UNIVERSITY OF LEICESTER, UNIVERSITY OF LOUGHBOROUGH

&

UNIVERSITY HOSPITALS OF LEICESTER NHS TRUST

JOINT RESEARCH SUPPORT OFFICE

STANDARD OPERATING PROCEDURES

UHL Research Support Office
SOP S-1041 UHL V1 March 2019

Standard Operating Procedure for the processing and reporting of Medical Device Deficiencies, Serious Adverse Events, Serious Adverse Device Effects, and Unexpected Serious Adverse Device Effects for Non CE Marked and Proof of Concept Medical Device Studies (NOT requiring MHRA Approval) Sponsored by University Hospitals of Leicester NHS Trust

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 (UHL) for identifying, documenting and reporting all adverse events (AEs) for medical device studies (NOT requiring MHRA approval) sponsored by University Hospitals of Leicester.

In order to comply with the appropriate legislation, all researchers must be aware of the definitions and procedures in relation to AEs for medical device studies. This legislation includes:

- Medical Device Regulations 2002
- European Commission Guidelines on Medical Devices MEDDEV 2.7/3

1 SCOPE

This SOP applies to all staff and external individuals involved in research activity involving CE Marked Devices utilised within their intended purpose and Proof of Concept studies NOT requiring MHRA approval.

2 DEFINITIONS

Medical Device
A medical device is defined as any instrument, apparatus, appliance, material or other article, whether used alone or in combination with any software necessary for its proper application which is:

a) Intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purpose(s) of:
• diagnosis, prevention, monitoring, treatment or alleviation of disease
• diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury
• investigation, replacement, modification, or support of the anatomy or of a physiological process
• supporting or sustaining life
• control of contraception
• disinfection of medical devices

b) which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its intended function by such means.

This definition of medical device is as per ISO 14155 Clinical investigation of medical devices for human subjects - Good Clinical Practice and **does not apply to in vitro** diagnostic medical devices (which is covered by ISO 13485:2003).

**Investigational Medical Device**
An Investigational Medical Device is a medical device being assessed for safety or performance in a clinical investigation. This includes medical devices already on the market that are being evaluated for new intended uses, new populations, new materials or design changes.

**Device Deficiency**
Inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use error and inadequate labelling.

**Device Malfunction**
Failure of an investigational medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or Clinical Investigation Plan (CIP).

**CE Marked Device Studies**
Post-marketing studies where the product is used within its intended purpose.

**Proof of Concept Studies**
Devices manufactured in-house in a healthcare establishment that are usually produced as a one-off model or in small numbers to determine ‘proof of concept’. Provided such devices are used within the same legal entity and on patients of that Trust, then the device(s) are **not** subject to the provisions of the Medical Devices Regulation.

**Clinical Investigation Plan (CIP)**
A document that states the rationale, objectives, design and proposed analysis, methodology, monitoring, conduct and record keeping of the clinical investigation.

**Investigator’s Brochure (IB)**
A compilation of the current clinical and non-clinical information on the investigational medicinal device relevant to the clinical investigation.
Adverse Event (AE)
An adverse event (AE) is an untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device/intervention.

An AE can therefore be any unfavourable and unintended sign (including abnormal laboratory results), symptom or disease temporarily associated with the use of the investigational medical device/intervention, whether or not considered to be related to the investigational medical device/intervention.

Adverse Device Effect (ADE)
An adverse device effect (ADE) is an adverse event that is deemed to be related to the use of an investigational medical device. This includes any adverse event resulting from insufficiencies or inadequacies in the instructions for use, the deployment, the implantation, the installation, the operation, or any malfunction of the investigational medical device.

An ADE includes any event that is a result of use error or intentional misuse. Use error refers to an act or omission of an act that results in a different device response than intended by the manufacturer or expected by the user. An unexpected physiological response of the subject does not in itself constitute a use error.

Serious Adverse Event (SAE)
In medical device studies a Serious Adverse Event (SAE) is defined by ISO14155:2011 guidelines for medical device studies as an untoward occurrence in a trial subject that:
- led to a death
- led to serious deterioration in the health of the participant, that either resulted in:
  - a life-threatening illness or injury, or
  - a permanent impairment of a body structure or a body function
  - in patient hospitalisation or prolonged in-patient hospitalisation
  - medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function.
- led to foetal distress, foetal death or a congenital abnormality or birth defect.

NOTE 1: This also includes device deficiencies that might have led to a SAE if:
- suitable action have not been taken
- intervention had not been made
- if circumstances had been less fortunate

NOTE 2: A planned hospitalisation for a pre-existing condition, or procedure required by the Clinical Investigation Plan (CIP) without a serious deterioration in health is not considered to be a serious adverse event.
Serious Adverse Device Effect (SADE)
A SADE is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

Anticipated Serious Adverse Device effect (ASADE)
A serious adverse device effect which by its nature, incidence, severity or outcome has been previously identified in the current version of the Risk Assessment or the Investigator’s Brochure.

Unanticipated Serious Adverse Device Effect (USADE)
A serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the Risk Assessment and/or Investigator’s Brochure.

3 IDENTIFICATION AND RECORDING OF ADVERSE EVENTS/DEVICE DEFICIENCIES
The Principal Investigator (PI) at site or designee, is responsible for the identification of any AE as defined in the protocol/CIP. AE/ADEs defined as non-serious in nature must be recorded in the medical records and the Adverse Event/Device Effect record (Appendix 2). Device Deficiencies must be reported on Appendix 8 and retained with the case report form (CRF), unless it forms part of the CRF and is agreed by the Sponsor.

All AE and ADEs must be observed to ensure that they do not escalate to an SAE/SADE. There are no requirements to report these events to the Sponsor or Regulatory Agencies unless the AE meets the criteria of a SAE where the procedure described in section 5 must be followed.

5 REPORTING OF ADVERSE EVENTS

5.1 REPORTING TO SPONSOR
All SAEs/SADEs/USADEs and Device Deficiencies in studies sponsored by UHL must be reported to the Sponsor within 24 hours of the research team becoming aware of the event unless they are listed in the protocol/clinical investigation plan as expected events. UHL Serious Adverse Event/Device Effect Report Form C for medical device studies (Appendix 3) must be used. This form and associated completion guidance document (Appendix 4) are both available on the UHL Website: www.leicestersresearch.nhs.uk. This form and any documents provided to the Sponsor in support of the SAE/SADE/USADE MUST be anonymised and MUST not contain any patient identifiable data.
For UHL Sponsored studies, the Chief Investigator (CI) or Principal Investigator (PI) or the Sponsor delegated qualified individual is responsible for the review and sign-off of all serious adverse event/effects. In the event that the CI/PI is unable to sign the report immediately, the research team/site should not delay sending the report, however a CI/PI signed copy must be forwarded to the Sponsor as soon as possible (and within 7 days of the initial reporting). The research team/site must provide any additional information actively following-up the subject until either:

- The SAE/SADE/USADE resolves, or
- Until 30 days after the discontinuation of use of the medical device

After discussion with, and in 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.

5.1.1 Multi-Centre studies

SAEs and SADEs and Device Deficiencies from all sites must be sent to the Sponsor utilising the multicentre serious adverse events/serious adverse device effect line listing table (Appendix 5) and Device Deficiency Report Form (Appendix 8) SOP 1041. Where sites are managed through a third party contractor (e.g., a Clinical Trials Unit (CTU)), it may be appropriate to make alternative arrangements for reporting. These arrangements will be specifically detailed in the third party agreement. All SAE/SADE and Device Deficiency reports will be reviewed by the Director of R&I at the monthly R&I Management Meeting.

5.2 REPORTING TO MHRA

Device related events involving a CE marked device/proof of concept studies in a post market surveillance study must be reported to the MHRA Adverse Incident Centre [https://aic.mhra.gov.uk/](https://aic.mhra.gov.uk/). Individual guidance on the reporting requirements for certain types of devices can be found on the MHRA website [https://www.gov.uk/government/collections/medical-devices-guidance-for-manufacturers-on-vigilance](https://www.gov.uk/government/collections/medical-devices-guidance-for-manufacturers-on-vigilance).
5.3 Reporting to REC

The following SAEs/SADEs are considered reportable to the REC that gave the favourable ethical opinion:
- Those related to the administration of the medical device or any of the research procedures.
- USADEs- i.e. unanticipated events not listed in the Risk Assessment/Protocol as an anticipated occurrence.

Reports should be submitted within 15 days of the Chief Investigator becoming aware of the event using the Non-CTIMP Safety Report Form to the REC published on the HRA website [http://www.hra.nhs.uk/](http://www.hra.nhs.uk/).

The Chief Investigator is also required to include a report of the safety of participants in the annual progress report to the REC.

Individual reports will be reviewed by the REC at a subcommittee or committee meeting. Any requests for further information should be provided as applicable and all correspondence should be copied to the Sponsor.

5.4 Reporting to NHS Trust
Where applicable, SAEs, SADE or USADEs, Device Deficiencies which occur at site must be reported on the Trusts electronic incident reporting system (e.g. Datix). Reporting of incidents must be carried out in accordance with the Trusts Incident and Accident reporting policy.

6 Assessment of Adverse Events

All assessments of AEs must be made by the Chief Investigator (CI)/Principal Investigator (PI) or the Sponsor agreed delegated medically qualified individual. The study Delegation of Authority and Signature Log must reflect this (Appendix 1 SOP S-1006 Informed consent for research sponsored by UHL).

Each AE must be assessed for seriousness, severity, causality and expectedness. Where there are two assessments of causality, for example, the CI/PI assessment do not concur, the causality made by the Investigator cannot be downgraded.

6.1 Assessment of seriousness

The assessor should make an assessment of seriousness as defined in section 3 Serious Adverse Events.

6.2 Assessment of Severity

The relationship between the investigational medical device and the occurrence of each adverse event must be assessed utilising the device event categorisation flow chart (Appendix 1).
<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>Non Device Related</th>
<th>Device or Procedure Related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-serious</td>
<td>Adverse Event (AE)</td>
<td>Adverse Device Effect (ADE)</td>
</tr>
<tr>
<td>Serious</td>
<td>Serious Adverse Event (SAE)</td>
<td>Serious Adverse Device Effect (SADE)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anticipated</td>
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<td></td>
<td></td>
<td>Unanticipated</td>
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<tr>
<td></td>
<td></td>
<td>Anticipated Serious Device Effect (ASADE)</td>
</tr>
</tbody>
</table>

### 6.2 ASSESSMENT OF CAUSALITY

The assessor of any causality assessments will use clinical judgement to determine the relationship. The assessor must consult the current version of the Risk Assessment and/or the Investigator’s Brochure where available.

When making a causality assessment, the following definitions should be used:

**Not related**  
There is no evidence of causal relationship to the Investigational Device.

**Unlikely**  
The relationship with the use of the investigational medical device seems not relevant and/or the event can be reasonably explained by another cause.

**Possible**  
The relationship with the use of the investigational medical device is weak but cannot be ruled out completely.

**Probable**  
The relationship with the investigational medical device seems relevant and/or the event cannot reasonably be explained by another cause.

**Causal Relationship**  
The serious event is associated with the investigational medical device beyond reasonable doubt.
6.3 ASSESSMENT OF EXPECTEDNESS

The assessor must consult the current version of the Investigator Brochure and/or Risk Assessment to determine where an event is expected. Where applicable in blinded studies, unblinding must occur to assess treatment assignment.

If the event is classified as an anticipated effect, which by its nature, incidence severity or outcome has been previously identified in the Risk Assessment and/or Investigator Brochure (IB) and/or the Protocol. This event does not require reporting to the Sponsor or Regulatory Agencies but must be recorded in the medical records and the adverse event record (Appendix 2). This document must be retained with the case report form unless it forms part of the case report form (CRF) and is agreed by the Sponsor.

Where an event could be related to the medical device and is unanticipated in relation to the Investigator Brochure (IB)/Risk Assessment, the Investigator must report this event immediately or within 24hrs to the Sponsor/Manufacturer and to the Regulatory Agencies within the required timelines.

7 QUARANTINE OF DEVICES

The device must not be returned to the manufacturer until the MHRA has been given the opportunity to carry out/completion an investigation. In addition, the device should not be:

- Discarded
- Repaired
- Returned to the manufacturer

All material evidence i.e. devices/parts removed, replaced or withdrawn from use following an incident, instructions for use, records of use, repair and maintenance records, packaging materials, or other means of batch identification must be:

- clearly identified and labelled
- stored securely

Evidence should not be interfered with in any way except for safety reasons or to prevent its loss. Where appropriate, a record should be made of all readings, settings and positions of switches, valves, dials, gauges and indicators, together with photographic evidence and eyewitness reports.

N.B: Consideration should be given to the practicality and implications of quarantining the device; for example if the device is an implantable device all further supplies of the device should be quarantined as a precaution until further advice is sought.

The Investigator and the Sponsor will undertake any requirements outlined in the MHRA investigation and follow-up as instructed.
8 FOLLOW UP OF ADVERSE EVENTS BY SPONSOR

Acknowledgement will be issued to the Investigator from the Sponsor via email within 7 days of receipt of a fully completed form, and this must be filed in the TMF/ISF.

Each SAE/SADE/USADE will be registered on the recognised Sponsor database and reviewed by the Sponsor or their delegate, as per Appendix 6 (Medical Device SAE/SADE review process flowchart). This review may lead to queries being issued by the Sponsor/delegate to request signed documentation, clarify information or complete event outcome. All queries will be sent via email and must be responded to within the stated timeframe as per the SAE/SADE Template Email (Appendix 7).

All SAE/SADE/USADE reported to the Sponsor will be reviewed at the R&I Management Meeting by the Director of R&I.

9 Documentation

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

- SAE, SADE, USADE reports and follow-up information
- Adverse event/device effect document (Appendix 2)
- Device Deficiency Report Form (Appendix 8)
- Evidence of submission and receipt of SAE/SADEs to the Sponsor and Regulatory Agencies within the required timeframe
- Evidence of timely notifications to the MHRA and main REC

The investigator must ensure that all SAE/SADE/USADE information is recorded accurately in the medical notes and the study CRF.

10 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 CI/PI/Delegated individual</td>
<td>CI/PI/Delegated individual</td>
<td>Report all serious adverse events/device effects to the Sponsor (except those identified as exempt).</td>
</tr>
<tr>
<td>2 CI/PI/Delegated Individual</td>
<td>CI/PI/Delegated individual</td>
<td>Follow up the initial report with a detailed written follow up/report if not all information is available at the time of initial reporting.</td>
</tr>
<tr>
<td>3 CI/Delegated Individual</td>
<td>CI/Delegated Individual</td>
<td>Completion of adverse event/adverse device effect/Device Deficiency reports and/or line listing and review and sign off by Chief Investigator.</td>
</tr>
<tr>
<td>4 Sponsor</td>
<td>Sponsor or designee</td>
<td>Ensures that all reportable events are notified to the MHRA and REC within mandatory timelines.</td>
</tr>
<tr>
<td>5 CI/PI/Delegated individual</td>
<td>CI/PI/Delegated individual</td>
<td>Supply the Sponsor, and the REC with any additional information requested.</td>
</tr>
<tr>
<td>6 Sponsor</td>
<td>Sponsor</td>
<td>Monitor all SAE/SADE line listings reported on a monthly basis to identify and if necessary act upon any emerging safety issues.</td>
</tr>
<tr>
<td>7 Sponsor</td>
<td>Clinical Trial Monitor</td>
<td>The Monitor will review SAE/SADE submissions and request further clarification/information as required to ensure SAE/SADE report completion. The CI/PI will be provided with Sponsor acknowledgement of receipt of the completed SAE/SADE.</td>
</tr>
</tbody>
</table>

11 Responsibilities

This table is used to track the development and approval of the document and any changes made on revised / reviewed versions.

<table>
<thead>
<tr>
<th>DEVELOPMENT AND APPROVAL RECORD FOR THIS DOCUMENT</th>
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<tbody>
<tr>
<td>Author / Lead Officer: Julie James</td>
</tr>
<tr>
<td>Reviewed by: Carolyn Maloney</td>
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<tr>
<td>Approved by: Professor Nigel Brunskill</td>
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<td>Date Approved: 08-07-19</td>
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<th>REVIEW RECORD</th>
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<th>DISTRIBUTION RECORD:</th>
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<tr>
<td>Date</td>
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</table>
Event Categorisation Flow Chart

1. Adverse Event
   - Does it meet seriousness criteria?
     - Yes → SAE
     - No → Is it Device-Product related?
       - Yes → ADE
       - No → AE

2. If Yes to Device-Product related:
   - Is it anticipated?
     - Yes → Anticipated SADE
     - No → Unexpected Serious Adverse Device Effect
<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Adverse event/ Device Effect Description</th>
<th>Start Date (DD/MMM/YYYY)</th>
<th>End Date (DD/MMM/YYYY)</th>
<th>Relationship to Procedure: 1=not related OR 2=mot likely OR 3=possible OR 4=probable OR 5=causal relationship</th>
<th>Relationship to Device: 1=not related OR 2=mot likely OR 3=possible OR 4=probable OR 5=causal relationship</th>
<th>SAE or Device Deficiency? Y/N</th>
<th>Expectedness Assessment: 1=Expected 2=Unexpected</th>
<th>Outcome: 1=Resolved 2=Resolved with sequelae 3=Ongoing 4=Fatal 5=Unknown</th>
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SOP S-1041 Appendix 2 Adverse Event/Adverse Effect Record V1 March 2019
Serious Adverse Event/Effect Report - Form C
UHL Sponsored Medical Device Studies

Sponsor Ref Number:  | IRAS Ref Number:  | MHRA Ref Number:  
Study Title:  
Patient Study Number and Initials:  
Site:  

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

1. Type of Report
(Tick one box only)

- [ ] Initial
- [ ] FollowUp
- [ ] Final
- [ ] Initial & Final

Date of Report

Date of Onset

Date of Study

Team Aware

Time team became aware (24 hr clock) [ ] : [ ]

Date reported to MHRA (if applicable)

Date reported to REC (if applicable)

2. Event
Enter keywords that best summarise the event

3. Serious Criteria:
(Tick one box only)

- [ ] Death
- [ ] Life threatening illness & injury
- [ ] Hospitalisation or prolongation of hospitalisation
- [ ] Permanent impairment of body structure or body function
- [ ] Medical or surgical intervention required to prevent any of the above
- [ ] Led to foetal distress, foetal death or congenital anomaly or birth defect
- [ ] Other (maybe protocol specific) – Specify

4. Narrative - Briefly describe the event (attach anonymised supporting documentation if applicable)

Admission Date [ ] [ ] [ ] [ ] Discharge Date [ ] [ ] [ ] [ ]

Event narrative:

SOP S-1041 Appendix 3 Serious Adverse Event/Effect Report Form C Version 1 March 2019
5. Study Medical Device Information:

Subject has been fitted/used/treated with the device?  If No □ - Give Reason (i.e. screening)

If Yes, provide details below:

<table>
<thead>
<tr>
<th>Name of Device</th>
<th>Indication for use</th>
<th>Route of administration/use</th>
<th>Date of first use</th>
<th>Date of last use</th>
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</tbody>
</table>

6. Assessment

If more than one device is being used, please complete an assessment for each device.

Name of Device (if applicable): 

Both the Causality & Expectedness MUST be completed by the CI/PI or other delegated medically qualified Investigator, as agreed by the Sponsor.

Causality and Expectedness:

Detail all possible and suspected causes including relevant medical history.

Causality: Relationship to Procedure
Not Related □ Unlikely □ Possibly □ Probable □ Casual Relationship (Related) □

Causality: Relationship to Device
Not Related □ Unlikely □ Possibly □ Probable □ Casual Relationship (Related) □

Expectedness

The assessment of expectedness must be based on the information contained in the approved Investigator Brochure and/or Risk Analysis Report and/or Protocol

Anticipated □ Unanticipated □
If more than one device is being used, please complete an assessment for each device

Name of Device (if applicable): ________________________________

Both the Causality & Expectedness MUST be completed by the CI/PI or other delegated medically qualified Investigator, as agreed by the Sponsor.

Causality and Expectedness:

Detail all possible and suspected causes including relevant medical history:

Causality: Relationship to Procedure
Not Related ☐ Unlikely ☐ Possibly ☐ Probable ☐ Casual Relationship (Related) ☐

Causality: Relationship to Device
Not Related ☐ Unlikely ☐ Possibly ☐ Probable ☐ Casual Relationship (Related) ☐

Expectedness

The assessment of expectedness must be based on the information contained in the approved Investigator Brochure and/or Risk Analysis Report and/or Protocol

Anticipated ☐ Unanticipated ☐

If the event is related and unanticipated it is an Unexpected Serious Adverse Device Event (USADE) and requires expedited reporting. Inform the Sponsor immediately. Telephone number 0116 252 5308 / 223 1660

7. Is the Study Device Blinded or Unblinded?
   Blinded ☐ Unblinded ☐

8. Has the subject been unblinded?    Yes ☐ No ☐ N/A ☐

9. Was the event related to a protocol violation?
   Yes ☐ No ☐
10. Was the subject withdrawn due to this event?
   Yes ☐ No ☐

11. Action taken regarding study device:
   ☐ None
   ☐ Device schedule adjusted
   ☐ Device Permanently Removed/Discontinued Date:
   ☐ Other – provide details

Detail treatment given

☐ Unknown at time of report
☐ Not applicable

12. Outcome of the Event
   ☐ Recovered Date of Recovery: ☐ ☐ ☐ ☐
   ☐ Recovered with Sequelae Date of Recovery: ☐ ☐ ☐ ☐
   ☐ On-going – details:

☐ 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/SADE

<table>
<thead>
<tr>
<th>Person completing report:</th>
<th>Principal Investigator/delegated medically qualified individual as agreed by the Sponsor:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name:</td>
<td>Name:</td>
</tr>
<tr>
<td>Role:</td>
<td>Role:</td>
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<td>Signature:</td>
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<tr>
<td>Date:</td>
<td>Date:</td>
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<tr>
<td>Contact No:</td>
<td>Contact No:</td>
</tr>
</tbody>
</table>

Please return the completed form and copies of any additional anonymised documents to the Research Governance Office or by email to RIAdmin@uhl-tr.nhs.uk

Reporting of USADEs to the Research Ethics Committee and Regulatory Authority for UHL sponsored studies will be undertaken in accordance with SOP S-1041
Serious Adverse Event/Effect Report - Form C
UHL Sponsored Medical Device Studies

Sponsor Ref Number:  IRAS Ref Number:  MHRA Ref Number:

Study Title:  

Patient Study Number and Initials:  

Site:  

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

1. Type of Report  
   (Tick one box only)  
   
   Initial  
   FollowUp  
   Final  
   Initial & Final  

Date of Report  

Date of Onset  

Date of Study  

Team Aware  

Time team became aware (24 hr clock)  

Date reported to MHRA (if applicable)  

Date reported to REC (if applicable)  

2. Event  
   Enter keywords that best summarise the event  

3. Serious Criteria:  
   (Tick one box only)  
   
   Death  
   Life threatening illness & injury  
   Hospitalisation or prolongation of hospitalisation  
   Permanent impairment of body structure or body function  
   Medical or surgical intervention required to prevent any of the above  
   Led to foetal distress, foetal death or congenital anomaly or birth defect  
   Other (maybe protocol specific) – Specify  

4. Narrative - Briefly describe the event (attach anonymised supporting documentation if applicable)  

   Admission Date  
   
   Discharge Date  

Event narrative:  

SOP S-1041 Appendix 3 Serious Adverse Event/Effect Report Form C Version 1 March 2019
5. Study Medical Device Information:

Subject has been fitted/used/treated with the device?  If No □ - Give Reason (i.e. screening)

If Yes, provide details below:

<table>
<thead>
<tr>
<th>Name of Device</th>
<th>Indication for use</th>
<th>Route of administration/use</th>
<th>Date of first use</th>
<th>Date of last use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

6. Assessment

If more than one device is being used, please complete an assessment for each device.

Name of Device (if applicable):

Both the Causality & Expectedness MUST be completed by the CI/PI or other delegated medically qualified Investigator, as agreed by the Sponsor.

Causality and Expectedness:

Detail all possible and suspected causes including relevant medical history.

**Causality: Relationship to Procedure**
Not Related □ Unlikely □ Possibly □ Probable □ Casual Relationship (Related) □

**Causality: Relationship to Device**
Not Related □ Unlikely □ Possibly □ Probable □ Casual Relationship (Related) □

**Expectedness**

The assessment of expectedness must be based on the information contained in the approved Investigator Brochure and/or Risk Analysis Report and/or Protocol

Anticipated □ Unanticipated □
If more than one device is being used, please complete an assessment for each device

Name of Device (if applicable): ______________________________________

Both the Causality & Expectedness MUST be completed by the CI/PI or other delegated medically qualified Investigator, as agreed by the Sponsor.

Causality and Expectedness:

Detail all possible and suspected causes including relevant medical history:

Causality: Relationship to Procedure
Not Related □ Unlikely □ Possibly □ Probable □ Casual Relationship (Related) □

Causality: Relationship to Device
Not Related □ Unlikely □ Possibly □ Probable □ Casual Relationship (Related) □

Expectedness
The assessment of expectedness must be based on the information contained in the approved Investigator Brochure and/or Risk Analysis Report and/or Protocol

Anticipated □ Unanticipated □

If the event is related and unanticipated it is an Unexpected Serious Adverse Device Event (USADE) and requires expedited reporting. Inform the Sponsor immediately. Telephone number 0116 252 5308 / 223 1660

7. Is the Study Device Blinded or Unblinded?
   Blinded □ Unblinded □

8. Has the subject been unblinded?  Yes □ No □ N/A □

9. Was the event related to a protocol violation?
   Yes □ No □

SOP S-1041 Appendix 3 Serious Adverse Event/Effect Report Form C Version 1 March 2019
10. Was the subject withdrawn due to this event?
   Yes ☐ No ☐

11. Action taken regarding study device:
   ☐ None
   ☐ Device schedule adjusted
   ☐ Device Permanently Removed/Discontinued Date:
   ☐ Other – provide details ____________________________________________
   Detail treatment given

   ☐ Unknown at time of report
   ☐ Not applicable

12. Outcome of the Event
   ☐ Recovered Date of Recovery: ☐ ☐ ☐ ☐
   ☐ Recovered with Sequelae Date of Recovery: ☐ ☐ ☐ ☐
   ☐ On-going – details: ____________________________________________
   ☐ 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/SADE

<table>
<thead>
<tr>
<th>Person completing report:</th>
<th>Principal Investigator/delegated medically qualified individual as agreed by the Sponsor:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name:</td>
<td>Name:</td>
</tr>
<tr>
<td>Role:</td>
<td>Role:</td>
</tr>
<tr>
<td>Signature:</td>
<td>Signature:</td>
</tr>
<tr>
<td>Date:</td>
<td>Date:</td>
</tr>
<tr>
<td>Contact No:</td>
<td>Contact No:</td>
</tr>
</tbody>
</table>

Please return the completed form and copies of any additional anonymised documents to the Research Governance Office or by email to RIAadmin@uhl-tr.nhs.uk

Reporting of USADEs to the Research Ethics Committee and Regulatory Authority for UHL sponsored studies will be undertaken in accordance with SOP S-1041
Serious Adverse Event/Effect Report Form C

UHL Sponsored Medical Device Studies

Guidance Document

All Serious Adverse Events and Serious Adverse Device Effects MUST be reported within 24 hours of the research team becoming aware of the event.

The initial report may be submitted without a PI/delegated medically qualified individual (as agreed by the Sponsor) 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 days. If the patient is still an inpatient or there is an unavoidable delay in the provision of further information, inform the Research Governance 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 Research Governance Office. This MUST be documented to enable the Research Governance Office to identify the study.

IRAS Ref  IRAS reference can be located on HRA approval letter.

MHRA Ref  MHRA Reference number can be located on Clinical Trial Authorisation document.

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.

Site  Enter site name.

NO OTHER PATIENT IDENTIFIABLE DATA MUST BE ENTERED ON THIS FORM

1. Type of Report  Tick one box only

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.

SOP S-1041 Appendix 4 Form C Medical Device studies Guidance Document V1 March 2019
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 and outcome of the event are complete on the first submission of the report.

Date of Report
Date you are completing this report. If you are sending amended, follow-up or final reports, please ensure that you are using the current date and are not back-dating reports to the date on the report from the original submission.

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 UK/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/SADE must be submitted within 24 hours of this date.

Time Team Aware
Where possible the time that study team were made aware should be entered. If this is not known mark as unknown (UK).

Date Reported to MHRA
All reportable events as detailed in SOP S-1043 where there is an imminent risk of death, serious injury, or serious illness and that requires prompt remedial action for other patients must be reported to the MHRA immediately but no later than 2 calendar days after becoming aware of the event. Any other reported event must be reported immediately, but no later than 7 calendar days after becoming aware of the event.

Date Reported to REC
All reportable events as detailed in SOP S-1043 should be reported to the REC within 15 days of becoming aware of the event.

2. Event
Enter keywords that best summarise the event

3. Seriousness Criteria
Choose one box only from the menu. If there is more than one criteria, choose the most significant one. Multiple Serious Adverse Event/Effects MUST be reported on individual forms.

4. Narrative
If the SAE/SADE is due to an admission to hospital, provide the admission and discharge dates (if known). 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/SADE, who may not be experts in the disease area or investigational medicinal/device products. Abbreviations of clinical conditions should not be used. Summarise any relevant laboratory or diagnostic tests. Include details of discharge if appropriate and if known.

Where applicable enter date of admission and date of discharge if known.
5. Study Medical Device Information

Indicate by ticking the box, if applicable whether or not the subject has been fitted with/used or treated with the device.

If Yes: Complete boxes to indicate the name of the device or devices if multiple the route of administration and use. Also include the date of first and last use.

6. Assessment

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

Provide details of possible causes for the device issue (i.e. malfunction).

Consider any relevant medical history which may have had an effect.

Complete the causality assessment - relationship to procedure and device:

- **Not related**
  - There is no evidence of causal relationship to the procedure/Investigational Device.

- **Unlikely**
  - The relationship with the use of the procedure/device seems not relevant and/or the event can be reasonable explained by another cause.

- **Possibly**
  - The relationship with the use of the procedure/device is weak but cannot be ruled out completely.

- **Probable**
  - The relationship with the procedure/device seems relevant and/or the event cannot reasonably be explained by another cause.

**Causal Relationship:** The serious event is associated with the procedure/device beyond reasonable doubt.

The expectedness of the event must be based on the safety information available with regards to the device. This safety information may be found in the Investigator's Brochure/Risk Analysis Report and the Clinical Investigation Plan/Protocol.

If more than one device is under investigation the additional section should be completed. Where required addition sections can be added to the form.

**If the event is related and unexpected it is an Unexpected Serious Adverse Device Effect (USADE) and requires expedited reporting. Inform the Sponsor (Research Governance Office) office immediately. Telephone number 0116 258 8351 email UHLSponsor@tr-nhs.uk**

7. Is the study Blinded

Detail if the study device that subjects are using/treated with are known to the
<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>8. Has the study been Unblinded?</td>
<td>Investigator and research team or are the Investigator and research team blinded.</td>
</tr>
<tr>
<td>9. Is the event related to a protocol violation?</td>
<td>If the event is classified as a USADE where the research team are blinded. The subject must be unblinded as per the study unblinding procedure.</td>
</tr>
<tr>
<td>10. Was the subject withdrawn due to this event?</td>
<td>Answer Yes or No.</td>
</tr>
<tr>
<td>11. Action taken with regard to the study device(s)?</td>
<td>Answer Yes or No.</td>
</tr>
<tr>
<td>12. Outcome of event</td>
<td>Tick one box only to indicate action taken following the event. Where device not utilised marked as not applicable</td>
</tr>
</tbody>
</table>

**NOTE:** All supporting documentation must be anonymised and have all patient identifiable data removed. The documents MUST only be identified with the addition of the patient 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 and Signature Log.

---

**Reporting and completion of Serious Adverse Events/Serious adverse Device Effects for Medical Device Studies**

Must be undertaken in accordance with UHL SOP S-1041 Standard Operating Procedure for Processing and Reporting Serious Adverse Events, Serious Adverse Device Effects and Unexpected Serious Adverse Device Effects for Medical Device Studies sponsored by UHL Hospitals NHS Trust (UHL).

If you have queries regarding your SAE/SADE submission, please contact the Research Governance Office 0116 258 8351
## UHL Sponsored Multi Centre
### Serious Adverse Event/Serious Adverse Device Effect Line Listing Table

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

<table>
<thead>
<tr>
<th>Date of event</th>
<th>Relationship to Procedure?</th>
<th>Serious Criteria</th>
<th>Patient Study ID</th>
<th>Brief Description of Event</th>
<th>Relationship to Device?</th>
<th>Expectedness assessment</th>
<th>Outcome</th>
<th>Date of event resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 = Not related</td>
<td>1 = Led to death</td>
<td></td>
<td></td>
<td>1 = Not related</td>
<td>1 = Expected</td>
<td>1 = Resolved</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = Unlikely</td>
<td>2 = Life threatening</td>
<td></td>
<td></td>
<td>2 = Unlikely</td>
<td>2 = Unexpected</td>
<td>2 = Resolved with sequela</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 = Possible</td>
<td>3 = In patient hospitalization/prolongation of hospitalization</td>
<td></td>
<td></td>
<td>3 = Possible</td>
<td>3 = Ongoing</td>
<td>3 = Ongoing</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 = Probable</td>
<td>4 = Permanent impairment of body function</td>
<td></td>
<td></td>
<td>4 = Probable</td>
<td>4 = Fatal</td>
<td>4 = Fatal</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 = Causal relationship</td>
<td>5 = Medical/surgical intervention to prevent life threatening illness/injury</td>
<td></td>
<td></td>
<td>5 = Causal relationship</td>
<td>5 = Unknown</td>
<td>5 = Unknown</td>
<td></td>
</tr>
</tbody>
</table>

If the serious adverse device effect is related and unexpected, it is an Unexpected Serious Adverse Device Effect (USADE) and requires expedited reporting as per SOP S-1041

SOP S-1041 Appendix 5 Multi Centre Serious Adverse Event/Serious Adverse Device Effect Line Listing V1 March 2019
UHL Medical Device SAE/SADE Sponsor Review Process Flowchart

SAE/SADE received by EMAIL - Date stamped

Yes

USADE identified

Enter onto database within 96 hours

Immediately report to the Sponsor

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

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

Sponsor to review and send reminder if report not returned. Further 7 days given for return of completed SAE/SADE.

No

Completed / Signed off

Requires Follow-up

Completed final / follow-up SAE/SADEs reviewed and if no further information is required will be signed off by Sponsor within 7 days

Sponsored to review and send reminder. Further 7 days given for return of completed SAE/SADE.

Incomplete SAE/SADE forms request for further information to be returned with 7 days

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

Signed SAE/SADEs to be scanned and entered into electronic folder and acknowledgement email sent within 96 hours

Responsibilities

Sponsor

Monitoring Team

SOP S-1041 Appendix 6: Medical Device SAE/SADE Review Process Flowchart V1 March 2019
Dear Study Team

Thank you for submitting the following SAE/SADE to the Research Governance Office:

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

<Delete as appropriate>

Further clarification/action is required as indicated below. Please amend/provide further information within the requested timeframe. Please be aware that where changes are made to the form after original PI signature, the PI will be required to review and resign and date the form.

Should you have any queries with regards to the request/s please feel free to contact me:

- An initial unsignatured report has been received. Please forward a signed copy of either the initial report or where available the final report within 7 days.
- An initial signed report has been received. Please forward a signed follow up report within 28 days.
- The type of report (SAE/SADE/USADE) field is incomplete. Please review/revise and return updated form within 7 Days
- The ‘serious criteria’ field is incomplete. Please review/revise and return updated form within 7 Days
- The ‘device information’ field is incomplete. Please review/revise and return updated form within 7 Days
- The ‘causality assessment’ field is incomplete. Please review/revise and return updated form within 7 Days
- The ‘event expectedness’ field is incomplete. Please review/revise and return updated form within 7 Days
- The ‘study blinded/unblinded field’ is incomplete. Please review/revise and return updated form within 7 Days
- The ‘relationship to protocol violation’ field is incomplete. Please review/revise and return updated form within 7 Days
- The ‘action taken with regards to device’ field is incomplete. Please review/revise and return updated form within 7 Days
- The ‘outcome of the event’ field is incomplete. Please review/revise and return updated form within 7 Days
- The ‘cause of death’ field is incomplete. Please review/revise and return updated form within 7 Days
- Please provide evidence of submission to MHRA/REC within XX days.
- Other/comment. Return within xx days.

<Or delete as appropriate>

We have marked this SAE/SADE/USADE as COMPLETE and no further follow-up is necessary.

Please file this acknowledgement in your site file along with a copy of the report(s). Please updated the SAE log as appropriate.

Many thanks.
<table>
<thead>
<tr>
<th><strong>UHL Medical Device Deficiency Report Form</strong></th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>EudraCT number:</th>
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<table>
<thead>
<tr>
<th>Sponsor number:</th>
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</thead>
</table>

<table>
<thead>
<tr>
<th>Protocol title:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Site:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Subject number:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Device:</th>
</tr>
</thead>
</table>

**Device details**

Describe the nature of the device, its normal (label) applications and its application in the Clinical Investigation if different:

**Event details**

<table>
<thead>
<tr>
<th>Date of deficiency:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Description of deficiency</th>
</tr>
</thead>
</table>

Please indicate if the deficiency concerns identity, quality, durability, reliability, safety or performance of the device.

Please indicate if the deficiency is due to malfunction, use error or inadequate labelling.
<table>
<thead>
<tr>
<th>Action taken</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Additional information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name and contact details of person reporting and role</td>
</tr>
<tr>
<td>Date of report:</td>
</tr>
<tr>
<td>PI signature:</td>
</tr>
<tr>
<td>Date received by Sponsor:</td>
</tr>
<tr>
<td>Action:</td>
</tr>
</tbody>
</table>