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| Joint Research Office of Doncaster & Bassetlaw Hospitals NHS Foundation Trust, Rotherham Doncaster & South Humber NHS Foundation Trust and NHS Doncaster CCG | **Page 1 of 11** |
| Research Management & Governance | SOP No. RM&G0010, Version 1 |
| **Safety reporting in externally sponsored Clinical Trials of Investigational Medicinal Products (CTIMPs) hosted by Doncaster and Bassetlaw Hospitals NHS Foundation Trust** | **Supersedes:** Not applicable |
| | **Attachments:** 1 |
| | **Effective date:** 29th July 2013 |

Signatures:

| Role | Name | Function | Date (DD-MM-YYYY) | Signature |
|---|---|---|---|---|
| **Author** | Amy Beckitt | Clinical Research Development Manager | 25th July 2013 |  |
| **Reviewer** | Dr Trevor Rogers | Director of Research | 26th July 2013 |  |

*Reviewed every 2 years unless changes to applicable legislation require otherwise*

## 1.0 Definitions

Please refer to the current version of the SOP RM&G0002 for a glossary of all terms and acronyms.

**Adverse Event (AE) -** Any untoward medical occurrence in a subject to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product.

**Adverse Reaction (AR) -** Any untoward and unintended response in a subject to an investigational medicinal product which is related to any dose administered to that subject.

**Serious Adverse Event/Reaction (SAE/SAR) -** Any adverse event or adverse reaction that:

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
e. consists of a congenital anomaly or birth defect.

**Suspected Serious Adverse Reaction (SSAR) -** Any adverse reaction that is classed in nature as serious and which is consistent with the information about the medicinal product in question set out:

a. In the case of a licensed product, the summary of product characteristics (SmPC) for that product
b. In the case of any other investigational medicinal product, the Investigator's Brochure (IB) relating to the trial in question.

**Suspected Unexpected Serious Adverse Reaction (SUSAR) -** Any adverse reaction that is classed in nature as serious and which is not consistent with the information about the medicinal product in question set out:

a. In the case of a licensed product, the summary of product characteristics (SmPC) for that product
b. In the case of any other investigational medicinal product, the Investigator's Brochure (IB) relating to the trial in question.

*(Glossary taken from Medicines for Human Use (Clinical Trials) Regulations 2004)*

## 2.0 Purpose

The purpose of this SOP is to cover the procedures surrounding the recording, management and reporting of adverse events, for externally sponsored CTIMP research, hosted by Doncaster and Bassetlaw Hospitals NHS Foundation Trust. This Policy has been developed in accordance with the Medicines for Human Use (Clinical Trials) Regulations 2004 [and all subsequent amendments] and the Research Governance Framework 2005.

## 3.0 Scope

This SOP covers all personnel who are involved in CTIMP research hosted, but not sponsored by Doncaster and Bassetlaw Hospitals NHS Foundation Trust. It is extremely important that all

personnel involved in research activity within the Trust, are aware of the reporting requirements at site, and also the Trust ensures appropriate pharmacovigilance systems in place for the recording, management and reporting of the following events:

- Adverse Events (AE)
- Adverse Reactions (AR)
- Serious Adverse Events (SAE)
- Suspected Serious Adverse Reactions (SSAR)
- Suspected Unexpected Serious Adverse Reaction (SUSAR)

## 4.0 Procedure

There should be an ongoing assessment for safety throughout the course of the study. The Principal Investigator or delegated member of research team (delegate) should ask recruited patients at each study visit whether there has been any adverse events. Where aspects of this responsibility are delegated to a suitably qualified or experienced member of the research team, this should be clearly documented in the delegation log held within the local site file.

For all patients consented onto a CTIMP study, an interventional study notification sticker is placed on the Alert/Hazard Notification page of the patient casenotes, and the relevant fields completed. Any safety related event related to the patient should be brought to the immediate attention of the Principal Investigator or member of research team detailed in the patient casenotes.

All safety reports should be filed in the Investigator Site File, and should be signed by the Principal Investigator. Where international faxes are required to be sent to report safety events to the Sponsor, this can be done via the General Office at Doncaster Royal Infirmary or Switchboard at Bassetlaw Hospital.

### 4.1 Procedure for reporting Adverse Events (AE) and Adverse Reactions (AR) that occur within Doncaster and Bassetlaw Hospitals NHS Foundation Trust

Where a Principal Investigator or delegate identifies or is notified of an AE/AR, the following procedures must then be followed:

1. The Principal Investigator or delegate makes an assessment on the event causality, and whether it is related to the investigational medicinal product.

2. The Principal Investigator or delegate reports the AE/AR to the Sponsor, in accordance with the protocol specified requirements.

3. This report may be followed up by the sponsor, and any additional information must be provided by the Principal Investigator or delegate, within the sponsor specified timeframe.

4. The Principal Investigator or delegate should follow up AE/AR until resolved (if applicable).

5. The Principal Investigator or delegate records the AE/AR in full in the Case Report Form (CRF) and the research section of the patient casenotes.

### 4.2 Procedure for reporting Serious Adverse Events (SAE), Suspected Serious Adverse Reactions (SSAR), Suspected Unexpected Serious Adverse Reactions (SUSAR) that occur within Doncaster and Bassetlaw Hospitals NHS Foundation Trust

Where a Principal Investigator or delegate identifies or is notified of an SAE, the following procedures must then be followed:

1. The Principal Investigator or delegate confirms the event is serious using the ICH GCP definition, and the study protocol.

2. The Principal Investigator or delegate makes an assessment on the event causality in relation to the investigational medicinal product, and the expectedness of the event. Please refer to Appendix 1 for guidance on classification.

3. The Principal Investigator or delegate follows the procedure outlined in the study protocol for the reporting of SAE/SSAR/SUSARs to the sponsor. This report should be sent immediately and without the Principal Investigator if they are unavailable. A signed copy should be sent thereafter. Where a sponsor has not provided a safety reporting form, the Trust Serious Adverse Event/SUSAR report form should be used (attachment 1).

4. This report will be followed up by the sponsor, and any additional information must be provided by the Principal Investigator or delegate, within the sponsor specified timeframe. The sponsor confirms the classification of the event as an SAE, SSAR or SUSAR.

5. The Principal Investigator or delegate faxes a copy of the safety report form in addition to any relevant sponsor correspondence, to the Research office to: 01302 553254. This report should be sent immediately. The Research office will acknowledge receipt of the faxed notification by the close of business the next working day. Acknowledgement will be faxed to the fax number from which the breach was notified unless an alternative method of acknowledgement has been agreed with the Research office in writing. It is the responsibility of the reporting individual to contact the Research office immediately if no acknowledgement is received.

6. The Research office will make a decision on the continuation of the study in relation to the reported event, based on risk. The Research office reserves the right to withdraw or suspend Trust approval for any research study, where there are safety concerns about the continuation of the study. Where a decision is made to temporarily suspend the study, the PI and Sponsor will be notified in writing.

7. The Principal Investigator or delegate should follow up the event until resolved (if applicable).

8. The Principal Investigator or delegate records the event in full on the Case Report Form (CRF) and patient casenotes.

Where a Principal Investigator is notified of new safety information which may affect the Trust decisions as to whether to continue with the trial, they should notify the Research office immediately.

### 4.3 Urgent Safety Measures

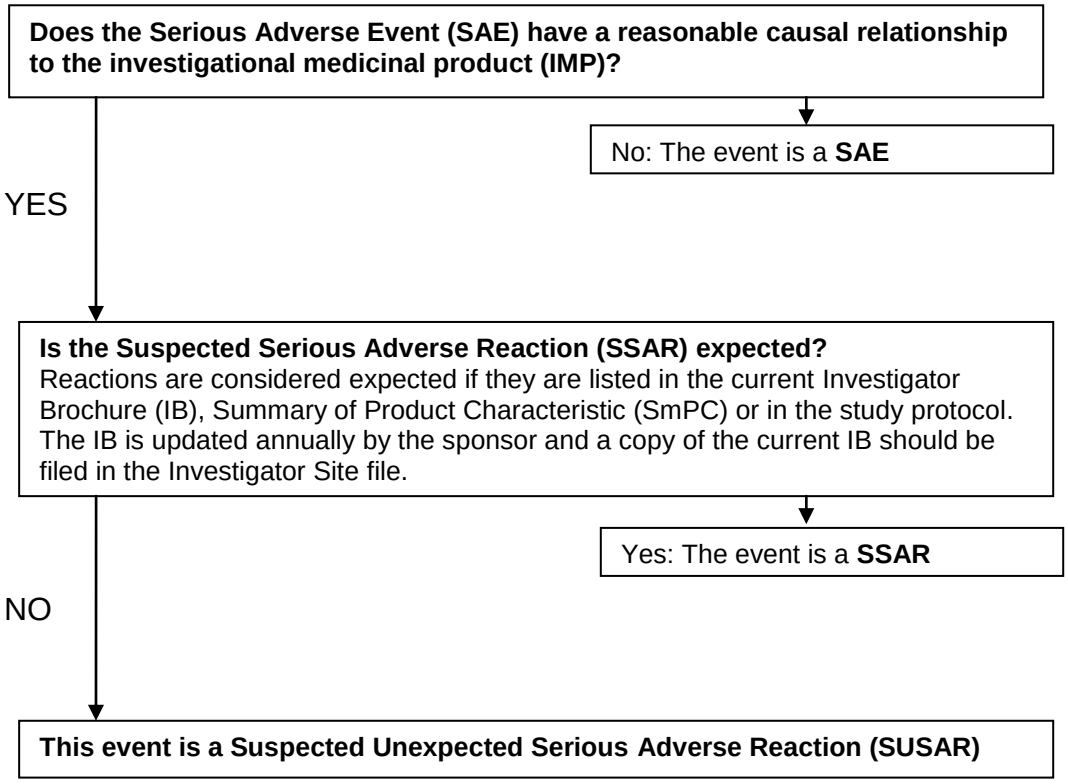
In accordance with the Clinical Trials Regulations, the Chief Investigator, Principal Investigator or study sponsor may take appropriate urgent safety measures in order to protect the participants of a CTIMP against any immediate hazard to their health or safety, without prior approval from the regulatory bodies or Trust Research Governance Department.

### Related SOPs and Documents

1. No associated SOPs at this time

**Appendix 1**

Flowchart to classify a safety event for CTIMPs



**Attachment 1**

The attachment consists of 4 pages excluding this page. The attachment has been independently page numbered 1 - 4. The following attachment has been included in the total number of pages as indicated on the header of the SOP.

Doncaster and Bassetlaw Hospitals NHS
NHS Foundation Trust

# Serious Adverse Event / SUSAR Report Form

This safety report form should be used where the sponsor have not provided a study specific report form.

## A STUDY DETAILS

**Short Title of Study**: ..... **DBHft Ref:**

**Name of Hospital**: ..... .....

**Principal Investigator**: .....

## B PATIENT DETAILS

| | | |
|---|---|---|
| **Patient Initials**: ☐☐☐ | **Height**: cm ☐☐☐ | **Patient Trial ID**: ..... |
| **Year of Birth**: Y Y Y Y | **Weight**: kg ☐☐☐ | |
| **Gender**: ☐ M / F | | |

## C DETAILS OF SAE

**Date SAE was identified**:

☐☐ ☐☐ ☐☐☐☐

dd mm yyyy

**Where did the SAE start?** ☐

1 Hospital
2 Out-patient clinic
3 Home
4 Nursing Home
5 Other - specify

.....

**Why was the event serious**? ☐

1 Resulted in death
2 Life-threatening
3 Required inpatient hospitalisation or prolongation of existing hospitalisation
4 Persistent/significant disability/incapacity
5 Congenital anomaly / birth defect

| Main adverse event diagnosis / symptom | Grade ☐<br>1 Mild<br>2 Moderate<br>3 Severe<br>4 Life-threatening<br>5 Death related to AE | Date of Onset<br>dd / mm / yyyy | SAE Status ☐<br>1 Resolved<br>2 Resolved with sequelae<br>3 Ongoing<br>4 Worsened<br>5 Fatal | Date Resolved<br>dd / mm / yyyy |
|---|---|---|---|---|
| | | | | |

**Associated symptoms**:

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# Serious Adverse Event / SUSAR Report Form

**Patient Trial ID No.** : …… **Date SAE was identified** D D M M Y Y Y Y

## D TRIAL MEDICATIONS (Refer to SmPC or IB for expectedness of main event for each trial drug)

| | | | | | Investigator's Opinion | |
|---|---|---|---|---|---|---|
| **Trial drug name** | **Date of first administration** dd / mm / yyyy | **Actual dose given at most recent administration** (assume actual IMP dosage) | **Date of most recent administration** dd / mm / yyyy | **Action taken due to SAE** 0 None 1 Dose reduction 2 Treatment delayed 3 Treatment reduced & delayed 4 Treatment stopped | **Causal relationship to SAE** 1 DEFINITELY * 2 PROBABLY * 3 POSSIBLY * 4 Unlikely 5 Not related *answer expectedness question | **Expectedness** (was the main event one of the recognised undesirable effects mentioned in SmPC or IB?) 1 = Expected 2 = Unexpected |
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**Did reaction abate after stopping drug?** Yes / No / N/A **Did reaction reappear after reintroduction?** Yes / No / N/A

## E OTHER TREATMENTS

(Exclude any therapy given for management of SAE; include all treatments **not** given for management of SAE e.g. concomitant medication, surgery. Continue on a separate sheet if necessary)

| | | | | | | | Investigator Opinion |
|---|---|---|---|---|---|---|---|
| **Treatment** Give generic name | **Total daily dose** | **Route** 1 Oral 2 Intravenous 3 Subcutaneous 4 Other | **Start date** dd / mm / yyyy | **Ongoing** 0 No 1 Yes | **End date** dd / mm / yyyy | **Action taken** 0 None 1 Dose reduction 2 Treatment delayed 3 Treatment reduced & delayed 4 Treatment stopped | **Causal relationship** 1 Definitely 2 Probably 3 Possibly 4 Unlikely 5 Not related |
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# Serious Adverse Event / SUSAR Report Form

**Patient Trial ID No.** : …… **Date SAE was identified** D D M M Y Y Y Y

## E OTHER TREATMENTS .....continued

| **Treatment** Give generic name | **Total daily dose** | **Route** 1 Oral 2 Intravenous 3 Subcutaneous 4 Other | **Start date** dd / mm / yyyy | **Ongoing** 0 No 1 Yes | **End date** dd / mm / yyyy | **Action taken** 0 None 1 Dose reduction 2 Treatment delayed 3 Treatment reduced & delayed 4 Treatment stopped | **Investigator Opinion Causal relationship** 1 Definitely 2 Probably 3 Possibly 4 Unlikely 5 Not related |
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## F DESCRIPTION OF SAE

| **Describe serious adverse event** (include manifestation and progression of event, any treatments given in response to the event and any relevant tests carried out e.g. WBC, neutrophil count. Continue on a separate sheet if necessary).<br><br>Please attach anonymised diagnostic tests where required, e.g. blood results, etc. |
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# Serious Adverse Event / SUSAR Report Form

**Patient Trial ID No.** : …… **Date SAE was identified** D D M M Y Y Y Y

**F DESCRIPTION OF SAE** .....continued

## G CAUSALITY NOT RELATED TO TREATMENT

**Do you consider it likely that this event was caused by something other than the treatments listed on this form?**

☐ 0 No
1 Yes: if yes, please specify: (include medical history, drug or alcohol abuse, family history, findings from special investigations)

## H SIGN OFF

**Form completed by**:

*Signature* | *Print Name* | **Date**

**Contact E-mail**: **Contact Telephone No**:

**Principal Investigator:**

*Signature* | *Print Name* | **Date**

Please fax this form to the Sponsor, in accordance with the protocol specified requirements

**SPONSOR REVIEW:** ……

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