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.

1.1)

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
- Medical Device Directives 90/385/EEC and 93/42/EEC, ISO 14155:2011 (Clinical investigations of medical devices for human subjects – Good Clinical Practice)

2. 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.

3. Definitions

3.1 CE Mark

CE marking is an administrative **marking** that indicates conformity with health, safety, and environmental protection standards for products sold within the European Economic Area

3.2 UKCA Mark

The UKCA (**UK Conformity Assessed**) marking is a new UK product marking that is used for goods being placed on the market in Great Britain (England, Wales and Scotland) from the 1st January 2021.

3.2.1

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:

3.2.1.1)

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
- Investigation, replacement, modification, or support of the anatomy or of a physiological process
- Supporting or sustaining life
- Control of contraception
- Disinfection of medical devices

3.2.1.2)

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.

3.2.1.3)

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).

3.3 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.

3.4 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.

3.5 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).

3.6 CE/UKCA Marked Device Studies

Post-marketing studies where the product is used within its intended purpose.

3.7 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.

3.8 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.

3.9 Investigator's Brochure (IB)

A compilation of the current clinical and non-clinical information on the investigational medicinal device relevant to the clinical investigation.

3.10 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.

3.10.1)

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.

3.11 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.

3.11.1)

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.

3.12 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-threating illness or injury, or
- A permanent impairment of a body structure or a bodyfunction
- 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.

3.12.1)

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

3.12.2)

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.

3.13 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.

3.14 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.

3.15 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.

4. Identification and Recording of Adverse Events / Device Deficiencies

4.1)
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.

4.2)
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 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 R&I Website. 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.

5.1.1)
For UHL Sponsored studies, the 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 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).

5.1.2)
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

5.1.3)
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.

5.1.4)
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/. 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

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/

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).

6.1)

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.

6.1.1 Assessment of Seriousness

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

6.1.2 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).

6.1.2.1)

Adverse Events	Non Device Related	Device or Procedure Related	
Non-serious	Adverse Event (AE)	Adverse Device Effect (ADE)	
Serious	Serious Adverse Event (SAE)	Serious Adverse Devise Effect (SADE)	
		Anticipated	Unanticipated
		Anticipated Serious Device Effect (ASADE)	Unanticipated Serious Device Effect (USADE)

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.

6.2.1)

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.

6.3.1)

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/complete an investigation. In addition, the device **should not** be:

- Discarded
- Repaired
- Returned to the manufacturer

7.1)

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

7.2)

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.

7.3)

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.

7.4)

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.

8.1)

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).

8.2)

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

9.1)
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.

11. Responsibilities

	Responsibility	Undertaken by	Activity
1	CI/PI/Delegated individual	CI/PI/Delegated individual	Report all serious adverse events/device effects to the Sponsor (except those identified as exempt).
2	CI/PI/Delegated Individual	CI/PI/Delegated individual	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.
3	CI/Delegated Individual	CI/Delegated Individual	Completion of adverse event/adverse device effect/Device Deficiency reports/and or line listing and review and sign off by Chief Investigator.
4	Sponsor	Sponsor or designee	Ensures that all reportable events are notified to the MHRA and REC within mandatory timelines.
5	CI/PI/Delegated individual	CI/PI/Delegated individual	Supply the Sponsor, and the REC with any additional information requested.
6	Sponsor	Sponsor	Monitor all SAE/SADE line listings reported on a monthly basis to identify and if necessary act upon any emerging safety issues.
7	Sponsor	Clinical Trial Monitor	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.

12. Who Guidelines Applies To

All staff within UHL and external to UHL who are delivering research.

13. Guideline Standards and Procedures

This SOP is detailed so the process can be clearly followed. Supporting SOP flowcharts can be found in SOP S-1040 Appendices 1 & 6.

14. Education and Training

None

15. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Sponsor Audit	Randomly chosen for audit	Carolyn Maloney	As and when	A report will be produced

16. Supporting Documents and Key References

SOP S-1041 Appendix 1, 2, 3, 4, 5, 6, 7 & 8

SOP S-1006

SOP S-1016

Medical Device Regulations 2002

Medical Device Directives

17. Key Words

Research, Innovation, EDGE, REC, Adverse Event, Medical Device, CE, Non CE

18. Contact and Review Details

CONTACT AND REVIEW DETAILS	
Guideline Lead (Name and Title) Lisa Wann R&I manager	**Executive Lead** **Medical Director**
Details of Changes made during review: **Review and update**	

19.

This line signifies the end of the document

19.1)

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

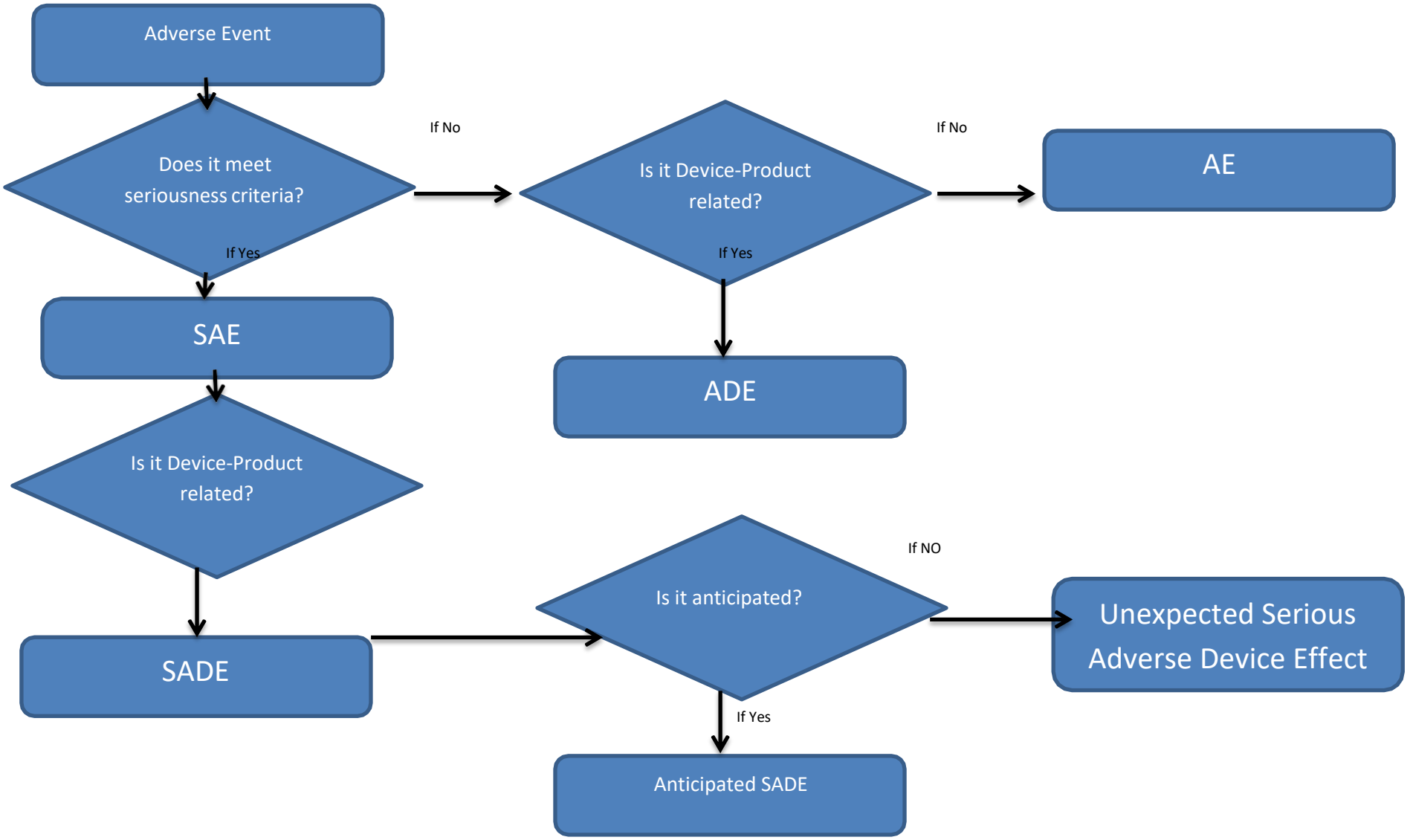
19.2)

DEVELOPMENT AND APPROVAL RECORD FOR THIS DOCUMENT		
Author / Lead Officer:	Julie James/Carolyn Maloney	**Job Title:** Clinical Trials Monitor & Trainer / Head of Research Operations
Reviewed by:	R&I Governance Meeting	
Approved by:	Professor Nigel Brunskill	**Date Approved:**

REVIEW RECORD			
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**
Feb 2021	2	CW,LW,JJ	Consistency checks. Update to include UKCA mark and definitions of CE and UKCA marking

DISTRIBUTION RECORD:			
Date	**Name**	**Dept**	**Received**

Event Categorisation Flow Chart



Adverse Event/Device Effect Record

For UHL Sponsored Medical Device Studies

Subject ID				**Subject Initials**			

	Adverse event/ Device Effect Description	**Start Date (DD/MMM/YYYY)**	**End Date (DD/MMM/YYYY)**	**Relationship to Procedure:** 1=not related **OR** 2=unlikely **OR** 3=possible **OR** 4=probable **OR** **5=**causal relationship	**Relationship to Device** 1=not related **OR** 2=unlikely **OR** 3=possible **OR** 4=probable **OR** **5=**causal relationship	**SAE or Device Deficiency?** **Y/N**	**Expectedness Assessment** **1=Expected** **2=Unexpected**	**Outcome** **1=Resolved** **2=Resolved with sequelae** **3= Ongoing** **4= Fatal** **5= Unknown**
1		--/--/----	--/--/----					
2		--/--/----	--/--/----					
3		--/--/----	--/--/----					
4		--/--/----	--/--/----					
5		--/--/----	--/--/----					
6		--/--/----	--/--/----					
7		--/--/----	--/--/----					

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** ☐ **Follow Up** ☐ **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:

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:

Name of Device	Indication for use	Route of administration/use	Date of first use	Date of last use

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

Person completing report:	Principal Investigator/delegated medically qualified individual as agreed by the Sponsor:
Name:	Name :
Role:	Role:
Signature:	Signature:
Date:	Date:
Contact No:	Contact No:

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

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.

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 15days 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 beenfitted 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 or Unblinded ?

Detail if the study device that subjects are using/treated with are known to the Investigator and research team or are the Investigator and research team blinded.

8. Has the study been Unblinded?	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.
9. Is the event related to a protocol violation?	Answer Yes or No. If Yes - Further information should be supplied on a separate protocol deviation form.
10. Was the subject withdrawn due to this event?	Answer Yes or No.
11. Action taken with regard to the study device(s)?	Tick one box only to indicate action taken following the event. Where device not utilised marked as not applicable
12. Outcome of event	Tick one box only at the time of the report: **Ongoing** - the adverse event/effect must be followed-up until resolution. **Fatal** – Where the event is fatal details of the date of death and the cause of death **MUST** be obtained. Detail where the information was obtained to support cause of death. Supporting anonymised documents must be supplied with SAE/SADE.

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

Sponsor Number:		**Principal Investigator:**
Study Title:		**Study Site Name:**

Date of event	Relationship to Procedure? 1 =Not related 2 = Unlikely 3=Possible 4=Probable 5=Causal relationship	Serious Criteria 1 = Led to a death 2 = Lifethreatening 3 = In patient hospitalization/prolongation of hospitalization 4= permanent impairment of body structure/ function 5 = medical/surgical intervention to prevent life threatening illness/injury 6 = led to foetal distress/death or birth defect	Patient Study ID	Brief Description of Event	Relationship to Device? 1 =Not related 2 = Unlikely 3=Possible 4=Probable 5=Causal relationship	Expectedness assessment 1 = Expected 2 =Unexpected	Outcome 1 =Resolved 2 =Resolved with sequalae 3 =Ongoing 4 =Fatal 5 =Unknown	Date of event resolution
--/--/----								--/--/----
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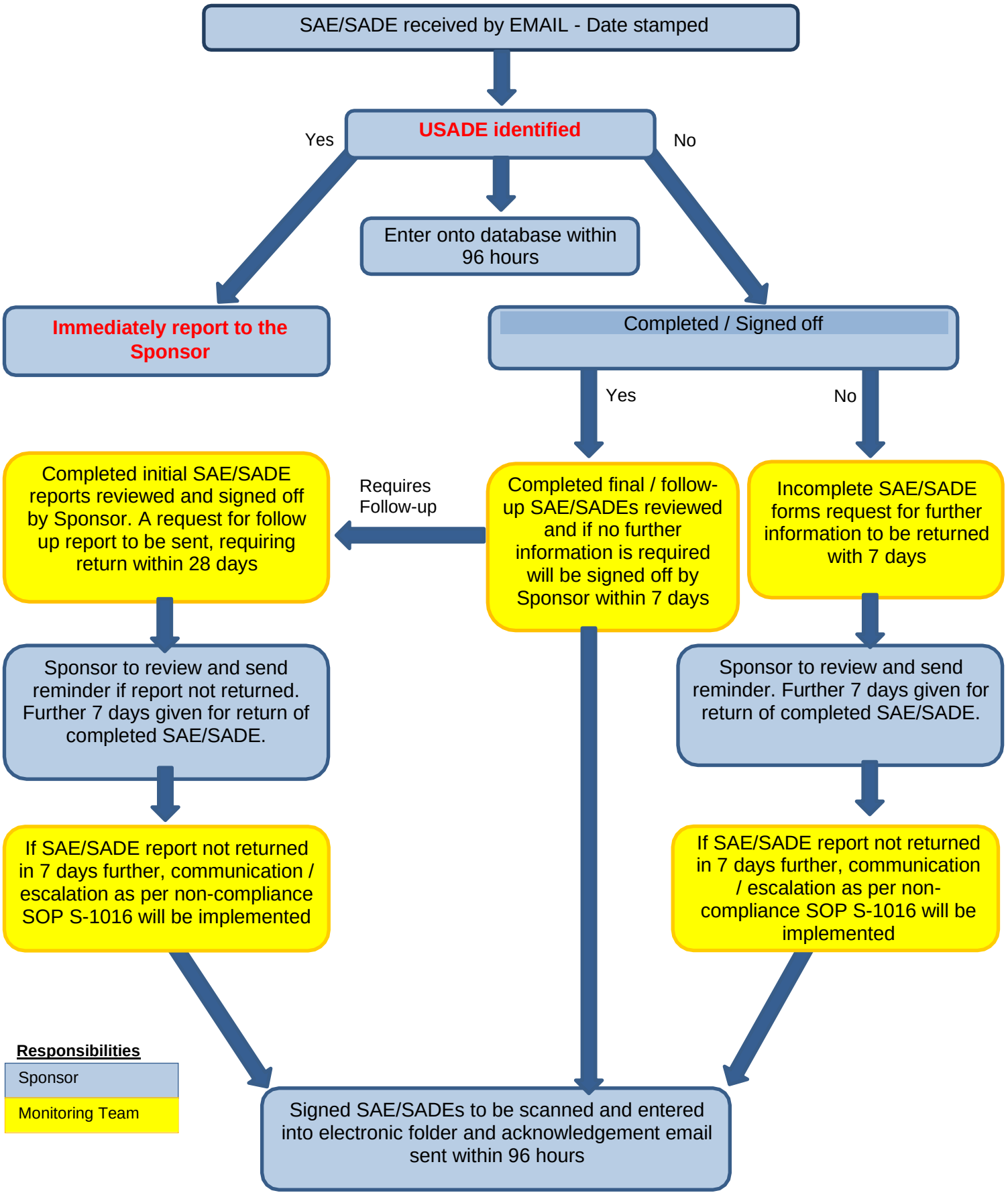
If the serious adverse device effect is related and unexpected, it is an Unexpected Serious Adverse Device Effect (USADE) and requires expedited reporting as per SOP S-1041

UHL Medical Device SAE/SADE Sponsor Review Process Flowchart



Dear Study Team

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

Patient ID	
Centre	
Study	
Sponsor Ref	
Onset date	
Event	
Type of Report	
Date of Report	

<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 unsigned 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 'patient withdrawn as a result of this event' 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.

UHL Medical Device Deficiency Report Form

EudraCT number:	
Sponsor number:	
Protocol title:	
Site:	
Subject number:	
Device:	
Device details	
Describe the nature of the device, its normal (label) applications and its application in the Clinical Investigation if different:	
Event details	
Date of deficiency:	
Description of deficiency	
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.	

Action taken

Additional information	
Name and contact details of person reporting and role	
Date of report:	
PI signature:	
Date received by Sponsor:	
Action:	