Standard Operating Procedure (SOP)

<table>
<thead>
<tr>
<th>SOP Title</th>
<th>Adverse Events Monitoring, Reporting and Recording</th>
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<tbody>
<tr>
<td>SOP Reference</td>
<td>SOP 11</td>
</tr>
<tr>
<td>Version Number</td>
<td>4</td>
</tr>
<tr>
<td>Effective Date</td>
<td>September 2011</td>
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<td>Next Review Date</td>
<td>September 2013</td>
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<table>
<thead>
<tr>
<th>Author</th>
<th>Deborah Main</th>
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<tr>
<td>Reviewed by</td>
<td>Charlotte Davies</td>
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<tr>
<td></td>
<td>Operations Manager</td>
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| Approved by                | Dr Brian Thomson                                   |
|                            | Director of Research & Innovation                  |
|                            | Signature                                           |
|                            | Date                                               |
|                            | 19/9/11                                             |

| Approved by                | Dr Stephen Fowlie                                   |
|                            | Medical Director                                    |
|                            | Signature                                           |
|                            | Date                                               |
|                            | 6/11/11                                             |

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<th>Version</th>
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<td>4</td>
<td>05/09/11</td>
<td>Annual Review</td>
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1. **Introduction**

In order to comply with the Medicines for Human Use (Clinical Trials) Regulations 2004 and Standards for Good Clinical Practice (GCP), it is important that all researchers are aware of the different definitions related to adverse events in research and how to record, report and review each of these specific occurrences.

2. **Scope**

This SOP is applicable to all researchers undertaking projects that fall within the Medicines for Human Use (Clinical Trials) Regulations 2004. The principles within this document must be followed, however, if applicable, and only with prior agreement with the sponsor the content may be modified to be study specific and meet the needs of individual studies.

3. **Definitions**

Adverse events in research can be classified into the following categories:

3.1 **Adverse Event (AE)**

Any untoward medical occurrence in a patient/participant administered a medicinal product that does not necessarily have a causal relationship with this treatment. An AE can therefore be described as any unfavourable and unintended sign (including abnormal laboratory results), symptom or disease temporally (timely) associated with the use of a medicinal product, whether or not related to the product.

**Additional Information relating to Medical Devices/Equipment**

Adverse events also include any incident that was possibly linked to a device or with shortcomings in the information supplied that might lead to death or serious deterioration in health if it recurred.

3.2 **Serious Adverse Event (SAE)**

Any untoward medical occurrence in a patient/participant administered a medicinal product, which does not necessarily have a causal relationship with this treatment, and that at any dose results in:

- Death
- Is life-threatening i.e. the subject is at risk of death at time of event
- Results in persistent or significant disability/incapacity
- Requires in-patient hospitalisation or prolongs a current hospitalisation
- Results in congenital anomaly or birth defect
  OR
- May jeopardise the patient or may require intervention to prevent one of the outcomes listed above

**N.B.** The study protocol may have been written to exclude reporting of certain conditions related to the disease under investigation or natural disease progression. These events would not be classed as serious adverse events. All NUH sponsored protocols should report AEs.

### 3.3 Adverse Drug Reaction (ADR)
Any noxious and unintended (harmful and unwanted) “response to a medicinal product normally” used in man for prophylaxis, diagnosis or therapy of diseases, or for modification of physiological function, and is suspected to be related to the medicinal product.

The phrase “response to a medicinal products” means that a causal relationship between a study medication and an AE is at least a reasonable possibility, i.e., the relationship cannot be ruled out.

All cases judged by either the reporting medically qualified professional or the sponsor as having a reasonable suspected causal relationship to the study medication qualify as adverse reactions.

### 3.4 Serious Adverse Drug Reaction (SADR)
An adverse drug reaction that is serious (see SAE criteria in 3.2)

### 3.5 Expected Serious Adverse Reactions
These will be outlined in the protocol, the SmPC and Investigators Brochure. Any serious adverse events/reactions that could be reasonably expected when taking into account the likely course of the disease or condition during the course of the study or expected from the study medication(s) will be outlined in the protocol.

### 3.6 Suspected Unexpected Serious Adverse Drug reaction (SUSAR)
A SUSAR is serious ADR where the nature or severity is not consistent with the applicable product information e.g. Investigator Brochure for an unapproved investigational medicinal product or Summary of Product Characteristics (SmPC) for a product with a marketing authorisation.

### 4. Recording, Reporting and Reviewing of Adverse Events
Specific procedures should be followed when recording, reporting and reviewing all adverse events/occurrences in research.
24hr Medical Cover: Arrangements will be requested from all active clinical trials sponsored by the NUH Trust to provide a 24hr contact card for participants, where appropriate. This will be audited by NUH R&D trial monitors.

4.1 Recording
It is the researcher’s responsibility to maintain an accurate and up to date record of all adverse events/occurrences in research. This record, including details of nature, onset, duration, severity, outcome and any relationship to investigational product, should be made on the relevant documentation.

4.2 Reporting
The adverse event/occurrence must be reported to the sponsor as per study protocol or upon request. The researcher should use medical terminology to describe any event and avoid vague terms such as “sick”. For details on assessing causality see section 9.

4.3 Reviewing
Event reviewing is the responsibility of the researcher and as such must ensure that the participants are not compromised. Any appropriate action must be taken to protect the participants, research team and the Trust whilst ensuring validity of the results. If the action taken leads to suspension, cessation or amendment of the study, then the sponsor, MHRA, the relevant Research Ethics Committee and subsequently R&D must be notified.

4.4 Adverse Events and Adverse Drug Reaction
- All adverse events must be recorded in the participant’s medical records in accordance with standards of good clinical practice.
- When documenting adverse events, researchers should utilise proformas or logs. This may consist of a form supplied by the sponsor/coordinating body/funder or one developed by the researcher. See appendix A for a generic “Adverse Event Recording Form”.

4.5 Serious Adverse Events or Serious Drug Reactions
- All adverse events must be recorded in the participant’s medical records in accordance with standards of good clinical practice.
- When documenting serious adverse events researchers should utilise the appropriate documentation provided by the sponsor and reported to the sponsor in accordance with the protocol by the researcher.

- Where Nottingham University Hospitals NHS Trust is the Sponsor, the researcher must complete the “Serious Event Reporting Form” See appendix C. This must be sent to R&D < 24hrs from becoming aware. The completed “Serious Event Reporting Form” can either be emailed, faxed or
hand-delivered but NOT mailed to the R&D Department, E11 Curie Court, QMC Campus, email: rdsae@nuh.nhs.uk, Fax. No: 0115 8493295 or internal fax no. 35295.

4.6 Suspected Unexpected Serious Adverse Drug Reactions (SUSARs)

- An event is unexpected if it is NOT listed in the Investigators Brochure (IB) or Summary of Product Characteristics (SmPC).

- Sponsors of clinical trials conducted in the European Union (EU) must ensure that all relevant information about SUSARs is recorded and reported in an expedited fashion to the Competent Authorities in all the Member States concerned (in the UK this is the MHRA) and to the main Ethics Committees which gave the favourable opinion.

**Trial Sponsor Responsibilities:**

SUSARs must be recorded on the appropriate documentation provided by the sponsor and reported to the sponsor in accordance with the protocol by the researcher. Reports of SUSARs can be made in the CIOMS-1 format available at [www.cioms.ch/cioms.pdf](http://www.cioms.ch/cioms.pdf) and is widely accepted as the standard reporting form.

Where incomplete information is available at the time of initial reporting, all the appropriate information for an adequate analysis of causality should be provided as follow-up reports as soon as it becomes available.

- Where **Nottingham University Hospitals NHS Trust is the Sponsor**, the researcher must complete the “Serious Event Reporting Form” See appendix C. (The CIOMS-1 format is also acceptable available at [www.cioms.ch/cioms.pdf](http://www.cioms.ch/cioms.pdf)). The researcher is required to complete the minimum reporting criteria denoted on this form, which must be received by the NUH R&D Department within 1 working day or <24hrs of becoming aware.

A final detailed report must follow within 7 calendar days. The completed “Serious Event Reporting Form” can either be emailed, faxed or hand-delivered but NOT mailed to the R&D Department, E11 Curie Court, QMC Campus, email: rdsae@nuh.nhs.uk, Fax. No: 0115 8493295 or internal fax no. 35295.
R&D Internal processing of Adverse Events (Appendix F)

NUH is the sponsor:

All CTIMP trials sponsored by NUH will be registered on the MHRA eSUSAR online reporting website: esusar@mhra.gsi.gov.uk

- Upon receipt of all SAE reports, a member of the R&D team will review the “Serious Event Reporting Form” for accuracy and complete a “Serious Event Tracking Form”. If the event is a SUSAR, a copy of the report form must be emailed to the eSUSAR website and to the Ethics Committee which gave favourable opinion within the specified timeframe below:
  
  i) For fatal and life threatening SUSARs this will be no later than 7 calendar days from discovery of the event, for the initial notification, with the final report forwarded no later than a further 8 days (15 calendar days in total from discovery)
  
  ii) For non fatal/ life threatening SUSARs this will be no later than 15 calendar days (from discovery) in total for both the initial and final report

- If the University of Nottingham Clinical Trials Unit (CTU) is responsible for the Trial, it is the CTUs responsibility to report to the MHRA, REC and then notify the R&D.

- All SUSARs reported from NUH sponsored trials will be assessed by an appointed independent Medical Assessor.

- Follow up Reports will be provided by the Investigator each time new information is available. All follow up reports will be placed in the R&D SAE file until the SUSAR resolves or until a decision is made not to continue follow up. Upon completion of the SAE then all of the information held in the R&D SAE file and will be filed in the study File

  - Fax machine, mail tray and RDSAE reporting folder to be checked twice daily for any reports received by R&D administration according to a rota set up with agreement of all individuals involved, allowing for absence and leave cover.

  - Upon checking all three routes of contact, a rota form will be signed /dated and the time documented. Admin staff will also ensure the fax machine is maintained.
• A copy of the “Serious Event Reporting Form”, “Serious Event Tracking Form” and acknowledgement of fax/email sent to be kept in:
  
  i) The relevant project file
  ii) Departmental Serious Event File

SUSAR Reports to Concerned Investigators

• It is the responsibility of the Sponsor to ensure that SUSARs are reported to all concerned investigators. A concerned investigator is any investigator in trials sponsored by the same Sponsor who is using the same IMP.

• Note: Any immediate safety concerns must be communicated to all concerned investigators in an expedited fashion.

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

5. Un-blinding:

Breaking the Blind in an Emergency, refer to SOP 9 Un-blinding Procedures for NUH Sponsored IMP Clinical Trials (CTIMPS)

• CTIMP

• For blinded trials an independent assessment of the causality of the SAE being probably, or definitely as a result of the IMP and unexpected will be made by a delegate not involved in the running of the trial.

• The appointed individual/Clinical Trials Pharmacist will un-blind the subject following the procedure for un-blinding as described in the study protocol and SOP 9.

• No member of the investigating team will un-blind a subject or be notified of the result of un-blinding for the purpose of assessing an SAE (see appendix D).

• The delegate will consider whether further action is required and will discuss this with the PI/CI and the R&D Director/Deputy Director.

• The competent authorities (MHRA, UK) and main REC will be notified.

• Non-Investigational Medicinal Products (NIMPs)
- Products that are not the object of investigation (i.e. other than the tested product, placebo or active comparator) may be supplied to subjects participating in the trial and used in accordance with the protocol. This might be, for example, medicinal products such as support or rescue/escape medication for preventative, diagnostic or therapeutic reasons and/or to ensure that adequate medical care is provided for the subject.

- These medicinal products do not fall within the definition of investigational medicinal products (IMPs) in Directive 2001/20/EC and are called non-investigational medicinal products (NIMPs).

- If, following un-blinding, it is revealed that the subject received the comparator drug, but the event still meets the criteria of a SUSAR, in that it is unexpected according to the comparator reference document (which should be defined in the protocol), then it should be reported in an expedited fashion to the drug company holding the Marketing Authorisation (MA) for the comparator. The MA holder should be named in the Summary of Product Characteristics (SmPC).

- If un-blinding reveals the IMP to be placebo this will not require expedited reporting unless, in the opinion of the delegated individual, and the Investigator that the event was related to a reaction to the placebo.

- Other NIMPs used in the trial may also be subject to reporting requirements and details should be provided in the study protocol. The following scenarios when an adverse reaction to a NIMP would require reporting:

  a). If the adverse reaction is suspected to be linked to an interaction between a NIMP and an IMP and is serious and unexpected

  b). If a SUSAR is reported and it might be linked to either a NIMP or an IMP but cannot be attributed to only one of these

  c). If an adverse reaction associated with the NIMP is likely to affect the safety of the trial subjects

- SAEs associated with a NIMP should be reported to the Marketing Authorisation Holder (MAH) in order that this information may be used in the MAH’s ongoing safety monitoring procedures. The MAH should be named in the SmPC.
• A SAE associated with a NIMP which does not have a Marketing Authorisation in the UK must be notified to the MHRA.

• In addition to the above, there are other rare safety issues where the same SUSAR reporting requirements apply. A list of these can be found in the detailed guidance document for adverse reaction reporting, see http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/21_susar_rev2_2006_04_11.pdf

6. Annual Safety Reports (ASR)

The collection and reporting of adverse event (AE) data to the appropriate competent authority (CA), (in the UK MHRA) is compulsory, in accordance with the European Clinical Trials Directive 2001/20/EC (EUCTD).

The sponsor may delegate the responsibility for writing and submission of the annual safety report to the chief investigator (CI) of each trial. CI’s must submit their annual safety reports to the MHRA and the main REC and copy these reports and any accompanying correspondence to the R&D department. It may be necessary for the CI to confer with the medical advisor or Data Safety Monitoring Committee (DSMC) prior to preparation of the report. http://www.ct-toolkit.ac.uk/_db/_documents/Joint_Project_Guidance_on_Pharmacovigilance.pdf

The annual safety report is due annually:

• The date on the CTA approval letter is referred to as the birth date for that trial. The annual safety report is based on data collected in the year following the birth date and is due on the anniversary of the birth date

• If a trial has a CTA but has not yet started, once a CTA has been granted, annual safety reports will be due as described above, regardless of whether the trial has actually started.

If the trial is also being conducted outside the UK this will include CA’s and appropriate REC’s of the European member states involved. ASR’s must be submitted to the CA (MHRA), main REC and copied in to R&D within 60 days of the due date.

7. Pregnancy during a trial
Pregnancy occurring in a participant or in a female partner of a male participant in a Clinical Trial of Investigational Medicinal Product (CTIMP), while not considered an adverse event or serious adverse event requires monitoring and follow up by the investigator. PI/CI must collect all information to determine outcome, including spontaneous or voluntary termination, details of birth, and the presence or absence of birth defects, congenital abnormalities, or maternal and/or newborn complications. Any occurrences that result in an SAE should be reported as per this guidance document.

Any pregnancy should be reported by the CI to the sponsor using either a study specific or the pregnancy reporting form in appendix E.

Guidance on the procedure for recording and reporting pregnancy should be included in the study protocol.

8. **Trust Reportable Incidents**

An adverse event that occurs during research may also fulfil the definition of a NUH Trust reportable “near miss”, untoward incident or serious untoward incident. In addition to informing the sponsor, the Ethics Committee and the R&D Department, where appropriate it is the researcher’s responsibility to complete a Trust untoward incident form.


When completing this form it is necessary to identify that the individual concerned is a research team member or participant involved in a research project, and what the relationship to any medicinal product or to the conduct of the research project is.

9. **Assessment of Causality**

The Clinical Trial Regulations 2004 (amendment 2006) require the relationship of the adverse event to the medicinal product being studied be determined. The classification system below can be utilised to assess causality, however it is not mandatory to use these categories.

**Not related:** Where a temporal (timely) relationship of the onset of the event, relative to the administration of the product is not reasonable e.g. cut finger, or where another cause can explain the occurrence of the event by itself e.g. headache associated with migraine.

**Unlikely:** Where a temporal (timely) relationship of the onset of the event, relative to the administration of the product is unlikely but cannot be ruled out eg mouth ulcer following administration of oral drug.

**Possibly related:** Where a temporal (timely) relationship of the onset of the event, relative to the administration of the product is reasonable, but the event could have been due to an equally likely cause e.g. headache.

**Probably related:** Where a temporal (timely) relationship of the onset of the event, relative to the administration of the product is reasonable and the event is more likely
to be explained by the medicinal product than any other cause e.g. nausea and vomiting

**Definitely related:** Where a temporal (timely) relationship of the onset of the event, relative to the administration of the product is reasonable and there is no other cause to explain the event (or a re-challenge is positive) e.g. bone marrow depression following administration of cytotoxic chemotherapy.

Out of these 5 categories, “possibly”, “probably” and “definitely” related to a medicinal product qualify as **adverse reactions.** “Unlikely” and “not related” do not qualify as a reasonable causal relationship

**Procedure for downgrading of causality assessments**

If there is a difference in opinion between the CI and PI over causality assessment, both assessments are recorded with the most conservative assessment being taken for regulatory purposes.

The Sponsor cannot downgrade the Investigators opinion. If there is disagreement record both.

**10. Useful links**

**MRC/DH Clinical Trials Tool Kit – trial management and closure:**

http://www.ct-toolkit.ac.uk/route_maps/stations.cfm?current_station_id=317&view_type=map

**European Clinical Trial Database (EudraCT) supporting documentation:**

*i) Detailed Guidance Documents:*


*ii) CT Regulations:*

http://www.uk-legislation.hmso.gov.uk/si/si2004/20041031.htm

**Good Clinical Practice Guidelines:**


**Trust Reportable Incidents:**
11. Review period
R&D Manager or RG facilitator will review this SOP on a biennial basis, unless new local national and/or international recommendations require and earlier review.
### ADVERSE EVENT RECORDING FORM

<table>
<thead>
<tr>
<th>(1) Project and Subject Identifiers: (If applicable)</th>
<th>(2) Project Title:</th>
</tr>
</thead>
<tbody>
<tr>
<td>EudraCT No:</td>
<td></td>
</tr>
<tr>
<td>CSP No:</td>
<td></td>
</tr>
<tr>
<td>Initials:</td>
<td></td>
</tr>
<tr>
<td>R&amp;D:</td>
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</table>

<table>
<thead>
<tr>
<th>(3) Description of Event (include date and time of onset)</th>
<th>(4) Causal relationship to Project/ Intervention/ Project Specific Action (Please tick one)</th>
<th>(5) Seriousness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Definite □</td>
<td>Mild □</td>
</tr>
<tr>
<td></td>
<td>Probable □</td>
<td>Moderate □</td>
</tr>
<tr>
<td></td>
<td>Possible □</td>
<td>Severe/Serious*</td>
</tr>
<tr>
<td></td>
<td>Unlikely □</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unrelated □</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>(6) Event/Reaction Outcome</th>
<th>(7) Action taken/Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recovered      Yes □ No □</td>
<td>If yes, date of recovery …………</td>
</tr>
<tr>
<td>Improved        Yes □ No □</td>
<td>If yes, date ……………………</td>
</tr>
<tr>
<td>On-going        Yes □ No □</td>
<td>If yes, details ……………………</td>
</tr>
<tr>
<td>Worsened        Yes □ No □</td>
<td>If yes, date ……………………</td>
</tr>
</tbody>
</table>

(8) Reviewing of all events is the responsibility of the researcher and as such must ensure that the participants are not compromised. Any appropriate action must be taken to protect the participants, research team and Trust whilst ensuring validity of the results. If the action taken leads to suspension, cessation or amendment of the study, then the sponsor, R&D and the relevant ethics committee must be notified.

(9) Completed by:

Name: .................................................. Signature: .................................. Date:
In some circumstances an adverse event that occurs during research may also fulfill the definition of a “near miss”, untoward incident or serious untoward incident. In addition to informing the sponsor, ethics committee and R&D department, where appropriate, it is the researchers responsibility to complete a trust untoward incident form. (See part 5 of the Guidance Notes).

A generic “Event Recording form” can be found in appendix A.

Copies of the “Serious Event Reporting form” can be found in appendix C.

If documentation is not provided, the NUH “Serious Event Reporting form” can be utilised.

The project report is sent out to the lead researcher annually for completion and return to R&D.

Reviewing of all events is the responsibility of the researcher and as such must ensure that the participants are not compromised by any appropriate action must be taken to protect the participants whilst ensuring validity of the results. If the action taken leads to suspension, cessation or amendment of the study, then the sponsor must inform R&D and the relevant ethics committee.
Appendix C

SERIOUS EVENT REPORTING FORM

When completing this form please refer to “SOP Guidance on Adverse Event Recording, Reporting & Reviewing for Researchers”

1. Project Identifiers: (where applicable)

<table>
<thead>
<tr>
<th>R&amp;D No.</th>
<th>Ethics No.</th>
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<tbody>
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<table>
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<tr>
<th>EudraCT No.</th>
<th>CSP No.</th>
<th>OTHER</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
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</tbody>
</table>

2. Project Title:


3. Sponsor Organisation:


4. Subject Identifiers:

<table>
<thead>
<tr>
<th>Initials:</th>
<th>Date of Birth:</th>
<th>Age:</th>
<th>Sex:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Male</td>
</tr>
</tbody>
</table>

Unique Study Identifier:


5. Does this event meet the definition of a SUSAR? Yes [ ] No [ ]

6. Event/Reaction Information:

<table>
<thead>
<tr>
<th>Date of Onset:</th>
<th>Time of Onset:</th>
</tr>
</thead>
<tbody>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

Description of Event: *e.g. Lab Tests/Results, Signs & Symptoms related to Diagnosis*
6.1. **Result: (Please tick one)**

- Death
- Hospitalisation/Prolongation of a current hospitalisation (i.e., ‘In Patient study’)
- Congenital anomaly
- Or birth defect
- Persistent or Significant Disability or Incapacity
- Life Threatening

7. **Suspected Medicinal Product Information (tick if not applicable)**

<table>
<thead>
<tr>
<th>Name of Medicinal Product (s):</th>
<th>Daily Dose (s):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication(s) for use:</td>
<td>Route of Administration:</td>
</tr>
<tr>
<td>Start/End Date of Therapy:</td>
<td>Was Medicinal Product Discontinued: Yes ☐ No ☐</td>
</tr>
</tbody>
</table>

- What is the Causal Relationship of the Reaction to the Medicinal Product? *(Please tick one below)*
  - Definite
  - Probable
  - Possible
  - Unlikely
  - Unrelated

- Has Unblinding Occurred? (Please tick one, if yes please provide details below)
  - Yes ☐ No ☐

8. **Concomitant Medications and Relevant Medical History:**

- Concomitant Meds: State Dose, Route and Start/End Dates (exclude those used to treat reaction)

- Other Relevant Medical History:
### 9. Event/Reaction Outcome:

<table>
<thead>
<tr>
<th>Event/Reaction</th>
<th>Outcome</th>
<th>Yes:</th>
<th>No:</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Recovered</td>
<td></td>
<td></td>
<td></td>
<td>If yes, date of recovery:</td>
</tr>
<tr>
<td>2) Improved</td>
<td></td>
<td></td>
<td></td>
<td>If yes, date:</td>
</tr>
<tr>
<td>3) Ongoing</td>
<td></td>
<td></td>
<td></td>
<td>If yes, details:</td>
</tr>
<tr>
<td>4) Worsened</td>
<td></td>
<td></td>
<td></td>
<td>If yes, date:</td>
</tr>
<tr>
<td>5) Subject Died</td>
<td></td>
<td></td>
<td></td>
<td>If yes, date of death:</td>
</tr>
</tbody>
</table>

### 10. Project Management Outcome:

<table>
<thead>
<tr>
<th>Project Management</th>
<th>Outcome</th>
<th>Yes:</th>
<th>No:</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the project continuing?</td>
<td></td>
<td>Yes:</td>
<td>No:</td>
<td>If yes, give details:</td>
</tr>
<tr>
<td>Have any changes/amendments been made to the project?</td>
<td>Yes:</td>
<td>No:</td>
<td>If yes, give details:</td>
<td></td>
</tr>
<tr>
<td>Has the project been suspended?</td>
<td>Yes:</td>
<td>No:</td>
<td>If yes, date of suspension:</td>
<td></td>
</tr>
<tr>
<td>Decision to suspend taken by:</td>
<td></td>
<td></td>
<td></td>
<td>.........................................................</td>
</tr>
<tr>
<td>Has the project been terminated?</td>
<td>Yes:</td>
<td>No:</td>
<td>If yes, date of termination:</td>
<td></td>
</tr>
<tr>
<td>Decision to terminate taken by:</td>
<td></td>
<td></td>
<td></td>
<td>.........................................................</td>
</tr>
</tbody>
</table>

### Additional Criteria for final/follow-up report
**GENERAL INSTRUCTIONS**

**SAE’s**

Retain this form in the Trial Master File.

**SUSAR’s**

1. **Hand-deliver a copy of the above form to:**
   - Research and Development (SUSAR Report)
   - E11 Curie Court
   - Nottingham University Hospitals NHS Trust
   - Queen's Hospital Campus
   - Derby Road
   - Nottingham
   - NG7 2UH
   
   OR

2. **email a copy to rdsae@nhs.nuh.uk,** Fax a copy to 35295 (Internal), 0115 8493295 (External) and phone R&D Dept on ext 61049 to confirm arrival.

   Any queries please contact a member of staff in the R&D department:

   Telephone: 0115 9709049 or 0115 9249924 ext 61049

<table>
<thead>
<tr>
<th>Name of Person Completing the Form:</th>
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<tr>
<td>Signature:</td>
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<tr>
<td>Designation in Relation to Study:</td>
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<td>Name of Investigator:</td>
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<td>Signature:</td>
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SOP 11 Adverse Events Monitoring, Reporting and Recording for Investigators
Serious adverse reaction

Assess expectedness

DO NOT EXPEDITE  EXPECTED

Test product(s)

EXPEDITE

DO NOT EXPEDITE

1 for any of the test products administered to that subject

EXPECTED

UNEXPECTED

Assess expectedness for comparator product

Break blind

2 If the reaction is unexpected for the actual test or comparator product administered to that trial subject

EXPEDITE

EXPEDITE

Placebo

EXPEDITE (if reaction to component of placebo)
Appendix E

**PREGNANCY NOTIFICATION FORM**

1. **MATERNAL INFORMATION**
   - **DOB (dd/mm/yyyy)**
   - **Date of last menstrual period (dd/mm/yyyy)**
   - **Expected date of delivery (dd/mm/yyyy)**
   - Method of contraception
   - Contraception used as instructed?
     - ☐ Yes
     - ☐ No
     - ☐ Uncertain

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)
   - **Gestation week**
   - **Outcome including any abnormalities**
   
<table>
<thead>
<tr>
<th>Week</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>1</td>
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<tr>
<td>2</td>
<td></td>
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<tr>
<td>3</td>
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</tbody>
</table>

4. **DRUG INFORMATION** (list all therapies taken prior to and during pregnancy)
   - **Name of drug**
   - **Daily dose**
   - **Route**
   - **Date started (dd/mm/yyyy)**
   - **Date stopped (dd/mm/yyyy)**
   - **Indication**
   - **Treatment start (week of pregnancy)**
   - **Treatment stop (week of pregnancy)**

5. **PRENATAL INFORMATION**
   - Have any specific tests, eg amniocentesis, ultrasound, maternal serum AFP, been performed during the pregnancy so far?
     - ☐ No
     - ☐ Yes
     - ☐ Not known
   - If yes, please specify test date and results:

6. **PREGNANCY OUTCOME**
   - **Abortion:**
     - ☐ Therapeutic
     - ☐ Planned
     - ☐ Spontaneous
   - Please specify the reason and any abnormalities (if known):
   - **Delivery:**
     - ☐ Normal
     - ☐ Forceps/Ventouse
     - ☐ Caesarean
   - Maternal complications or problems related to birth:
7. MATERNAL PREGNANCY ASSOCIATED EVENTS:
If the mother experiences an SAE during the pregnancy, please indicate here and complete an SAE form and submit to DCTU immediately

8. CHILD OUTCOME
- Normal
- Abnormal
- Stillbirth
If any abnormalities, please specify and provide dates

Sex
- Male
- Female

<table>
<thead>
<tr>
<th>Height</th>
<th>Weight</th>
<th>Apgar scores</th>
<th>Head circumference</th>
</tr>
</thead>
<tbody>
<tr>
<td>cm</td>
<td>kg</td>
<td>1 min</td>
<td>5 mins</td>
</tr>
</tbody>
</table>

9. ASSESSMENT OF SERIOUSNESS (OF PREGNANCY OUTCOME)
- Non serious
- Life-threatening
- Results in persistent or significant disability/incapacity
- Other seriousness criteria
- Congenital anomaly/birth defect
- Other significant medical events

10. ASSESSMENT OF CAUSALITY (OF PREGNANCY OUTCOME)
Please indicate the relationship between pregnancy outcome
- Unrelated
- Possibly*
- Probably*
- Definitely*
If any of the *fields have been checked, the outcome is considered to be RELATED to the study drug.

11. ADDITIONAL INFORMATION

12. INFORMATION SOURCE
Name, address and telephone number of PI:

Date of report (dd/mm/yyyy)

PI signature

13 ECTU TRACKING (INTERNAL USE ONLY)
Report received by

ALL REPORTS MUST BE SIGNED AND DATED BY THE PRINCIPAL INVESTIGATOR. PLEASE SEND ALL REPORTS TO NHS R&D, Pharmacovigilance

Email: rdsae@nuh.nhs.uk
Fax: 0115 8493295
<table>
<thead>
<tr>
<th>R&amp;D reference:</th>
<th>Centre (if multicentre trial):</th>
<th>DO NOT SEND IDENTIFIABLE DATA OR SOURCE DOCUMENTS WITH THIS REPORT</th>
</tr>
</thead>
<tbody>
<tr>
<td>EudraCT number:</td>
<td>Subject ID:</td>
<td></td>
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<tr>
<td>Study Title:</td>
<td>Subject initials:</td>
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</tr>
</tbody>
</table>

Report received on (dd/mm/yyyy)

Action taken
## SERIOUS EVENT TRACKING FORM

**PROJECT TITLE:**  

<table>
<thead>
<tr>
<th>R&amp;D No:</th>
<th>Ethics No:</th>
<th>Eudract No.</th>
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</table>

**Sent From:**  

<table>
<thead>
<tr>
<th>CHECKLIST</th>
<th>Initial Report Received by email/fax/hand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reviewed by:</td>
<td>Date: ………………...</td>
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<tr>
<td>Date reviewed:</td>
<td>Date: ………………...</td>
</tr>
<tr>
<td>Date Faxed to competent authority (MHRA)</td>
<td>Date: ………………...</td>
</tr>
</tbody>
</table>

| Final report Received by email/fax/hand |
| Reviewed by: | Date: ………………... |
| Date reviewed: | Date: ………………... |
| Date Faxed to competent authority (MHRA) | Date: ………………... |

If SUSAR  

| Date Faxed to competent authority (MHRA) | Date: ………………... |
| Date informed Lead REC | Date: ………………... |

| If fatal/life threatening to report within 7 days (+ for further information 8 days, non-fatal/life threatening within 15 days) | Date: ………………... |
| Copy and report sent to R&D Department | Date: ………………... |

**COPY FOR PROJECT FILE:**  

**COPY FOR R&D SERIOUS EVENTS FILE:**  

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SOP 11 Adverse Events Monitoring, Reporting and Recording for Investigators
Fax machine/ mail tray/ RDSA E server
folder to be checked twice daily by Admin for
SAE/SUSAR Forms: establish if the report is
an Initial or Final report.

Forward the report to Research Managers the RM &
Governance facilitators for immediate attention

Complete the R&D departmental Serious Event Tracking
form located in departmental SAE file

Is the SAE a SUSAR?

NO

YES

SAE/SAR/ADR reports to be retained
in the project file and one copy in the
R&D Serious Events file.
Save all documents in the electronic
study file

NUH are the sponsor so the trial will be registered
with the MHRA eSUSAR website and must be reported
via this route

esusar@mhra.gsi.gov.uk

If the CTU is responsible for the Trial, they will report to the
MHRA and to the Ethics Committee which gave favourable
opinion and then notify the R&D.

INITIAL NOTIFICATION OF A FATAL OR LIFE THREATENING SERIOUS
EVENTS MUST BE RECEIVED BY THE MHRA WITHIN 7 CALENDAR DAYS
AFTER THE RESEARCHER HAS FIRST KNOWLEDGE OF THE EVENT, AND
THE FINAL REPORT MUST BE RECEIVED WITHIN A FURTHER 8 CALENDAR
DAYS.

Retain the receipt of fax/report in the serious event file. Place one
copy of both the SUSAR form and the tracking form in the relevant
project file and one copy in the R&D Serious Events file.
Document the follow up and the outcome of the event and any
action required by R&D. Save all documents in the electronic study
file.