SAEs (SPONSORED)

Research & Development

Standard Operating Procedure for Identifying, Recording and Reporting Serious Adverse Events in Trust Sponsored Drug Clinical Trials

SOP Number : SOP-02-09	**Effective Date:** October 2021
Version Number: v09	**Review Date:** 2-3 years

1.0 BACKGROUND

This document sets out the adverse event reporting procedures to be followed by all West Hertfordshire Hospitals Trust (WHHT) staff who are involved in setting up and running research studies managed or sponsored by WHHT.

It provides guidance on the responsibilities delegated to the Chief Investigator (CI) or delegated individual (DI) by the Sponsor regarding adverse event reporting.

2.0 PURPOSE

- To outline responsibilities for assessment of seriousness, causality, severity and expectedness of safety events by the Sponsor and investigator
- To outline procedures for Adverse Event (AE)/Serious Adverse Event (SAE)/Serious Adverse Reaction (SAR) recording and reporting requirements for Trust sponsored clinical trials
- To outline the Suspected Unexpected Serious Adverse Reaction (SUSAR) reporting process to the Sponsor, the Medicines and Healthcare products Regulatory Agency (MHRA), ethics and participating sites (for multicentre trials)
- To outline Development Safety Update Report (DSUR) submission
- To outline details of safety event trend analysis and monitoring by Sponsor and/or investigator

3.0 APPLICABLE TO

Any Trust employee involved with clinical research including, but not limited to, Chief Investigators (CI), Principal Investigators (PI), Consultants, Co-Investigators, Clinical Trial Pharmacists, Research Managers, Statisticians, Research Nurses, Allied Health Professionals, Trial Coordinators,

Administrative Staff and Clinical Trial Administrators.

4.0 RESPONSIBILITIES

For Trust sponsored drug trials, the responsibility for pharmacovigilance is delegated to the CI. The CI should ensure the pharmacovigilance responsibilities are delegated to appropriately trained and qualified individuals and is recorded in a delegation log (see SOP-06).

The CI shall also ensure that all study personnel involved in conducting sponsored trials attend SOP training sessions provided by the R&D Office and evidence of this maintained with the study personnel training files (see SOP-07).

5.0 PROCEDURE

5.1 Recording and Reporting Adverse Events (AEs) and Adverse Reactions (ARs)

5.1.1 All AEs/ARs should be recorded in the source data (medical records, unless the protocol states particular AEs/ARs are exempt from recording or reporting).

5.1.2 AEs/ARs should be reviewed by a clinician.

5.1.3 The severity of adverse events and adverse reactions should also be graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version stated in the protocol.

5.1.4 For multicentre trials, the CI/DI may not always agree on the grading of an event. Please ensure that the highest grading is used for reporting purposes.

5.1.5 Events considered serious, should follow procedures outlined in 5.2.

5.2 Recording and Reporting Serious Adverse Events

5.2.1 A Serious Adverse Event (SAE) or Serious Adverse Reaction (SAR) must be recorded and reported according to the protocol.

5.2.2 Any member of the research team who observes an SAE is responsible for notifying the CI/DI within 24 hours of knowledge, unless the protocol states this event is exempt from immediate reporting. If this is the case, the SAE should be recorded in the patient's Case Report Form (CRF) and the relevant SAE log.

5.2.3 **Seriousness Assessment**

Seriousness must always be assessed by a medically qualified doctor.

The CI or DI should review whether the event is classed as serious, i.e. if the event results in one or more of the criteria listed above or has been identified within the protocol or reference document (e.g. Investigator's Brochure (IB) or Summary of Product Characteristics (SPC)) as an SAE.

5.2.4 The CI/DI should record the classification of the seriousness as per protocol recording requirements (e.g. CRF/SAE form)

5.2.5 **Causality Assessment**

Causality must always be assessed by a medically qualified doctor. The Sponsor may also make an independent assessment of causality.

The CI/DI should assess the causality of the event, by considering whether the event has any relationship to the administered study medication, as follows:

- Events which are Definitely, Probably or Possibly related are Serious Adverse Reactions
- Events which are Unlikely or Unrelated are Serious Adverse Events

This assessment should be recorded as per protocol requirements.

All adverse events judged by either the investigator or Sponsor as having a reasonable suspected causal relationship to an Investigational Medicinal Product (IMP) qualify as ARs.

The investigator's decision should be independent of the Sponsor. In the case where the Sponsor assessment differs from that of the investigator's assessment, under no circumstances should the Sponsor downgrade the investigator's assessment. If the Sponsor disagrees with the investigator's causality assessment, both the opinion of the investigator and the Sponsor should be provided on the report. This disagreement should also be fully documented.

5.2.6 **Expectedness Assessment**

For SARs, the CI/DI should carry out the expectedness assessment using the reference information (SmPC) or IB) as stated in the protocol. If the nature, seriousness, severity or outcome of the reaction(s) is not consistent with the reference information for the IMP, they should be considered unexpected.

The Sponsor's representative will review the expectedness of all SARs against the Reference Safety Information (RSI).

5.2.7 Expectedness decisions must be based purely on the content of the RSI in either the IB or SPC; other factors such as the subject population and subject history should not be taken into account. Expectedness is not related to what is an anticipated event within a particular disease.

5.2.8 Current versions of the SPC should be printed and a hard-copy kept in the Trial Master File (TMF). The Research Team should check periodically for updates to the SPC. If the SPC has not been updated since the last check, then the previous copy can be kept in the file, with a file note listing the dates of update checks.

5.2.9 IBs should either be kept in the TMF or in a central file with a file note stating the current version and its location.

5.2.10 When IBs are updated with no change to the safety information, please send a copy to the R&D Department for notification.

5.2.11 When IBs are updated with a change to the safety information, this should be treated as a substantial amendment (see SOP-09). An electronic copy of the IB should also be forwarded to the R&D Department.

5.2.12 Where electronic copies are not available, a hard-copy of the front sheet should be forwarded to the R&D Department.

5.2.13 The CI/DI should ensure that the seriousness, causality, expectedness and severity assessments are documented according to the protocol.

5.2.14 All SAEs should be followed-up until resolution and this must be documented in the source information and/or study specific documents.

5.2.15 The SAE flow chart (appendix 2) can be used to assess SAEs and decide if the event requires further expedited reporting.

5.2.16 All SAEs should be followed up until resolution and subsequent follow-up reports submitted as per protocol requirements.

5.2.17 Events listed as expected and not requiring expedited reporting in the protocol do not need reporting but will need to be recorded according to the protocol and included in the annual line-listing (see SOP-16).

5.3 Recording and Reporting SUSARs

5.3.1 Events identified as serious, related (or possibly/probably related) and unexpected, should be classed as Suspected Unexpected Serious Adverse Reactions (SUSARs).

5.3.2 For Trust sponsored studies, the CI/DI is responsible for reporting SUSARs to the regulatory authorities and any participating sites according to the protocol and site agreements.

5.3.3 SUSARs must be reported to:

- The Medicines and Healthcare products Regulatory Agency (MHRA) through one of the options below:
    - eSUSAR website
      The R&D Department has been provided with a login and administrator status and can delegate reporting responsibilities to the Research Team and provide them with a login to the eSUSAR database. SUSAR details need to be entered into this database and a copy filed in the TMF.
    - ICSR Submissions, which replaces the EudraVigilance website (EVWB). The ICSR Submissions route is used to submit single reports.
    - MHRA Gateway, which replaces the Eudravigilance Gateway. The Gateway route is used to submit bulk reports. To gain access to the MHRA Gateway you need to register to another portal called MHRA Submissions.
- Health Research Authority (HRA): Safety Reporting Form (CTIMPs)
- R&D Office: SUSAR Reporting Form (Appendix 3)

5.3.4 The timelines for SUSAR reporting purposes starts at day ‘0’, which is the day that the Sponsor actually receives the information containing the minimum reporting criteria and not the day the Sponsor picks up and processes this information.

5.3.5 Initial reports for fatal or life-threatening SUSARs must be reported to the MHRA and the Research Ethics Committee (REC) within 7 calendar days from knowledge. Any follow-up reports must be reported and submitted within a further 8 days. The R&D Office must also be notified as soon as the Research Team become aware of the SUSAR.

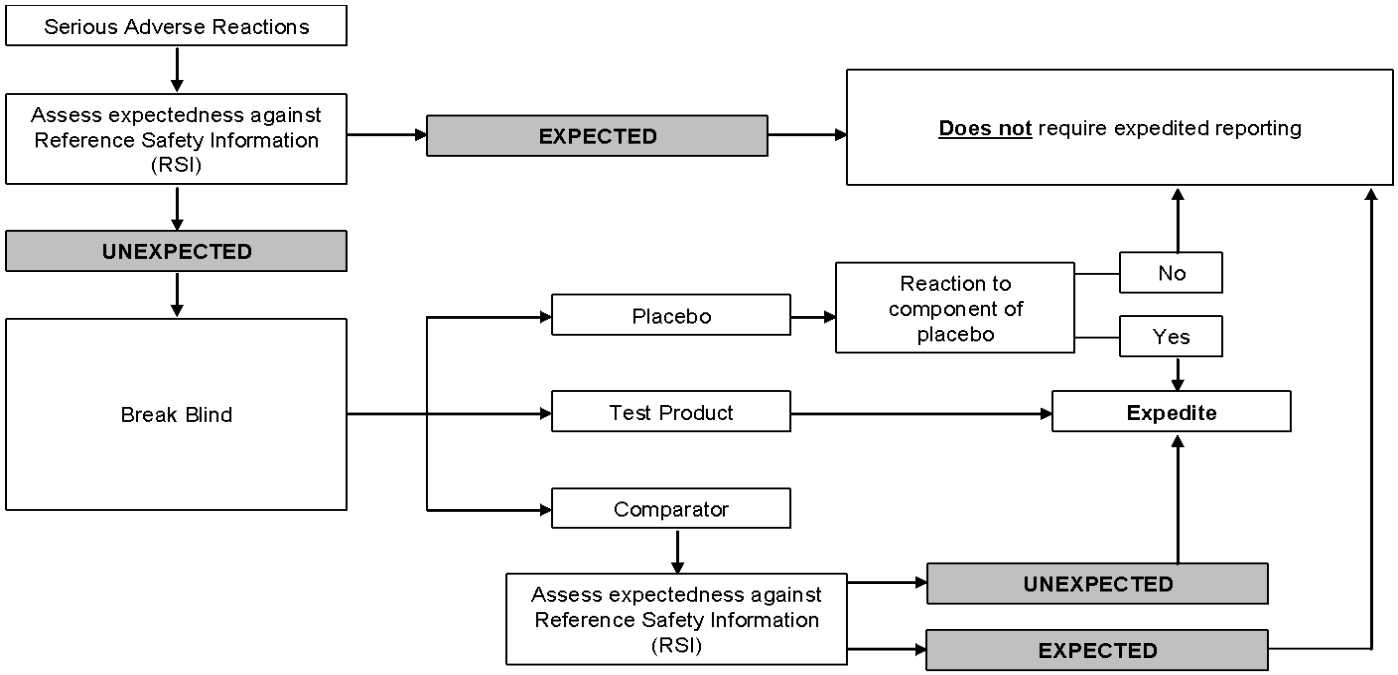
5.3.6 For all other SUSARs, the initial report should be submitted within 15 calendar days to the MHRA, ethics and R&D Office. Follow-up reports should be submitted as soon as available or as per protocol.

5.3.7 If there is any suspicion that a SAR is caused by a non-IMP interacting with an IMP, then this should be reported as a SUSAR.

5.38 As a general rule treatment codes should be broken by the Sponsor before reporting a SUSAR to the MHRA and ethics committee. The unblinding of a single subject should only be carried out if it is important to the subject's safety. For further guidance, refer to MHRA Guidance.

5.3.9 If the CI/DI decides not to unblind a SUSAR during the expedited reporting process, appropriate documented justification for this decision should be made. A copy of the documentation should be filed within the TMF and a copy provided to the R&D Office with the SUSAR report form.

Unblinding in relation to SUSAR Reporting:



5.3.10 Completed SUSAR report forms should be sent in the first instance, as Word documents or a PDF file to the R&D Department. Signed hard copies of completed SUSAR forms should also be sent to the R&D Department as soon as possible.

5.3.11 Reporting **Timeframes**
The table below specifies the reporting timeframes during which the CI should respond to any SAEs, SARs and SUSARs.

Event	**Reported by**	**Report to**	**Time**
All SAEs/SARs (not identified in the protocol as expected) and SUSARs	Researchers/ DI	Chief Investigator	within 24 hours

Follow-up reports			ASAP
All fatal/life-threatening SUSARs Follow-up reports	CI or DI	MHRA, HRA & R&D Office	within 7 days Further 8 days
All other SUSARs Follow-up reports	CI or DI	MHRA, HRA & R&D Office	within 15 days As soon as information is available
All SAEs, SARs and SUSARs per IMP for Trust sponsored trials (both expected and unexpected), with a summary of any issues affecting safety of participants.	CI or DI	MHRA, HRA & R&D Office	Development Safety Update Report or Annual Report (SOP-16)

5.4 Pregnancy

5.4.1 Pregnancy in itself is not regarded as an adverse event unless there is suspicion that the study medication may have interfered with the effectiveness of the contraceptive or that it might be harmful to the foetus.

5.4.2 Should a pregnancy occur, it should be recorded and reported in accordance with the procedures described in the protocol.

5.4.3 A pregnancy report form should be completed with the CI/PI's signature (attached as Appendix 5).

5.4.4 The mother should be followed-up during the course of the pregnancy and the baby should be followed-up for a minimum of three months after birth.

5.4.5 The mother should give consent for additional follow-up during the course of the pregnancy and once the baby is born.

5.4.6 Similarly, if the partner of a patient on a clinical trial becomes pregnant, the baby should be monitored for at least three months after birth. Consent needs to be obtained for this additional follow-up.

5.4.7 Any event meeting the serious criteria (death, life-threatening, congenital abnormality, birth-

defects) should be reported as an SAE. This should be reported accordingly (see section 5.2)

5.5 Sponsor's Review of Safety Events

5.5.1. The CI should review all SAEs, SARs and SUSARs on an ongoing basis; however independent review by the R&D Department and members of the R&D Steering Group (RDSG) will also take place. Annual reports will be submitted and reviewed by the R&D Office.

5.5.2 A log of all safety events (SAEs/SARs/SUSARs) should be maintained in a chronological order from study commencement. The R&D Department will monitor safety trends on an ongoing basis based on study risk. Compliance with safety recording and reporting timeframes will also be routinely assessed as part of the trial monitoring plan however separate pharmacovigilance audits may be performed where necessary.

5.5.3 A DSUR is required to be submitted annually to the MHRA and REC (see SOP-16).

5.5.4 It is the responsibility of the CI to ensure a DSUR is submitted per drug on the anniversary of the Development International Birth Date (DIBD). (see SOP-16).

5.5.5 A DSUR template will be prepared in conjunction with the R&D Office (see SOP-16).

5.6 Urgent Safety Measures (USMs)

5.6.1 USMs are actions which need to be taken to protect participants from any immediate hazard relating to the conduct of the trial or new developments with the IMP, which may affect the safety of the participants.

5.6.2 USMs may be taken without prior notification to the MHRA. However, the CI/DI must inform the MHRA, the REC and the R&D Office of the new events, the measures taken and the plan for further action as soon as possible (as outlined in SOP-09).

Please contact the R&D office urgently and start completion of the form attached as appendix 4.

5.7 Safety Reporting Requirements for nIMPs

5.7.1 nIMPs are products that are used in accordance with the trial protocol, but which fall outside the IMP definition (e.g. medicines used to assess clinical trial end points such as a radiopharmaceutical used to measure organ function after administration of an IMP, concomitant medication given as part of standard of care for a condition that is not the indication for which the IMP is being tested).

5.7.2 SUSARs related to nIMPs, where there is a possibility of an interaction between a nIMP and IMP, must be reported as SUSARs.

5.7.3 If a SUSAR occurs which may be linked to either a nIMP or an IMP, but cannot be attributed to only one of these, the SUSAR must be reported.

5.7.4 If an AR associated with the nIMP is likely to affect the safety of the trial subjects, the Sponsor must report this to the MHRA/REC as a USM, a substantial amendment or via a notification to terminate the trial, as applicable.

6.0 RELATED DOCUMENTS

- SOP-06- TMF (Sponsored)
- SOP-07- Research Staff Training
- SOP-09- Amendments
- SOP-10- Serious Breaches (Sponsored)
- SOP-16- DSURs (Sponsored)
- ICH Topic E2B – Clinical Safety Data Management
- ICH Topic E2F - Development Safety Update Reports (DSUR)
- MHRA website for guidance

7.0 APPENDICES

Appendix 1.0- Definitions
Appendix 2.0- SAE Reporting Flowchart
Appendix 3.0- SUSAR Report form
Appendix 4.0- Urgent Safety Measures form
Appendix 5.0-Pregnancy Notification

8.0 VERSION HISTORY

Revision Chronology:		
Version Number	**Effective Date**	**Reason for Change**
SOP-02-09	**October 2021**	1. Change from general Standard Operating Procedures (gSOP) to SOP 2. Removal of the '10.0 Agreement' from the template - all agreement signatures will be collated on a new 'SOP Signature Sheet Document' 3. Updates to Recording and Reporting SUSARs in line with guidance 4. Other minor amendments and clarification of terms following review
gSOP-02-08	**October 2017**	Minor amendments following review
gSOP-02-07	**01/10/2015**	Minor amendments following review
gSOP-02-06	**07/05/2014**	Minor amendments following review
gSOP-02-05		SOP modified for implementation at ENHT/WHHT. gSOP-02-05 replaces 2011-161
gSOP-02-04		SOP modified for implementation at MVCC
	03/10/2011	Section 4.2.9 – location of SPCs and IBs Section 4.4 - an updated section on pregnancy has been added. Section 4.5.4 - DSURs now replace Annual Safety Reports. Section 4.5.4 - reference to the amended gSOP-16 - Standard Operating Procedure for the Generation and Submission of Development Safety Update Reports for RMH and ICR Sponsored Drug Trials* . Section 5.0 - a section on Urgent Safety Measures has been incorporated.

gSOP-02-04		The SAE reporting flowchart has been updated – attached as Appendix 2.0. The SUSAR report form (version 3.3 July 09) has been updated to version 4.0 29th August 2011 – attached as Appendix 3.0 A new SAE form version 1.0 April 2011 has been included for trials without a trial- specific SAE form – attached as Appendix 4.0. The form for reporting Urgent Safety Measures is attached as appendix 5.0. The form for reporting pregnancies is attached as Appendix 6.0
gSOP-02-03	**01/03/2009**	Updated SAE flow chart and R&D cover sheet Review /update of overall SOP format
gSOP-02-02	**01/03/2009**	Section 4 – amended to include details of seriousness, causality, expectedness and severity assessments. Blinded trials SUSAR reporting process. Section 4.1 –amended to include additional recording requirements. Section 4.3.5 – amended to include review of SAE frequency and changes in severity. Section 4.3.6 – amended to include reference to gSOP-10. Update to Appendix 2
gSOP-02-01	**08/08/2006**	Amendment to flow chart & text on section 3 to read the following: **Co-sponsor agreements**: This SOP does not apply when pharmacovigilance responsibility has been delegated to a co-sponsor that is not RMH/ICR as part of the sponsorship agreement. Section 4.3.2: addition of R&D contacts details for reporting SAEs. Section 4.3.3: Notification to external site Section 4.3.6 Notification of serious breaches of GCP and Urgent Safety Measures. Appendix 2: updated form v2.4 for SAE reporting.

9.0 AUTHORSHIP & APPROVAL

Author

Signature  **Date** 28/10/2021

R & D Steering Group Approval

Signature  **Date** 28/10/2021

Appendix 1: Definitions

Adverse Event (AE)

An unfavourable outcome that occurs during or after the use of a drug or other intervention, but is not necessarily caused by it.

Adverse Reaction (AR)

Any untoward and unintended response to an investigational medicinal product related to any dose administered. Comment: All adverse events judged by either the reporting investigator or the sponsor as having a reasonable causal relationship to a medicinal product would qualify as adverse reactions. The expression 'reasonable causal relationship' means to convey, in general, that there is evidence or argument to suggest a causal relationship.

Chief Investigator (CI)

The investigator with overall responsibility for the research. In a multi-site study, the CI has co-ordinating responsibility for research at all sites. All applications for ethical review should be submitted by the CI.

Clinical Trial of Investigational Medicinal Product (CTIMP)

A clinical trial that is within the scope of the UK Medicines for Human Use (Clinical Trials) Regulations 2004. An investigation in human subjects, other than a non-interventional trial, intended: a) to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more medicinal products, b) to identify any adverse reactions, or c) to study absorption, distribution, metabolism and excretion, with the object of ascertaining the safety and/or efficacy of those products.

Delegated Individual (DI)

An individual delegated by a person of responsibility to carry out their task(s).

Pharmacovigilance

The science relating to the detection, assessment, understanding and prevention of the adverse effects of medicines.

Principal Investigator (PI)

The investigator responsible for the research site. There should be one PI for each research site. In the case of a single-site study, the chief investigator and the PI will normally be the same person.

Serious Adverse Event (SAE) or Serious Adverse Reaction (SAR)

Any adverse event or adverse reaction that results in:

- death
- is life-threatening*
- requires hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability or incapacity
- or is a congenital anomaly or birth defect

Comment: Medical judgement should be exercised in deciding whether an adverse event/reaction should be classified as serious in other situations. Important adverse events/reactions 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 of the other outcomes listed in the definition above, should also be considered serious.

* Life-threatening in the definition of a serious adverse event or serious adverse reaction 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 which hypothetically might have caused death if it were more severe.

Sponsor's Representative
The Director / Assistant Director of R&D will appoint an appropriate staff member to act as the Sponsor's Representative.

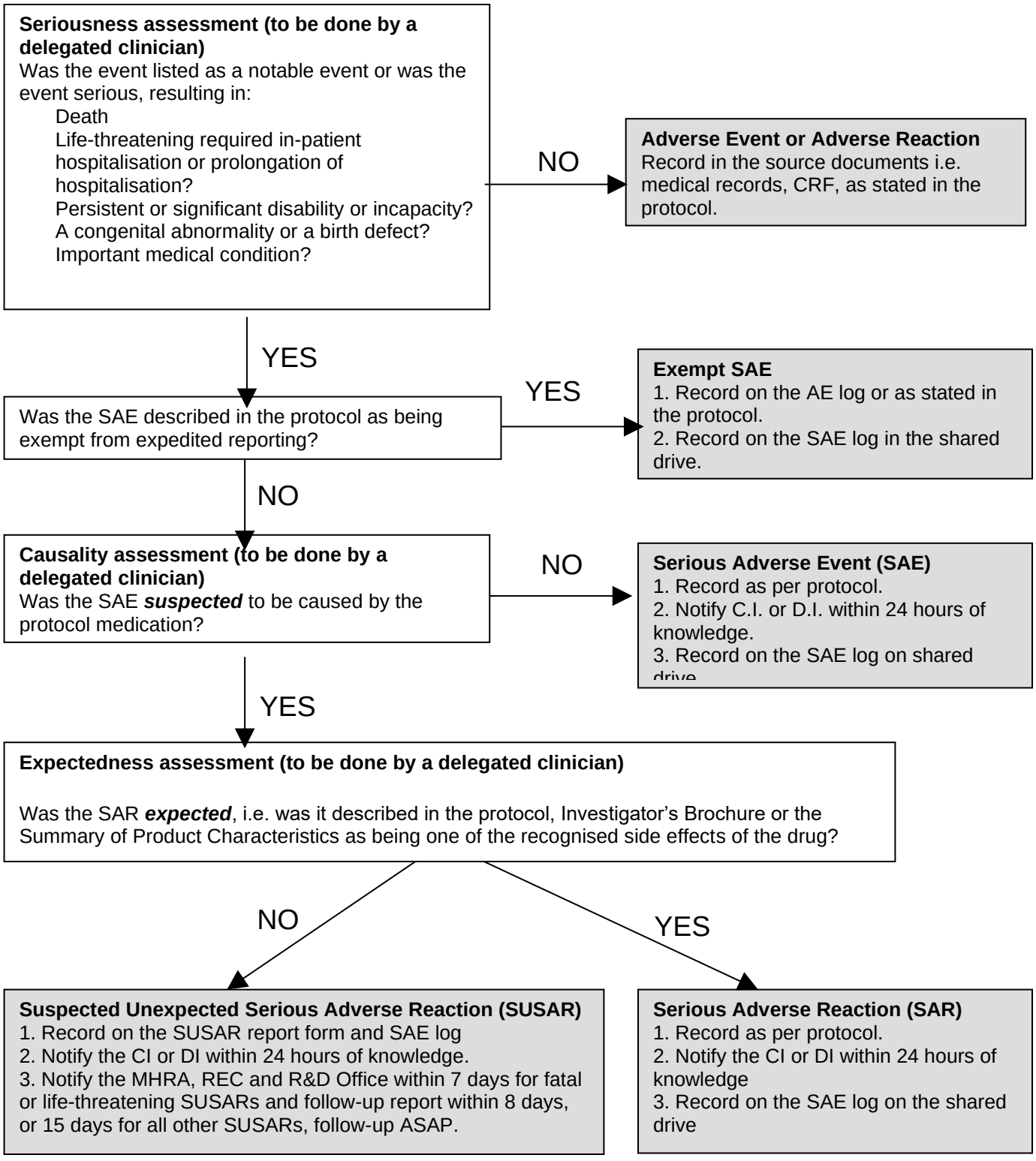
Suspected Unexpected Serious Adverse Reaction (SUSAR)
An adverse reaction that is both unexpected (not consistent with the applicable product information) and also meets the definition of a Serious Adverse Event/Reaction.

Unexpected Adverse Reaction
An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g. Investigator's brochure for an unauthorised investigational product or summary of product characteristics (SmPC) for an authorised product).

Unexpected SAE/SAR
An adverse event that meets the definition of serious and is not listed in the protocol, IB, SmPC or the most recent informed consent document for the study (list of unexpected SAE will be trial specific).

Appendix 2: SAE reporting flowchart

Please carry out the following assessments for all adverse events.



Appendix 3: SUSAR Report Form Version 7.0 2021

Date received by R&D Office	ID

Local Lead Researcher: **Department :** **Your reference:**

RD No. __ __ __ __ **Short title of study:**

Details of SUSAR - please provide details or circle all that apply.

1) Patient's Trial ID Number __ __ __ __

2) Is this a Trust patient? Yes No

3a) Patient's age ___ ___ **b) Gender** Male Female

4) Medical History

5) Concomitant Medication:

6) Details of SAE:

_____
_____
_____
_____
_____

7) Type of AE Report: Initial report Follow up report

8) Date of onset: __ __/__ __/__ __**Time of onset:** _ _ : _ _ **Date event resolved:** __ __/__ __/__ __ **Still ongoing - - - - - - - - - -**

9) Trial drug : **Date of last dose:** _ _ / _ _ / _ _ _ _ **Time of last dose:** _ _ : _ _

10a) Event terms and CTCAE grading:

10b) Which version of the CTCAE was used? Version 5.0 Version 6.0

11) Seriousness assessment (please circle)

Death Life-threatening Hospitalisation or Prolongation of existing hospitalisation

Disability Congenital abnormality Important medical event

12) Causality assessment by CI/ PI- is there a possible causal relationship between this adverse event and the trial drug?

Causality / Trial Drug	Definitely	Probably	Possibly	Unlikely	Unrelated

13) Severity of event: Mild Moderate Severe

14) Outcome: Recovered Recovering Recovered with sequelae Not recovered Unknown Fatal

15) Expectedness assessment by CI/ PI – is this event expected as described in the protocol, Investigator's Brochure (IB) or Summary of Product Characteristics (SPC)?

Expectedness / Trial Drug	Expected*	Unexpected

*(Expected events do not need to be reported to the R&D Office)

16) Please indicate which document(s) were used to check expectedness: Protocol IB SPC

For all SUSARs and SAEs please notify the sponsor as per their requirement. Where the Trust is the sponsor, please notify the MHRA and Research Ethics Committee of all SUSARs, in line with the Trust SOP SOP-02.

Local Lead Researcher Comments: (View on SUSAR and the implications for ongoing trial.)

Sponsor Assessment of Causality and Expectedness

Sponsor approval of Causality Assessment (Please circle): Yes No

If 'No' please provide details:

Sponsor approval of Expectedness Assessment (Please circle): Yes No

If 'No' please provide details:

Recommended Actions (where required):

Sponsor Representative Signature…… **Date**____/____/____

For Trust sponsored trials, please provide dates that this event was reported to:

MHRA __ __/__ __/__ __ **Main REC** __ __/__ __/__ __ **Other participating sites (for multi-centre studies)** __ __/__ __/__ _
For Trust hosted studies please give the date this event was reported to the sponsor __ __/__ __/__ __

CI/PI/DI signature…… **Date**____/____/____

Print Name ……
Return completed form, with accompanying Serious Adverse Event Report Form to: the R&D Department

Appendix 4: Notification of Amendment for Urgent Safety Measures

*Please complete this form to the R&D Office as soon as possible after implementation of Urgent Safety Measure. This form should only be in exceptional circumstances, for example to protect the participants from an **immediate** hazard to their welfare or safety*

Part A – Where to Send your Request

To: R&D Office

R&D Office use only

Date received:

Part B – Your Details

From:	
Tel:	
Fax:	
Email:	

Part C – Sponsor Details

(please tick)

Trust-sponsored ☐

Trust-hosted (please specify below) ☐

_____

_____

Part D – Study Details

Trial Name:							
CTIMP **OR** non-CTIMP (please delete as appropriate)							
RD reference number:	RD						
Chief Investigator:							
Principal Investigator:							

Part E – Urgent Measures

Measures taken:
Date effective from:

Why have these measures been taken:

Chief Investigator Signature	
Date	

Appendix 5: Pregnancy Notification Form version 2.0 13th January 2013

RD number _ _ _ _	**Your reference**
Short title of study	
Chief Investigator	**Department**
Patient's Trial ID Number __ __ __ __	**Date of birth ___ ___ / ___ ___ /___ ___**

1. MATERNAL INFORMATION			
Date of Birth	_ _/_ _/_ _ _ _		
Date of last menstrual period	_ _/_ _/_ _ _ _		
Expected Date of Delivery	_ _/_ _/_ _ _ _		
Method of contraception:			
Was contraception used as instructed?	Yes	No	Uncertain

2. MEDICAL HISTORY
Include information in familial disorders, known risk factors or conditions that may affect the outcome of the pregnancy. (If none, mark as N/A)

3. PREVIOUS OBSTETRIC HISTORY

(provide details on all previous pregnancies, including termination or stillbirth)
Gestation Week Outcome including any abnormalities

1

2

3

Patient's Trial ID Number __ __ __ __ **Date of birth** ___ ___ / ___ ___ /___

4. DRUG INFORMATION

Drug name	Dose	Route	Date start	Date stopped

5. PRENATAL INFORMATION

Have any specific tests, e.g. amniocentesis, ultrasound, maternal serum AFP, been performed during the pregnancy so far?

Yes No Not known

If Yes, please specify test date and results:

Test type and date _ _/_ _/_ _ _ _

Result

6. PREGNANCY OUTCOME

Patient's Trial ID Number __ __ __ __ **Date of birth** ___ ___ / ___ ___ /___ ___

7. MATERNAL PREGNANCY ASSOCIATED EVENTS

If the mother experiences an SAE during the pregnancy, please indicate here and complete an SAE form, complete with CI's signature.

8. CHILD OUTCOME

(**a) Abortion** Yes No

If Yes

Therapeutic Planned Spontaneous

Please specify the reason and any abnormalities (if known):

Date _ _/_ _/_ _ _ _

(b) Delivery Yes No

If Yes

Normal Forceps/Ventouse Caesarean

Date of delivery _ _/_ _/_ _ _ _

Delivery at week:

Delivery was: Normal Abnormal Stillborn

Please give dates and details of any abnormalities

Sex Male Female
Height cm
Weight kg
Head circumference cm

AGPAR score

1minute _ _ 5 minutes _ _ 10 minutes _ _

Patient's Trial ID Number __ __ __ __ **Date of birth** ___ ___ / ___ ___ /___ ___

9. ASSESSMENT OF SERIOUSNESS (OF PREGNANCY OUTCOME)

Not serious

Serious :

a) Mother died/baby died b) Life-threatening c) Involved prolonged inpatient hospitalisation

d) Results in persistent or significant disability/incapacity

e) Congenital anomaly/birth defect f) Other significant medical events

Date of death: _ _/_ _/_ _ _ _

10. ASSESSMENT OF CAUSALITY(OF PREGNANCY OUTCOME)

Please indicate the relationship between the trial drugs and the pregnancy outcome

Causality / Trial Drug(s)	Definitely	Probably	Possibly	Unlikely	Unrelated

Could the trial drugs have interfered with contraception?

a) Yes b) No c) Maybe

11. ANY ADDITIONAL INFORMATION

12. DETAILS OF PERSON SUBMITTING THIS REPORT

Signature …… Date _ _/_ _/_ _ _ _

Please print name ……..

CI/PI signature…… Date _ _/_ _/_ _ _ _