal product which has a marketing authorisation but is, for the purposes of the trial, being used or assembled (formulated or packaged) in a way different from the approved form or being used for an unapproved indication or when used to gain further information about an approved use.

Adverse Event (AE)
Any untoward medical occurrence in a study participant which does not necessarily have a causal relationship with the study treatment or procedure (e.g. abnormal laboratory findings, unfavourable symptoms or diseases) is classed as an ***adverse event (AE***).

Comment: An adverse event can therefore be any unfavourable and unintended sign (including abnormal lab results), symptom or disease temporally associated with the use of the medicinal product/intervention, whether or not considered to be related to the medicinal product/intervention.

Adverse Reaction (AR)

An ***adverse reaction (AR)*** is any untoward and unintended response in a subject to a product or study procedure where there is evidence or argument to suggest a causal relationship.

Any adverse event judged by either the reporting investigator or the sponsor as having reasonable causal relationship to a product or study procedure qualifies as an AR.

Note: All adverse reactions are adverse events.

Unexpected Adverse Reaction (UAR)

An ***unexpected adverse reaction*** is an adverse reaction the nature and severity of which is not consistent with the information about the event or the medicinal product in question set out –

(a) in the case of a product with a marketing authorisation, in the summary of product characteristics (SmPC or SPC) for that product,

(b) in the case of any other investigational medicinal product, in the investigator's brochure relating to the trial in question.

(c) in the study protocol (for non-CTIMP studies)

Comment: When the outcome of the adverse reaction is not consistent with the applicable product information this adverse reaction should be considered as unexpected. All unexpected adverse reactions are adverse events.

Serious Adverse Event (SAE)

An adverse event, adverse reaction, or unexpected adverse reaction is defined as ***serious*** if it:

(a) results in death,
(b) is life-threatening,
(c) requires hospitalisation or prolongation of existing hospitalisation,
(d) results in persistent or significant disability or incapacity, or
(e) consists of a congenital anomaly or birth defect
(f) is otherwise considered medically significant

Comment: Life threatening in the definition of an SAE/SAR refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event that hypothetically might have caused death if it were more severe. Medical judgement should be exercised in deciding whether an SAE/SAR is serious in other situations. Important SAE/SARs that are not immediately life-threatening or do not result in death or hospitalisation but may jeopardise the

subject or may require intervention to prevent one or the other outcomes listed in the definition above, should also be considered serious.

ALL AE/SAEs should be collected for all trial subjects from the commencement of any study related procedures (including screening procedures). This is the default position for all Trust sponsored studies and any deviation from this must be agreed by the Sponsor prior to the start of the study and documented accordingly.

Suspected Unexpected Serious Adverse Reaction (SUSAR)

A ***SUSAR*** is a suspected unexpected serious adverse reaction.

A **suspected unexpected serious adverse reaction (SUSAR)** is an SAR which is also "unexpected", meaning that its nature and severity are not consistent with the information about the medicinal product in question set out:

1. in the case of a product with a marketing authorisation, in the summary of product characteristics for that product;
2. in the case of any other investigational medicinal product, in the investigator's brochure relating to the trial in question.

Comment: All adverse events that are suspected to be related to an investigational medicinal product and that are both unexpected and serious are considered to be SUSARs.

Urgent Safety Measures

All urgent safety measure must be communicated to the CI and Sponsor ***IMMEDIATELY*** and discussed with the REC by telephone. (Please refer to section 7 R&D/S68).

Adverse Incident (AI)

An ***adverse incident (AI)*** is any incident/accident, near miss or untoward event which had or may have had the potential to cause harm, dissatisfaction or injury to persons, loss or damage to property. This definition includes hazards, accident, ill health, dangerous occurrences and near misses**.**

5 Reporting Procedures

The specific reporting requirements for Hosted Studies may vary depending on the nature of the study being undertaken. Details must be included in a distinct section of the study protocol. Where reporting requirements exist the following will apply.

Delegation of Responsibilities

- For multi-site studies, the Chief Investigator (CI) has overall responsibility for Pharmacovigilance and Safety Reporting at all participating sites.
- Each Principal Investigator (PI) is delegated responsibilities for Pharmacovigilance and Safety Reporting at their site.
- The Principal Investigator must ensuring that study personnel are suitably trained for the purposes of AE recording, assessment and reporting.
- Assessment of an adverse event is a medical decision and as such MUST be performed by a medically qualified team member. This may not be the PI if they are not medically qualified.

5.1 Adverse Events (AE) and Adverse Reactions (AR)

AEs/ARs must be documented in accordance with the Sponsor requirements.

As a minimum they should be documented patients' medical records and observed to ensure that they do not escalate to a serious adverse event. There may be an additional requirement to document these in case report forms (CRFs).

The investigator should keep an ongoing log of adverse events on EDGE (using the process detailed in appendix B) that must be made available to the Sponsor on request.

5.2 Serious Adverse Events (SAEs)

It is expected that all SAEs will be reported to the Sponsor in accordance with the Sponsor requirements. Generally, the requirement is that this is reported immediately after becoming aware of a reportable serious adverse event (and within 24 hours).

The initial report will include as much information as is available at the time and should be signed by a suitable qualified medical doctor, usually the PI or delegated investigator, to confirm their review and assessment of the SAE

The assessment criteria will be specified in the Research Protocol but is generally intensity, causality, expectedness and seriousness (see section 6).

The investigator should keep an ongoing log of SAEs on EDGE (using the process detailed in appendix 1) that must be made available to the Sponsor on request.

5.3 Serious Adverse Reactions (SARs)

It is expected that all SARs be reported to the Sponsor in accordance with the Sponsor requirements. Generally, the requirement is that this is reported immediately after becoming aware of a reportable serious adverse event (and within 24 hours).

There is an additional requirement to notify the R&D Unit in the event of a Serious Adverse Reaction (SAR) occurring in the Trust. This notification must be made in an expedited fashion to yhs-tr.research.governance@nhs.net.

The initial report will include as much information as is available at the time and should be signed by a suitable qualified medical doctor, usually the PI or delegated investigator, to confirm their review and assessment of the SAR.

The assessment criteria will be specified in the Research Protocol but is generally intensity, causality, expectedness and seriousness (see section 6).

The investigator should keep an ongoing log of SARs on EDGE (using the process detailed in appendix 1) that must be made available to the Sponsor on request.

5.4 SUSARs

SUSARs are a subset of suspected unexpected serious adverse reactions which are subject to strict mandatory reporting timelines to the Medicines and Healthcare products Regulatory Agency (MHRA) and the main Research Ethics Committee (REC).

In a study hosted by our Trust it is expected that all SUSARs will be reported to the Sponsor in accordance with the Sponsor requirements. SUSARs must be reported to the Sponsor with immediate effect and within 24 hours of the research team becoming aware of it.

There is an additional requirement to notify the R&D Unit in the event of a Suspected Unexpected Serious Adverse Reaction (SUSAR) occurring in the Trust. This notification must be made in an expedited fashion to yhs-tr.research.governance@nhs.net.

The responsibility to report to the MHRA through the eSUSAR system and the main REC is that of the Sponsor.

For all Hosted studies the Chief Investigator must inform all Principal Investigators of SUSARs occurring on the study. It is the responsibility of the CI to communicate all information to the PIs, in particular any information that could adversely affect the safety of subjects. This notification must be documented.

5.5 Adverse Incidents

In the same way that adverse incidents, including clinical, non-clinical and near misses can involve patients, staff and visitors during routine care, adverse incidents can also occur during research related activities. It is important that research related adverse incidents are treated in the same way as non-

research related adverse incidents. Research related Adverse Incidents must therefore be reported in accordance with the hosting Trust's own Adverse Incident Reporting Procedure/System.

Events that are both Adverse Incidents and Adverse Events MUST be reported independently following both processes or procedures.

All Adverse Incidents that are reported as occurring on research studies taking place in York Foundation Trust are reviewed by the R&D Unit and are assessed for trends quarterly.

6 Assessment of Adverse Events

6.1 Intensity

The assessment of intensity will be based on the investigator's clinical judgement using the following definitions:

- Mild: An event that is easily tolerated by the patient, causing minimal discomfort and not interfering with everyday activities.
- Moderate: An event that is sufficiently discomforting to interfere with normal everyday activities.
- Severe: An event that prevents normal everyday activities.

Comment: The term severity is often used to describe the intensity (severity) of a specific event. This is not the same as 'seriousness', which is based on patient/event outcome or action criteria.

6.2 Causality

The relationship between the intervention/procedure/product and the occurrence of each adverse event will be assessed and categorised as below. The investigator will use clinical judgement to determine the relationship. Alternative causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors etc. will be considered.

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

*Where an event is assessed as possibly related, probably related, definitely related, the event is an **adverse reaction (AR)**.

6.3 Expectedness

Adverse reactions must be considered as unexpected if they add significant information on the specificity or severity of an expected adverse reaction. The expectedness of an adverse reaction shall be determined according to the protocol or other reference documentation.

- Expected: Reaction previously identified and described in protocol and/or reference documents
- Unexpected: Reaction not previously described in the protocol or reference documents.

NB The protocol must identify the reference documentation used.

6.4 Seriousness

An event is considered serious if it meets one or more of the following criteria:

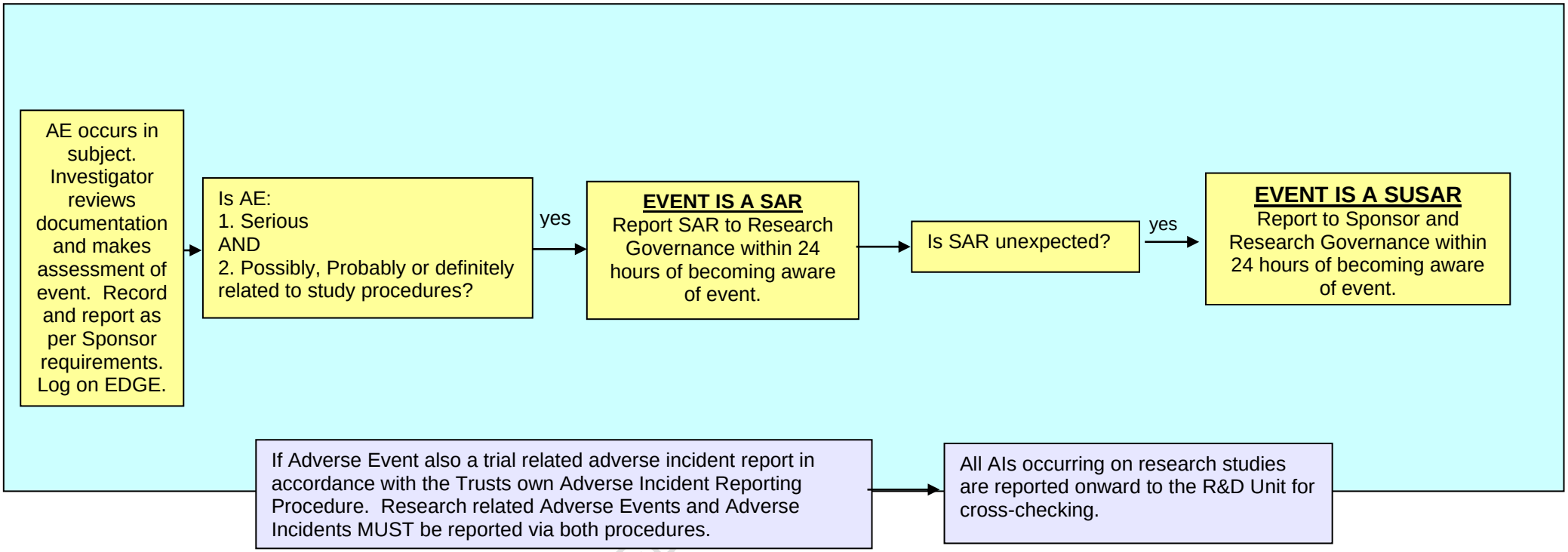
- Results in death
- Is life-threatening
- Requires hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability or incapacity
- Consists of a congenital anomaly or birth defect

7 Related SOPs and Documents

R&D/T02	Research Related Adverse Event (AE) Recording Template
R&D/F07	Research Related SAE/SUSAR Initial Report Form
R&D/F08	Research Related SAE/SUSAR Follow-up Report form
R&D/F09	Research Related SAE/SUSAR Sponsor Report Form
R&D/F46	AE/SAE Log
R&D/F121	Pregnancy Notification Form
R&D/S12	Receiving and Acknowledging Safety Notifications to the R&D Unit
R&D/S13	R&D SAE/SUSAR Handling Procedure
R&D/S06	Reporting Requirements During Research Studies

8 Appendix A

INVESTIGATOR RESPONSIBILITIES



9 Appendix B

Logging Safety Reports on EDGE

1. Go to the applicable project site page (red bar) in which the patient was recruited.
2. From here navigate to the participant tab and click on the relevant participant's name.
3. To the left-hand side there will be multiple tabs starting with "Overview" and ending with "Documents", navigate to the tab labelled "Safety Reporting".
4. From here click on the 

Button to the right-hand side of the page.
5. Fill out all the relevant information when/if it is known to you. Make sure to return to the form if more information becomes available.
6. Once you have filled out the form, click **Save**.
7. Once saved you can **Edit**, **View** or **Delete** the event by clicking on the corresponding action to the right of the event.
8. A notification will then go out to all the people working on the study with clinical access.