Standard Operating Procedure for Processing and Reporting of Serious Adverse Events, Serious Adverse Reactions and Suspected Unexpected Serious Adverse Reactions for all Research sponsored by University Hospitals of Leicester NHS Trust (UHL)

PGC Registration – C10/2014

OFFICE BASE
Research & Innovation
Leicester General Hospital
Gwendolen Road
Leicester
LE5 4PW
1. Introduction

This Standard Operating Procedure (SOP) describes the process required by the University Hospitals of Leicester NHS Trust (UHL) for identifying, documenting and reporting all Adverse Events and Reactions when UHL are acting as research Sponsor.

The outcome is that the UHL fulfills the requirements as Sponsor to identify, document and report all categories of Serious Adverse Events and Reactions.

2. Scope

This SOP applies to all staff and external individuals involved in research activity sponsored by the UHL.

3. Definitions

3.1 Adverse Event (AE)
Is defined as "any untoward medical occurrence in a patient or clinical trial subject administered a medicinal product and which does not necessarily have a causal relationship with this treatment."

3.2 Adverse reaction (AR)
Is defined as "an untoward and unintended response in a participant to an investigational medicinal product, related to any dose administered."

3.3 Serious Adverse Event (SAE) or Serious Adverse Reaction (SAR)
Is defined as any adverse event or adverse reaction in a trial subject that:

- Results in death
- Is life threatening (the subject was at risk of death at the time of event)
- Requires hospitalisation or prolongation of an existing hospitalisation
- Results in persistent or significant disability or incapacity
- Consists of a congenital anomaly or birth defect
- Other serious Important Medical Event - an event that may not be immediately life threatening or result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the outcomes listed above should be considered.

3.4 Suspected Serious Reaction
Is defined as an adverse reaction that in its nature is serious and which is consistent with the information about the medicinal product listed in the relevant reference documentation – Investigator Brochure (IB) or Summary of Product Characteristics (SPC).

3.5 Suspected Unexpected Serious Adverse Reaction (SUSAR)
Is defined as a serious adverse reaction, the nature and severity of which is not consistent with the applicable product information in the Investigator Brochure (IB) or Summary of Product Characteristics (SPC).
Although these are the standard definitions, the reporting requirements of each study may differ, dependent on the nature of the study and the patient population. Specific protocol reporting instructions should be followed.

4. Pregnancy Reporting

Although pregnancy in a study subject or their partner is not classified as a serious adverse event in itself, it is however an important event and there is a regulatory requirement to follow up all pregnancies occurring in Clinical Trials of Investigational Medicinal Products (CTIMPs) to outcome.

A Pregnancy Notification Form (Appendix 1) must be completed and sent to the Research Office. This is available on the R&I pages of the UHL public website.

5. Reporting Procedure

5.1 AE/AR (Adverse Events/Adverse Reactions)
There are no requirements to report these events to the sponsor or regulatory agencies unless they are identified as critical to evaluations of the safety of the study. AEs/ARs must be documented in the Case Report Form (CRF) and patients’ medical records (where appropriate), and observed to ensure that they do not escalate to a serious adverse event/reaction.

5.2 SAE/SAR – (Serious Adverse Event / Adverse Reactions)
All serious adverse events/reactions in studies sponsored by UHL must be reported to the Sponsor immediately and within 24 hours of the research team becoming aware of the event using the appropriate reporting form.

6. SAE/SAR Reporting Form

6.1 UHL Sponsored CTIMP studies
The UHL Serious Adverse Event for CTIMP (Clinical Trials of Investigational Medicinal Products) Form A must be used. This form and associated completion guidance document are both available on the R&I Website. This form and any documents provided to the Sponsor in support of the SAE MUST not contain any participant identifiable data.

6.2 UHL Sponsored Studies NOT involving Investigational Medicinal Products
For UHL sponsored studies NOT involving Investigational Medicinal products the UHL Serious Adverse Event Form B must be used. This form and associated completion guidance document are both available on the R&I website. This form and any documents provided to the Sponsor, in support of the SAE, MUST not contain any participant identifiable data.
6.3 Sign Off and of Review for UHL Sponsored Studies
For UHL Sponsored studies, the Principal Investigator (PI) is responsible for the review and sign off of all serious adverse events at their site. After discussion with, and agreement by the Sponsor it may be possible for additional medically qualified individuals to be delegated the responsibility for reviewing and signing off the SAE form. This must be recorded on the Delegation of Authority Log.

The Chief Investigator should regularly review SAE Listings with the PI and Sponsor (where agreed).

6.4 Multi-Centre

6.4.1 Where the study is a CTIMP all SAEs from all sites must be sent to the Sponsor as per UHL reporting requirements. Where sites are managed through a third party contractor e.g. a Clinical Trials Unit it may be appropriate to make alternative arrangements for reporting. These arrangements will be specifically detailed in the third party agreement.

Where alternative reporting arrangements have been agreed, details of all SAEs occurring at all sites, must be completed/reviewed by the Chief Investigator. The multi-centre CTIMP SAE Listing table (Appendix 6) could be used where an alternative is not available. The line listing must be submitted as detailed in the agreement. All SAE listings will be reviewed by the Director of R&I at the monthly R&I Management Meeting.

6.4.2 Where the study is a non CTIMP, the SAEs for the lead site must be submitted to the Sponsor. Details of SAEs occurring at collaborating sites must be completed by the Chief Investigator. The Multi Centre SAE listings table (Appendix 2) could be used where an alternative is not available. These must be submitted to the Sponsor as detailed within the agreement.

7. Causality – IMP studies ONLY

Any causality assessments must be made by the PI or the Sponsor agreed delegated medically qualified individual. The study delegation log must reflect this.

The definitions below can be used:

**Unrelated**
There is no evidence of causal relationship to the Investigational Medicinal Product

**Related**
There is evidence of causal relationship to the Investigational Medicinal Product.

Events relating to placebo or reference drugs must also be reported.
8. Expectedness – IMP Studies ONLY

The approved Reference Safety Information (RSI) i.e. Investigator Brochure or Summary of Product Characteristics MUST be used to determine Expectedness.

**Expected**  The event is **Expected** based on the information contained in the Investigator Brochure and/or the Summary of Product Characteristics.

**Unexpected**  The event is **Unexpected** based on the information contained in the Investigator Brochure and/or the Summary of Product Characteristics.

Events relating to placebo or reference drugs must be reported.

Events leading to the death of a study participant need to be reported to the Sponsor immediately once the Investigator becomes aware of the event, unless death is classified as an expected event and therefore exempt from reporting. Exemption to reporting events must be detailed in the approved protocol.

9. SAR/SUSARs (Serious Adverse Reaction/Suspected Unexpected Serious Adverse Reactions)

SAR/SUSARs are a subset of serious adverse reactions which are subject to mandatory expedited reporting timelines to the Medicines and Healthcare products Regulatory Agency (MHRA) and the main Research Ethics Committee (REC). accompanied by a CTIMP safety report form.

In a UHL sponsored study, the responsibility to evaluate whether or not a reaction is a SUSAR is delegated to the PI.

As for all SAEs, a SUSAR must be reported to the Sponsor with immediate effect and within 24 hours of the research team becoming aware of it. The responsibility to report to the MHRA through the eSUSAR system and the main REC is that of the Sponsor, but this is delegated to the CI for completion. An 'eSUSAR' reporting guidance document is available at Appendix 7. The Sponsor process for ensuring SUSARs are appropriately reported is available at Appendix 8. A template email notifying all sites (where multi-centre) is available at Appendix 9.

The initial report must be submitted as soon as possible and, within 7 calendar days for a death or life threatening SUSAR (and submit any follow up information within an additional 8 calendar days) or within 15 calendar days for other SUSARs. SUSARs for UHL Sponsored Studies are additionally tracked through EDGE.

9.1 UHL Sponsored CTIMP Studies

Where UHL is the Sponsor, the responsibility to report the SUSAR using eSUSAR to the MHRA is delegated to the CI or PI or appropriately qualified individual approved by the Sponsor. This delegated task will be discussed and confirmed with the individual during the Sponsor review process.
In addition the CI/PI is responsible for the completion of the CIOMS form which must be sent to the Sponsor, whose responsibility it will be to submit to the REC & MHRA.

9.2 Blinded Studies

In a blinded study, unblinding must be carried out prior to reporting a SUSAR to the MHRA, appendix 10. Study specific procedures for unblinding prior to reporting, will be discussed, and clearly documented, as part of the sponsor review process.

10. Urgent Safety Measures

The Sponsor and Investigator may take appropriate urgent safety measures to protect clinical trial subjects from any immediate hazard to their health and safety. The measures must be taken immediately; Sponsor, MHRA, REC, HRA & R&I approval is not required before implementation, however all parties must be informed in writing, in the form of a substantial amendment within three days. The process for submitting amendments as a result of Urgent Safety Measures is covered in SOP S-1018 UHL SOP S-1026 UHL.

11. Development Safety Update Reports (DSURs)

In addition to the expedited reporting required for SUSARs, Sponsors of CTIMP studies are required to submit a Development Safety Update Report to the MHRA and main REC once a year throughout the term of the clinical trial or on request. Reports must be provided at yearly intervals from the date of the approval of the first trial of the Investigational Medicinal Product anywhere in the world (the Development International Birth Date (DIBD)). Details about DSUR and the requirements may be found in SOP S-1004 UHL which is available on the R&I public website.

12. Ethics Committee Reports for Clinical Trials of Non-Investigational Medicinal Products where the event is related and unexpected.

SAEs occur in research that does not involve an Investigational Medicinal Product. These SAEs should be reported as per 6 above.

Where in the opinion of the PI the event was related (that is, it resulted from administration of any of the research procedures), and unexpected (that is, the type of event is not listed in the protocol as an expected occurrence). The SAE report form for non-CTIMPs, available from the Health Research Authority (HRA) website should be completed and sent to the main REC within 15 days of the PI becoming aware of the event. A copy of the SAE form must also be submitted to the Research Office.
13. Documentation

The following documentation must be available in the Trial Master File (TMF) / Investigator Site File (ISF)

- SAE, SAR and SUSAR reports and follow-up information
- AE / AR / SAE Logs
- Evidence of submission and receipt of SAEs to the Sponsor within the required timeframe.
- Evidence of timely SUSAR submission to the MHRA and main REC
- DSURs and evidence of their timely submission to the Sponsor and subsequent forwarding from the Sponsor to the main REC and the MHRA.

The investigator must ensure that all SAE information is recorded accurately in the study Case Report Form.

14. SAE Review Process

Sponsor acknowledgement will be issued to the Investigator within 7 days of receipt of a fully completed form. This acknowledgement must be filed in the TMF / ISF.

Each SAE will be registered on the recognised Sponsor SAE database and reviewed. With effect from 1st June 2018 the whole SAE process will be managed through the EDGE system. Please see Flow Chart (Appendix 4). The review may lead to queries being issued to request signed documentation, clarify information or complete outcome event. All queries will be sent via email and must be responded to within the stated timeframe as per the SAE Template Email (Appendix 5).

All SAE/SUSARs reported to the Sponsor will be reviewed and where appropriate formally signed off at the R&I Management Meeting by the Director of R&I.

15. Non-Compliance

Where evidence of non-compliance is identified the Non-Compliance SOP S-1016 UHL will be followed. Corrective actions will be expected in accordance with MAJOR findings.
<table>
<thead>
<tr>
<th>Responsibility</th>
<th>Undertaken by</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 PI/Delegated</td>
<td>PI/Delegated individual</td>
<td>Report all serious adverse events to the sponsor (except those identified as exempt)</td>
</tr>
<tr>
<td>individual</td>
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<tr>
<td>2 PI/Delegated</td>
<td>PI/Delegated individual</td>
<td>Follow up the initial report with a detailed written follow up/final report if not all information is available at the time of initial reporting</td>
</tr>
<tr>
<td>individual</td>
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<tr>
<td>3 CI/PI/Delegated</td>
<td>CI/PI/Delegated</td>
<td>Completion of SAE Line Listing and review and sign off by Chief Investigator</td>
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<tr>
<td>Individual</td>
<td>Individual</td>
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</tr>
<tr>
<td>4 CI/PI/Delegated</td>
<td>CI/PI/Delegated</td>
<td>Supply the Sponsor and the main REC with any additional information requested</td>
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<tr>
<td>Individual</td>
<td>Individual</td>
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<tr>
<td>5 CI/PI/Delegated</td>
<td>CI/PI/Delegated</td>
<td>Submit DSURs to Sponsor as per SOP S-1004 UHL</td>
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<tr>
<td>Individual</td>
<td>Individual</td>
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<tr>
<td>6 Sponsor</td>
<td>Sponsor</td>
<td>Ensures that all SUSARs are reported to the MHRA and REC within mandatory timelines</td>
</tr>
<tr>
<td>7 Sponsor</td>
<td>Sponsor</td>
<td>Monitor all SAEs/SAR Line Listings reported on a monthly basis to identify and if necessary act upon any emerging safety issues</td>
</tr>
<tr>
<td>8 Sponsor</td>
<td>Monitor</td>
<td>The Monitor will review SAE submissions and request further clarification/information as required to ensure SAE report completion. The CI/PI will be provided with Sponsor acknowledgement of receipt of the completed SAE</td>
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</tbody>
</table>
This table is used to track the development and approval of the document and any changes made on revised/reviewed versions.

### DEVELOPMENT AND APPROVAL RECORD FOR THIS DOCUMENT

<table>
<thead>
<tr>
<th>Author / Lead Officer:</th>
<th>Carolyn Maloney</th>
<th>Job Title: Head of Research Operations</th>
</tr>
</thead>
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<tr>
<td>Reviewed by:</td>
<td>UHL Research Management Meeting</td>
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<tr>
<td>Approved by:</td>
<td>Professor Nigel Brunskill</td>
<td></td>
</tr>
<tr>
<td>Date Approved:</td>
<td>18 Feb 19</td>
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### REVIEW RECORD

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<th>Issue Number</th>
<th>Reviewed By</th>
<th>Description Of Changes (If Any)</th>
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<tr>
<td>March 2014</td>
<td>2</td>
<td>Carolyn Maloney</td>
<td>Version 1 amended following review of Sponsor processes</td>
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<tr>
<td>March 2015</td>
<td>3</td>
<td>Carolyn Maloney</td>
<td>Version 2 amended Logo and corporate identity</td>
</tr>
<tr>
<td>May 2015</td>
<td>4</td>
<td>Carolyn Maloney</td>
<td>Version 3 amended following review of Sponsor processes</td>
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<td>October 2015</td>
<td>5</td>
<td>Carolyn Maloney</td>
<td>Version 4 amended to correlate with appendices</td>
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<tr>
<td>August 2016</td>
<td>6</td>
<td>CM, LW, JJ</td>
<td>Version 5 amended to update SOP for consistency with UOL SOP.</td>
</tr>
<tr>
<td>Dec 2016</td>
<td>7</td>
<td>CM, DD, JJ</td>
<td>Version 6 amended to update SOP to add extra appendix relating to multi-centre reporting requirements.</td>
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<tr>
<td>Feb 2017</td>
<td>8</td>
<td>Carolyn Maloney</td>
<td>Version 8 amended Logo</td>
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<td>June 2018</td>
<td>9</td>
<td>CM</td>
<td>Version 9 – wording changes. Addition of management through EDGE.</td>
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<td>September, November 2018</td>
<td>10</td>
<td>CCL, JJ</td>
<td>Version 10 – updated R&amp;I logo. Minor text formatting corrections in protocol &amp; SAE reporting &amp; guidance documents. Appendices 8, 9, 10 added</td>
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### DISTRIBUTION RECORD:

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<th>Date</th>
<th>Name</th>
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<th>Received</th>
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SOP S-1009 UHL Processing and Reporting of Serious Adverse Events, Serious Adverse Reactions and Suspected Unexpected Serious Adverse Reactions for all Research Sponsored by University Hospitals Leicester

Page 9 of 9
Version 10 September 2018

NB: Paper copies of this document may not be most recent version. The definitive version is held on the R&I Office website. [http://www.leicestersresearch.nhs.uk/](http://www.leicestersresearch.nhs.uk/)
University Hospitals of Leicester NHS Trust
Pregnancy Notification Form

PART 1 – Initial Pregnancy Notification

<table>
<thead>
<tr>
<th>Study Number</th>
<th>Subject ID</th>
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<tbody>
<tr>
<td>EudraCT Number</td>
<td>Study Sponsor</td>
</tr>
<tr>
<td>Study Title</td>
<td></td>
</tr>
</tbody>
</table>

DO NOT SEND IDENTIFIABLE DATA OR SOURCE DOCUMENTS WITH THIS REPORT

1. MATERNAL INFORMATION

Date of Birth: ___/___/___
Date of Last Menstrual Period: ___/___/___
Expected Date of Delivery: ___/___/___

Method of contraception: ___________________________________________________________________

Contraception used as instructed?

Yes 1  No 2  Uncertain 3

2. MEDICAL HISTORY (include information on 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)

<table>
<thead>
<tr>
<th>Gestation Week</th>
<th>Outcome Including Any Abnormalities</th>
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<td>1</td>
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</table>
4. TRIAL MEDICATION INFORMATION (list all trial therapies taken in the 3 months prior to and during pregnancy)

<table>
<thead>
<tr>
<th>Name of Drug</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Date Started</th>
<th>Date Stopped</th>
<th>Indication</th>
<th>Treatment Start (week of pregnancy)</th>
<th>Treatment Stop (week of pregnancy)</th>
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5. NON – TRIAL MEDICATION INFORMATION (list all other (non-trial) medication taken in the 3 months prior to and during pregnancy)

<table>
<thead>
<tr>
<th>Name of Drug</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Date Started</th>
<th>Date Stopped</th>
<th>Indication</th>
<th>Treatment Start (week of pregnancy)</th>
<th>Treatment Stop (week of pregnancy)</th>
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6. PRENATAL INFORMATION

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

Yes 1  No 2  Not known 3

If Yes, please specify test date and results:

Test ____________________ Date ____________
Result ____________________

Test ____________________ Date ____________
Result ____________________

Test ____________________ Date ____________
Result ____________________
7. MATERNAL PREGNANCY ASSOCIATED EVENTS
If the mother experiences an SAE during the pregnancy, please indicate here, complete an SAE form and submit to the R & I Office immediately.

8. INFORMATION SOURCE

PI details:
Name
Address
Date of report
CI/PI signature

ALL REPORTS MUST BE SIGNED AND DATED BY THE PRINCIPAL INVESTIGATOR
PLEASE MAKE A NOTE OF WHEN TO FOLLOW UP THE PREGNANCY OUTCOME

For internal use only
Report received by:
Report received on:
Action taken:

PLEASE EMAIL THIS REPORT TO THE R&I OFFICE TO RIAadmin@uhl-tr.nhs.uk
University Hospitals of Leicester NHS Trust
Pregnancy Notification Form

PART 2 – Pregnancy Outcome Notification

<table>
<thead>
<tr>
<th>Study Number</th>
<th>Subject ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>EudraCT Number</td>
<td>Study Sponsor</td>
</tr>
<tr>
<td>Study Title</td>
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</tbody>
</table>

1. PREGNANCY OUTCOME

a) Termination Yes/No  
 If yes, Therapeutic/Planned/Spontaneous  
 Specify the reason and any abnormalities (if known):  

b) Delivery Yes/No  
 If yes, Normal/Forceps/Ventouse/Caesarean  
 Maternal complications or problems related to birth:  

Date of Termination:  
Date of Delivery:

2. CHILD OUTCOME
Normal/Abnormal/Stilbirth
If any abnormalities please specify and provide dates:

<table>
<thead>
<tr>
<th>Sex</th>
<th>Male/Female</th>
<th>Apgar Scores (if known)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>cm</td>
<td>1 min</td>
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<tr>
<td></td>
<td>kg</td>
<td>5 mins</td>
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<tr>
<td></td>
<td>cm</td>
<td>10 mins</td>
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</table>

3. ASSESSMENT OF SERIOUSNESS (OF PREGNANCY OUTCOME)

Non serious  
Involved prolonged inpatient hospitalisation  
Results in persistent or significant disability/incapacity  
Life-threatening  
Mother died: Date of death:  
Stillbirth/neonate died: Date of death:  
Other seriousness criteria  
Congenital anomaly/birth defect  
Other significant medical event (Please provide details):
4. ASSESSMENT OF CAUSALITY (OF PREGNANCY OUTCOME)
Please indicate the relationship to pregnancy outcome to trial medication:
Unrelated Possibly* Probably* Definitely*

If any of the fields marked* have been ticked, the outcome is considered to be RELATED to the study drug.

5. ADDITIONAL INFORMATION


6. INFORMATION SOURCE

PI details:
Name
Address

Date of report

CI/PI signature

ALL REPORTS MUST BE SIGNED AND DATED BY THE PRINCIPAL INVESTIGATOR

For internal use only
Report received by:
Report received on:
Action taken:

PLEASE EMAIL THIS REPORT TO THE R&I OFFICE
TO RIAadmin@uhl-tr.nhs.uk
### UHL Sponsored Multi Centre Non CTIMP
### Serious Adverse Event Listing Table

<table>
<thead>
<tr>
<th>Sponsor Number</th>
<th>Principal Investigator:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Title</td>
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</table>

<table>
<thead>
<tr>
<th>Study Centre</th>
<th>Date of SAE</th>
<th>Patient Study ID</th>
<th>Brief Description of Event</th>
<th>Assessment of relationship to procedure/intervention Related/Unrelated</th>
<th>Outcome</th>
<th>Date of event resolution</th>
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# SAE Tracking Log

<table>
<thead>
<tr>
<th>Patient Study ID</th>
<th>Date of SAE</th>
<th>SAE Title</th>
<th>Date initial report sent to R&amp;I</th>
<th>Date follow up/final report sent to R&amp;I</th>
<th>R&amp;I acknowledgement received for final SAE</th>
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</table>
UHL SAE Review Process Flowchart

SAE received by Research Office

If a potential SUSAR report to Sponsor/Monitors immediately

Monitor to liaise with Investigator to ensure unblinding occurs (where applicable). If SUSAR that is related to IMP follow SUSAR Process Flowchart: Appendix 8

All SAEs to be entered on Sponsor database

Completed initial SAE reports reviewed and signed off by Trial Monitors. A request for follow up report to be sent, requiring return within 28 days

R&I Admin to review and send reminder if report not returned. Further 7 days given for return of completed SAE.

If SAE report not returned in 7 days further, communication / escalation as per non-compliance SOP S-1016 will be implemented

Completed final / follow-up SAEs reviewed and if no further information is required will be signed off by Trial Monitors with 7 days

Incomplete SAE form request for further information to be returned with 7 days

R&I Admin to review and send reminder if report not returned. Further 7 days given for return of completed SAE.

If SAE report not returned in 7 days further, communication / escalation as per non-compliance SOP S-1016 will be implemented

Signed SAEs to be scanned and entered into Sponsor database / electronic folder and acknowledgement email sent within 96 hours

SOP S-1009 Appendix 4 UHL SAE Process Flowchart Version 10 September 2018
Dear Study Team

Thank you for providing the R&I office with the following SAE:

<table>
<thead>
<tr>
<th>Participant</th>
<th>Centre</th>
<th>Study Title</th>
<th>Sponsor Ref</th>
<th>Onset date</th>
<th>Title of Event</th>
<th>Type of Report</th>
<th>Date of Report</th>
</tr>
</thead>
</table>

<Delete as appropriate>

The SAE form you provided requires amendment/further information or signature as indicated below:

- Initial unsigned report received. **A signed copy of the either in the initial report or the final report is required within 7 days.**
- An initial signed report received. **A signed follow up report is required within 28 days.**
- Serious Criteria not completed. **Return within 7 days.**
- Causality assessment incomplete. **Return within 7 days.**
- Event expectedness incomplete. **Return within 7 days**
- Relationship to study procedure incomplete. **Return within 7 days.**
- Relationship to protocol violation incomplete. **Return within 7 days.**
- Study medication information incomplete. **Return within 7 days.**
- Action taken with regards to IMP incomplete. **Return within 7 days.**
- Was patient withdrawn as a result of this event incomplete. **Return within 7 days.**
- Outcome of the event incomplete. **Return within 7 days.**
- Other/comment. **Return within X days.**

Once completed, we would be grateful if you could please send the updated form to RIAdmin@uhl-tr.nhs.uk

Many thanks.
UHL Sponsored Multi Centre CTIMP
Serious Adverse Event Listing Table

<table>
<thead>
<tr>
<th>Sponsor Number</th>
<th>Chief Investigator</th>
<th>Date of Report DD/MM/YYYY</th>
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<tbody>
<tr>
<td>Study Title</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Study Centre</th>
<th>Date of SAE</th>
<th>Type of Report 1-4</th>
<th>Subject Study ID</th>
<th>Brief Description of Event</th>
<th>Serious Criteria 1-6</th>
<th>Causality Related/unrelated</th>
<th>Expectedness Expected/unexpected</th>
<th>Outcome 1-5</th>
<th>Date of Resolution</th>
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</tbody>
</table>

Chief Investigator Name ------------------------------- Signature ------------------------------- Date------------------------

All SAEs that are not resolved at time of SAE line listing submission must be included on subsequent line listings until resolution confirmed.
### CTIMP Line Listing Guidance

1. **Study site**: list site name/number - If numbers utilised ensure that the Sponsor is provided with a listing of corresponding site names.
2. **Date of SAE**: Provide date of SAE
3. **Type of report**: List relevant number in column
   - Initial
   - Follow up
   - Final
   - Initial and Final
4. **Subject Study ID**: Provide details of subject’s unique study Identification Number. – Note No personal identifiable data must be used.
5. **Brief description of event**: Provide brief description of event and subsequent investigations/actions
6. **Serious Criteria**: List relevant number in column
   - 1 - Resulted in Death
   - 2 - Life Threatening
   - 3 - In-patient Hospitalisation/prolongation of existing hospitalization
   - 4 - Persistent or significant disability/incapacity
   - 5 - Congenital anomaly/birth defect
   - 6 - Other
7. **Causality**: record Related or Unrelated
8. **Expectedness**: record Expected or Unexpected

Where an event is related and unexpected it is a Suspected Unexpected Serious Adverse Reaction (SUSAR) and requires expedited reporting. Inform the Sponsor immediately.

9. **Outcome of event**
   - 1 - Resolved
   - 2 - Resolved with Sequelae,
   - 3 - Ongoing
   - 4 - Unknown at Present
   - 5 - Fatal

Where an event is Fatal further information will be required with regards to cause of death for the Sponsor.

10. **Date of resolution**: All SAES must be followed up until resolution
Completion of E-Susar – an Aide Memoire

In the absence of a ‘test’ or ‘practice’ site we have accessed the E-Susar and provided the following. Each page is a screen shot of the tabs that can be found on the E-Susar report when you ‘add a report’ to a study.

When you initially go into the E-Susar site, you will only be able to see studies that have been assigned to you. In the first instance you need to check that you can see the studies that you ‘should’ be assigned to, so that when / if you are required to submit an e-Susar report you are not going to fall at the very first hurdle!

The following screen-shots have been taken directly from the site, and the ‘help’ text is shown next to the button. This should aid you to prepare for when you have your first report to complete.

Please don’t ‘practice’ on the study as this will generate a report which will not be a real event.

e-Susar can be accessed by visiting: https://esusar.mhra.gov.uk/login

Appendix 7 - e-Susar walk through – an Aide Memorie V10 September2018
1. Select Trial

Select the trial for which the new report is to be created. Users can only create reports for active trials with which they have been associated.

By selecting the appropriate trial, the trial details are automatically populated into the report. You will then be guided through a series of pages collecting information on the trial subject, the reaction and the medication, before being invited to submit the report to the MHRA.

Fields that you must complete are marked with this symbol: <required>

Reference

Your available trials <required>

- 2017-000149-30 A Randomized, Double-Blind, Placebo-Controlled, Phase 2 Study of Safety, Tolerability and Efficacy of Pirfenidone in Patients with Rheumatoid Arthritis Interstitial Lung Disease

[Buttons: Step 1. Select Trial, Cancel, Save, Continue]
## 2. Subject Information

One patient identifier field (Initials, Sex, Age at time of adverse reaction or Subject ID Number) must be completed in order to proceed.

Fields that you must complete are marked with this symbol: ![required]

<table>
<thead>
<tr>
<th>Field</th>
<th>Instruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initials</td>
<td>Please enter the initials of the patient that has suffered the SUSAR</td>
</tr>
<tr>
<td>Sex</td>
<td>Please enter the gender of the patient that has suffered the SUSAR</td>
</tr>
<tr>
<td>Age at time of adverse reaction</td>
<td>Please enter the unique identification number used in the trial to identify the patient that has suffered the SUSAR</td>
</tr>
<tr>
<td>Subject ID Number</td>
<td>Please use the stone and pounds fields to convert your weight to kg</td>
</tr>
<tr>
<td>Patient weight (kg)</td>
<td>Please use the feet and inches fields to convert your height to metres.</td>
</tr>
<tr>
<td>Patient height (m)</td>
<td></td>
</tr>
</tbody>
</table>
Please enter details of any prior diseases the patient has suffered that are not being treated by the study medication.

Disease (required)

Start date
- DD
- MMM
- YYYY

End date
- DD
- MMM
- YYYY

Continuing (required)
- Yes
- No
- Unknown

Add another disease

This field is a predictive entry lookup against the MedDRA dictionary. Enter the first 3 characters then select a MedDRA term that matches the disease suffered by the patient.
This field is a predictive entry lookup against the MHRAs drug dictionary. Enter the first 3 characters then select the drug name from the list provided. If no match is found, enter the full drug name in the text field.
3. Reaction Details

Fields that you must complete are marked with this symbol: **required**

**Date sponsor was made aware of the SUSAR** **required**

[Calendar icon]

**Country of Origin** **required**

Please select the country the SUSAR occurred in.

**Narrative**

Please provide a narrative of the reactions, together with any other information relevant to the SUSAR report, in no more than 20,000 characters.

**Seriousness** **required**

- [ ] Death
- [ ] Life threatening
- [ ] Hospitalisation
- [ ] Disabling
- [ ] Congenital anomaly
- [ ] Other
Please enter details of the reactions suffered by the patient.

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Required</th>
<th>Help</th>
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</table>

This field is a predictive entry lookup against the MedDRA dictionary. Enter the first 3 characters then select a MedDRA term that matches the reaction suffered by the patient.

<table>
<thead>
<tr>
<th>Reaction Outcome</th>
<th>Required</th>
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<tbody>
<tr>
<td>Recovered</td>
<td></td>
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<tr>
<td>Recovering</td>
<td></td>
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<tr>
<td>Not Recovered</td>
<td></td>
</tr>
<tr>
<td>Recovered with sequelae</td>
<td></td>
</tr>
<tr>
<td>Fatal</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td></td>
</tr>
</tbody>
</table>

**Start date**

- Day
- Month
- Year

**End date**

- Day
- Month
- Year

Add another suspect reaction
Please enter details of any medical tests undertaken on the patient that are relevant to the SUSAR report.

**Test**
- **Required**
- [Help]

This field is a predictive entry lookup against the MedDRA dictionary. Enter the first 3 characters then select a MedDRA term that matches the test conducted.

**Result**
- **Required**
- [Help]

Please enter the test result. This field is restricted to 50 characters; any additional information should be included in the narrative.

**Unit**
- [Help]

Please enter the result unit. Where no unit is appropriate, this field may be left blank.

**Test date**
- [DD]
- [MMM]
- [YYYY]

Day
Month
Year

Add another test

Step 3. Reaction Details  Cancel  Save  Previous step  Continue
4. Medication Details

Please enter details of all medication the trial subject has taken in the last 3 months, including non-study medication. Each medicine should be characterised as either 'Suspect' or 'Concomitant'.

Note regarding Drug Name entry: A dictionary of drug terms and codes is associated with the eSUSAR reporting form. This is regularly updated with new terms that have been submitted to the MHRA in CTA applications. The term entered into the Drug Name field will be matched against the drug dictionary in real time. When no match is found, the user will be prompted to check and re-enter the term. When a match is found for a second time, the user will be permitted to continue and submit the report with an unmatched name.

Fields that you must complete are marked with this symbol: **required**

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<tr>
<th>Drug Name <strong>required</strong></th>
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<tr>
<th>Drug Characterisation <strong>required</strong></th>
<th>Help</th>
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<td>Please Choose</td>
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<th>Drug Dosage <strong>required</strong></th>
<th>Help</th>
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<th>Help</th>
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<th>Form <strong>required</strong></th>
<th>Help</th>
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<tbody>
<tr>
<td>Please Choose</td>
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</table>

Enter the drug substance term or code in the same format as in the CTA application. If the term or code matches a record in the MHRA dictionary the form will update to reflect this. Where possible please try to find a matching drug substance.

Select Suspect if the drug is the suspected cause of the SUSAR

Enter the dosage given to the patient.

Enter how often the dose is, or was, administered.
6. Overview

This page shows a summary of the SUSAR report prior to submission. Please check and ensure that all information is correct. Changes can be made at this stage by clicking on the link for the appropriate section.

If all the information is correct, click on the 'Submit Report' button at the bottom of the page to submit the report to the MHRA. Alternatively, the report can be saved for editing and/or submission at a later date by clicking on the 'Save' button.

You may print the report summary now to check it, then you will need to submit it later.

1. Trial Information

This stage has not yet been completed.
UHL SUSAR Process Flowchart

SAE reports Related Unexpected event -potential SUSAR.
Unblinding completed as per Appendix 10
SUSAR Confirmed for IMP or Comparator or placebo (if applicable)

Sponsor/Delegate to Liaise with Chief Investigator to ensure:
Initial eSUSAR
Submission within required regulatory Timelines:
as soon as possible and, within 7 calendar days for a death or life threatening SUSAR and
follow up information within an additional 8 calendar days.
For all other SUSAR within 15 calendar days for other SUSARS
Initial Notification to the Research Ethics Committee

Multi-Centre Studies
Sponsor/Delegate/Chief Investigator to ensure all Investigators informed of the
initial eSUSAR submission and confirm receipt received from all sites

Sponsor/Delegate to Liaise with Chief Investigator to ensure:
Follow up eSUSAR
Submission within required regulatory timelines (see above)
Follow up notification submitted to the Research Ethics Committee

Multi-Centre Studies
Sponsor/Delegate/Chief Investigator to ensure all Investigators informed of the
Follow-up eSUSAR submission and confirm receipt received from all sites

Sponsor/Delegate/Chief Investigator to respond to any queries received from
Competent Authorities/REC

SOP S-1009 Appendix 8 UHL SUSAR Flowchart Version 10 September 2018
SUSAR Safety Notification Email

Subject: Expedited Safety Report - Initial/Follow Up Report  (Study number, Title and IMP name)

Dear Investigator,

Study Title:

As a participating investigator in a clinical trial involving the investigational medicinal product xxxxxxx (name IMP/comparator), you are being notified of an initial/follow up safety report (delete as appropriate) that was submitted to the Regulatory Authorities and the Research Ethics Committee.

Please respond to this email to acknowledge receipt and review of this notification and attached documents and forward this email to your local R&I/R&D department for their records.

Kind regards

Name of Chief Investigator
Serious Adverse Reaction
Assess expectedness against Reference Safety Information (RSI)

If Serious Adverse Reaction is UNEXPECTED proceed to unblinding

Is Subject on Investigational Medicinal Product (IMP)
Expidite as SUSAR

Is Subject on Comparator
Assess expectedness against RSI for this product.
If expected - do not expedite
If unexpected - Expedite as SUSAR

Is Subject on Placebo
Consider reaction to component of placebo
If not related - do not expedite
If related - Expedite as SUSAR
(See Appendix 8)
Serious Adverse Event Report Form A

UHL Sponsored Clinical Trials of Investigational Medicinal Products

Guidance Document

All Serious Adverse Events MUST be reported within 24 hours of the research team being aware of the event. The initial report may be submitted without a PI signature, but must be followed up with a signed copy reporting expectedness and causality within 7 days.

Once a signed initial report is received a follow up or final report should be submitted within 28 day. If the participant is still an inpatient or there is an unavoidable delay in the provision of further information, inform the R&I office.

Should there be a requirement for clarification or further information required, an email detailing the request will be sent. Response to the request is required as per the timelines dictated in the email.

Sponsor Ref
Study identifier given by the R&I department. This MUST be documented to enable the R&I office to identify the study.

Study Title
Full or short version of the study title as entered on the IRAS form

Study Number/Initials
Enter unique subject identifier and subjects initials.

Centre
Enter centre name

NO OTHER PARTICIPANT IDENTIFIABLE DATA MUST BE ENTERED ON THIS FORM

1. Type of Report

Initial Report
The first time you are reporting this event this may be a signed or unsigned report. At this time point either, not all details are available, the form is unsigned, or the event is marked as ongoing.

Follow Up Report
Follow up information to an initial report is provided in this report. The event may still be marked as ongoing or resolved. If ongoing, further reports must be submitted until the resolution of the event.

Final report
When all follow up information is available for this Serious Adverse Event and the outcome for the event has been completed.
Initial and Final
All information on the SAE and outcome of the event are complete on the first submission of the SAE report.

Date of Report
Date you are completing this report. (Initial, Follow-up or Final)

Title of the Serious Adverse Event
Enter keywords that best summarise the event. i.e. admission for chest pain.

Multiple Serious Adverse Events MUST be reported on individual forms.

Date of Onset
Date of onset of the event reported. If a full date is not known either on the first or subsequent reports then UNK/ Month /Year should be completed.

Date study Team Aware
The date that the event was reported to/or the study team became aware of the event. The SAE must be submitted within 24 hours of this date.

2. Seriousness Criteria
Choose from the menu. If there is more than one criteria, choose the most significant one. Multiple Serious Adverse Events MUST be reported on individual forms.

3. Narrative
If the SAE is due to an admission to hospital, provide the admission and discharge dates. Provide an account of the event, similar to that of a discharge summary. The description must have sufficient details for evaluation by the individuals reviewing the SAE, who may not be experts in the disease area or investigational medicinal products. Abbreviations of clinical conditions should not be used. Summarise any relevant laboratory or diagnostic tests. Include details of discharge if appropriate.

4. Causality and Expectedness
This section must be completed by the Principal Investigator or other delegated medically qualified investigator, as agreed by the Sponsor, and delegated this role on the Delegation of Authority and signature Log by the Principal Investigator.

All Investigational drugs should be entered and their causal relationship and expectedness, or not, MUST be reported.

If more than two drugs are under investigation an additional section can be added.

Study Drug 1 Enter details of IMP involved.

Evaluation of Causal relationship to drug – Mark relevant box

Related – if the causal relationship between study drug 1 and the SAE is at least a reasonable possibility i.e. the relationship cannot be ruled out

Not Related-If there is no causal relationship between study drug 1 and the SAE
i.e. the event is caused by something other than the IMP e.g. underlying disease, a concomitant medication

Expectedness

The assessment of expectedness must be based on the information contained in the approved Reference Safety Information (RSI) e.g. Investigator Brochure and/or the Summary of Product Characteristics

Expected  The event is an expected reaction based on the information contained in the Investigator Brochure and/or Summary of Product Characteristics.

Unexpected  The event is unexpected based on the information contained in the Investigator Brochure and/or Summary of Product Characteristics.

Study Drug 2 Enter second drug completing all details as above

If the event is related and unexpected it is a Suspected Unexpected Serious Adverse Reaction (SUSAR) and requires expedited reporting. Inform the R&I office immediately Telephone number 0116 258 8351

5. Is the study drug Blinded or Unblinded  Detail if the study drug(s) the participants are receiving are known to the Investigator research team or are the research team blinded.

If a SUSAR has been reported, blinded studies must be unblinded as per unblinding procedure.

6. Event related to protocol violation  Answer Yes or No.
   If Yes - Further information should be supplied on a separate protocol deviation form.

7. Study Medication Information  Answer Yes or No.
   If Yes – Further information on when the study drug was given should be documented in the table provided within the form

8. Action taken with IMP  Please indicate action taken.
   If participant not taking IMP at time of event mark as not applicable.

9. Participant Withdrawn  Answer Yes or No
10. Outcome

Resolved The Serious Adverse event has resolved. e.g. participant has been hospitalised, received treatment and the event has been resolved. Provide details of the date of resolution of the SAE.

Resolved with Sequlalae The Serious Adverse Event is resolved but there are still some residual problems as a result of the SAE e.g. the patient hospitalised for DVT and then discharged on warfarin. The participant no longer requires hospital treatment but the pre-existing event continues.

Ongoing – The Event has not resolved at this time. This will require follow up until resolution of event.

Unknown at Present- Information is not available at the present time. Further information MUST be supplied until resolution of event.

Fatal- Where the event is fatal details of the date of death and the cause of death MUST be obtained.

Cause of death obtained- detail where the information was obtained to support cause of death. Supporting documents to be supplied with SAE.

NOTE: All supporting documentation must have all participant identifiable data removed. The documents MUST only be identified with the addition of the participant study ID and Initials.

Reporting Person
Supply full details as indicated of person reporting the event. Please ensure contact phone number and email address are complete.

Principal Investigator/Delegated Medically Qualified Individual
Supply full details. Please note the person signing this form must be either the Principal Investigator or a medically qualified individual as agreed by the Sponsor to undertake this role. The person must be named and delegated the duty on the delegation of authority log.

Reporting and completion of SAEs involving investigational medicinal products must be undertaken in accordance with SOP S-1009 UHL – Processing and Reporting of Serious Adverse Events, Serious Adverse Reactions and Suspected Unexpected Serious Adverse Reactions for all Research Sponsored by the University Hospitals of Leicester NHS Trust

Please return the completed form and any anonymised copies of supporting documents to the Research and Innovation Office, Leicester General Hospital by email to RIAdmin@uhl-tr.nhs.uk

If you have queries regarding your SAE submission, please contact the Clinical Trial Monitoring and training team. Contact details can be found on the R&I Website. http://www.leicestersresearch.nhs.uk
Serious Adverse Event Report Form B

For all studies EXCLUDING clinical trials of investigation medicinal products

Guidance Document

This form is for the reporting of Serious Adverse Events in studies that DO NOT involve Investigational Medicinal products. If your study involves Investigation Medicinal products you must use SAE Form A.

All Serious Adverse Events MUST be reported within 24 hours of the research team being aware of the event. The initial report may be submitted without a PI signature, but must be followed up with a signed copy within 7 days.

Once a signed initial report is received a follow up or final report should be submitted within 28 days. If the participant is still an inpatient or there is an unavoidable delay in the provision of further information, inform the Sponsor at the Research and Innovation office.

Should there be a requirement for clarification or further information required; an email detailing the request will be sent. Response to the request is required as per the timelines stated in the email.

Sponsor Reference Number
Study identifier given by the Sponsor. This can be found on the Sponsor green light letter. This MUST be given to enable Sponsor to identify the Trial.

Study Title
Full or short version of the study title as entered on the IRAS form

Study Number/Initials
Enter unique subject identifier and subjects initials.

Centre
Enter centre name.

NO OTHER PARTICIPANT IDENTIFIABLE DATA MUST BE ENTERED ON THIS FORM

1. Type of Report

Initial Report
The first time you are reporting this event. This may be a signed or unsigned report. At this time point either, not all details are available, the form is unsigned, or the event is marked as ongoing.

Follow Up Report
Follow up information to an initial report, is provided in this report. The event may still be marked as ongoing or resolved. If ongoing, further reports must be submitted until the resolution of the event.

UHL SAE Completion Guidance Document Form B Non- CTIMP Version 10 September 2018
Final report
When all follow up information is available for this Serious Adverse Event and the outcome for the event has been completed.

Initial and Final
All information on the SAE and outcome of the event are complete on the first submission of the SAE report.

Date of Report
Date SAE report completed.

Title of Serious Adverse Event
Enter keywords that best summarise the event e.g. admission for chest pain.
Multiple Serious adverse events MUST be reported on individual forms.

Date of Onset
Date of onset of the event reported. If a full date is not known either on the first or subsequent reports then UNK/ Month /Year should be completed.

Date study Team Aware
The date that the event was reported to/or the study team became aware of the event. The SAE must be submitted within 24hours of this date

2. Seriousness Criteria
Choose from the indicated menu.
If there is more than one criteria, choose the most significant one.
Multiple Serious Adverse Events MUST be reported on individual forms.

3. Narrative
Provide Admission and Discharge date information if applicable

Provide an account of the event, similar to that of a discharge summary. The description must have sufficient details for evaluation by the individuals reviewing the SAE, who may not be experts in the disease area. Abbreviations of clinical conditions should not be used. Summarise any relevant laboratory or diagnostic tests. Include details of discharge if appropriate.

Assessment of implications – if the event is related to a study device or procedure or intervention. Document the safety implications and how these will be addressed i.e. protocol amendment
If not relevant mark in box as not applicable
4. **Was the Event related to a study information**
   **Device/procedure or intervention**
   Answer Yes or No box as appropriate. If Yes - provide further information to the Sponsor.

   *If the SAE is related to the research procedures and is unexpected. An HRA Serious Adverse Event form must be submitted to the Research Ethics Committee that gave a favourable opinion of the research within 15 days of the CI becoming aware of the event. Website: http://www.hra.nhs.uk/resources/during-and-after-your-study/progress-and-safety-reporting/

5. **Event related to protocol violation**
   Answer Yes or No.
   If Yes - Further information should be supplied on a separate protocol deviation form/File note.

6. **Participant Withdrawn**
   Answer Yes or No

9. **Outcome**
   **Resolved** - The Serious Adverse Event is no longer present e.g., participant has been hospitalised/prolongation of hospitalisation, received relevant treatment and the event has been resolved. Provide details of the date of resolution of the SAE.

   **Resolved with Sequelae.** The Serious Adverse Event is resolved but there are still some residual problems as a result of the SAE. e.g. The participant was hospitalised for a DVT and discharged home on warfarin. The participant no longer requires hospital treatment but the pre-existing event continue.

   **Ongoing** – The Adverse Event has not resolved at this time. This will require follow up until resolution of event.

   **Unknown at Present** - Information is not available at the present time. Further information **MUST** be supplied until resolution of event.

   **Fatal** - Where the event is fatal; details of the date of death and the cause of death **MUST** be obtained.

   Cause of death obtained - detail where the information was obtained to support cause of death. Supporting documents to be supplied with SAE

**Note** All supporting documentation must have all patient identifiable data removed. The documents **MUST** only be identified with the addition of the participant study ID and Initials.

**Reporting Person**
Supply full details as indicated of person reporting the event. Please ensure contact phone number and email address are complete.
Principal Investigator/Delegated Supply full details. Please Note* the person signing this form must be
Medically qualified individual either the Principal Investigator or a medically qualified individual as
agreed by Sponsor to undertake this role. The person must be
named and delegated the duty on the delegation of authority log.

Reporting and completion of SAEs not involving investigational medicinal products must be
undertaken in accordance with SOP S-1009 – Processing and Reporting of Serious Adverse
Events, Serious Adverse Reactions and Suspected Unexpected Serious Adverse Reactions for
all Research Sponsored by the University Hospitals of Leicester NHS Trust (UHL)

Please return the completed form and any anonymised copies of supporting documents to the
Research and Innovation Office, Leicester General Hospital by email to RIAdmin@uhl-tr.nhs.uk

If you have queries regarding your SAE submission, please contact the Research and
Innovation Office. Contact details can be found on the UHL Website.
http://www.leicestersresearch.nhs.uk
SERIOUS ADVERSE EVENT REPORT FORM A
FOR UHL SPONSORED CLINICAL TRIALS OF INVESTIGATIONAL MEDICINAL PRODUCTS

Sponsor Reference Number

Study Title:

Participant Study Number and Initials

Centre:

This form is to be completed within 24 hours of becoming aware of the Serious Adverse Event

1. Type of Report
   - Initial
   - Follow Up
   - Final
   - Initial & Final
   (Tick relevant box)

Date of Report

Title of Serious Adverse Event

Date of Onset

Date of Study Team Aware

NB If the event is a pregnancy it should be reported on a UHL Pregnancy Notification Form

2. Serious Criteria (tick one box only):
   - ☐ Resulted in death
   - ☐ Life threatening
   - ☐ In-patient hospitalisation or prolongation of existing hospitalisation
   - ☐ Persistent or significant disability/incapacity
   - ☐ Congenital anomaly/birth defect
   - ☐ Other

3. Narrative - Briefly describe the event (attach anonymised supporting documentation if applicable)
   
   Admission Date
   
   Discharge Date

Page 1 of 4
Both the Causality & Expectedness MUST be completed by the Principal Investigator or other delegated medically qualified Investigator as agreed by the Sponsor.

Causality

4a. Evaluation of causal relationship with study drug 1

Related- If the casual relationship between study drug 1 and the SAE is at least a reasonable possibility
Un-Related- If there is no causal relationship between study drug 1 and the SAE

(Name of study drug 1) ........................................................................................................

  Related  ☐  Unrelated  ☐

4b. Expectedness: The assessment of expectedness must be based on the information contained in the approved Reference Safety Information (RSI) e.g. Investigator Brochure and/or the Summary of Product Characteristics

  Expected  ☐  Unexpected  ☐

If the event is related and unexpected it is a Suspected Unexpected Serious Adverse Reaction (SUSAR) and requires expedited reporting. Inform the Sponsor immediately. Telephone number 0116 258 8351

4a. Evaluation of causal relationship with study drug 2

Related- If the casual relationship between study drug 1 and the SAE is at least a reasonable possibility
Un-Related- If there is no causal relationship between study drug 1 and the SAE

(Name of study drug 2) ........................................................................................................

  Related  ☐  Unrelated  ☐

The assessment of expectedness must be based on the information contained in the approved Reference Safety Information (RSI) e.g. Investigator Brochure and/or the Summary of Product Characteristics

  Expected  ☐  Unexpected  ☐

If the event is related and unexpected it is a Suspected Unexpected Serious Adverse Reaction (SUSAR) and requires expedited reporting. Inform the Sponsor immediately. Telephone number 0116 258 8351
5. Is the Study Investigational Medicinal Product Blinded or Unblinded?

Blinded □  Unblinded □

6. Was the event related to a protocol violation/deviation?

Yes □  No □

7. Study Medication Information:

<table>
<thead>
<tr>
<th>Participant has been Administered Study Drug?</th>
<th>Yes (Provide details in box below)</th>
<th>No (Give reason i.e. screening)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name of Medication</td>
<td>Indication(s) for Use</td>
<td>Dose (units)</td>
</tr>
<tr>
<td>-------------------</td>
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</tbody>
</table>

8. Action taken with investigational product due to event:

□ Dose not changed
□ Temporarily discontinued Date:
□ Permanently discontinued Date:
□ Dose reduced - provide details __________________________________________
□ Other – provide details __________________________________________
□ Not applicable

9. Was the participant withdrawn from the study as a result of this event? Yes □ No □

10. Outcome of the Event

□ Resolved Date of Resolution: □ □ □ □ □ □ □
□ Resolved with Sequelae
□ Ongoing
□ Unknown at present
□ Fatal Date of Death:

Cause of Death .................................................................................................................

UHL SAE Report Form A CTIMP, Version 10 September 2018
Cause of death obtained from (tick one)

Working Diagnosis [ ] Coroners Inquest [ ] Death Certificate [ ]

Supporting documentation to be supplied with SAE

<table>
<thead>
<tr>
<th>Reporting Person:</th>
<th>Principal Investigator/Delegated medically qualified individual as agreed by the sponsor:</th>
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<tbody>
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Please return the completed form and copies of any additional anonymised documents to the Research & Innovation Office, to RIAdmin@uhl-tr.nhs.uk

Reporting of SUSARs to the Research Ethics Committee and Regulatory Authority for UHL sponsored studies will be undertaken in accordance with SOP S-1009 UHL. Processing and Reporting of Serious Adverse Events, Serious Adverse Reactions and Suspected Unexpected Serious Adverse Reactions for all Research Sponsored by the University Hospitals of Leicester NHS Trust.

For Office Use Only

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<tr>
<td>Initial &amp; Final</td>
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SERIOUS ADVERSE EVENT REPORT FORM B

(For all studies excluding Clinical Trials of Investigational Medicinal Products)

Sponsor Reference Number
Study Title:
Participant Study Number and Initials
Centre:

This form is to be completed within 24 hours of becoming aware of the Serious Adverse Event

1. Type of Report (Tick relevant box)
   - Initial
   - Follow Up
   - Final
   - Initial & Final

   Date of Report

   Title of the Serious Adverse Event:

   Date of Onset

   Date Study Team Aware

2. Serious Criteria (Tick one box only):
   - Resulted in death
   - Life threatening
   - In-patient hospitalisation or prolongation of existing hospitalisation
   - Persistent or significant disability/incapacity
   - Congenital anomaly/birth defect
   - Other
3. Narrative - Briefly describe the event (attach supporting documentation if applicable)

Admission Date          Discharge date

What is your assessment of the implications, if any, for the safety of study participants and how will these be addressed?

Questions 4 & 5 must be completed by the Principal Investigator.

4) Was the event related to a study device/procedure or intervention?

☐ Yes ☐ No

5) Was the event related to a protocol violation/deviation?

☐ Yes ☐ No

6) Was the participant withdrawn from the study as a result of this event?

☐ Yes ☐ No
7) Outcome of the Event
   - Resolved  Date of Resolution: __ __ __
   - Resolved with Sequelae
   - Ongoing
   - Unknown at present
   - Fatal  Date of Death:
   
   Cause of Death: .................................................................
   Cause of death obtained from (tick one)
   - Working Diagnosis
   - Coroner's Inquest
   - Death Certificate
   Supporting documentation to be supplied with SAE

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Reporting and completion of SAEs not involving investigational medicinal products must be undertaken in accordance with SOP S-1009 UHL Processing and Reporting of Serious Adverse Events, Serious Adverse Reactions and Suspected Unexpected Serious Adverse Reactions for all Research Sponsored by the University Hospitals Leicester NHS Trust (UHL)

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UHL SAE Report Form B Non CTIMP, Version 10
September 2018