Safety Reporting for clinical investigations of medical devices (MHRA regulated device trials)

Research & Innovation SOP S-1040

University Hospitals of Leicester NHS
NHS Trust

Trust Ref: B15/2021

1. Introduction

This Standard Operating Procedure (SOP) describes the process required by the University Hospitals of Leicester (UHL) NHS Trust for identifying, documenting and reporting all adverse events (AEs) and device deficiencies for clinical investigations of medical devices that are not CE/UKCA marked or used outside their intended purpose (requiring approval by the MHRA) sponsored by UHL.

Devices are regulated under the Medical Devices Regulations 2002 (SI 2002 No 618, as amended) (UK MDR 2002).

2. Scope

This SOP applies to all staff and external individuals involved in the conduct of research investigating non-CE/UKCA marked devices, or CE/UKCA marked devices that are being used outside their intended use(s) (MHRA regulated device trials).

3. Identification and Recording of Adverse Events

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 (T1021) 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.

4. Reporting of Adverse Events

4.1 Reporting to the 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 to RIGovernance@uhl-tr.nhs.uk. UHL Serious Adverse Event/Adverse Device Effect Report Form C for medical device studies (T1022) must be used. This form and associated completion guidance document (T1026) 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.

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). 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

All **device deficiencies** related to lack of identity, the quality, durability, reliability or performance/failure of the device to perform in accordance with its intended purpose should be reported to UHL Sponsor utilising the device deficiency form (T1025). Where an adverse event is the unexpected consequence associated with the device deficiency or malfunction this should be reported as an ADE or USADE accordingly.

For Multi-centre studies all SAEs and SADEs and device deficiencies from all sites must be sent to the Sponsor unless alternative arrangements have been agreed with the Sponsor. Where sites are managed through a third party contractor e.g. a Clinical Trials Unit, it may be appropriate to make alternative arrangements for reporting. These arrangements will be specifically detailed in the third party agreement. Where alternative reporting arrangements have been agreed, details of all SAEs occurring at all sites, must be completed/reviewed by the CI.

4.2 Reporting to the MHRA

All SAEs and device deficiencies should be reported MHRA (devices) Adverse Incident Centre and should include all serious adverse events, whether initially considered to be device related or not, that have occurred in all participating centres, whether European or non-European. If these indicate an imminent risk of death, serious injury, or serious illness and that requires prompt remedial action for other patients/subjects, users or other persons they must be reported immediately, but not later than 2 calendar days after awareness by sponsor of a new reportable event or of new information in relation with an already reported event. Any other reportable SAEs should be reported immediately but not later than 7 calendar days following the date of awareness by the sponsor of the new reportable event or of new information in relation with an already reported event.

The Sponsor or Designee must notify the MHRA using the template tabulation form detailed in the appendix of the MEDDEV 2.7/3 document DocsRoom - European Commission (europa.eu). The table gives a cumulative overview of the reportable events per clinical investigation and must be updated and transmitted to the MHRA every time a new reportable event or new finding to an already reported event is received.

The Sponsor or Designee shall identify the new/updated information in the status column of the tabular form as outlined below:

a = Added (new reportable event)
m = Modified (new finding/update to an already reported event)
u = unchanged

Changes in lines should be highlighted in bold and/or colour in the respective column.

The report should be sent as an Excel file to aic@mhra.gsi.gov.uk quoting MHRA's CI reference number or upload through MORE htttps://aic.mhra.gov.uk/ including the MHRA's CI reference number in the "incident description" field. All correspondence must be copied to the Sponsor.

The letter of no objection from the MHRA will also detail whether summary reports (including their frequency) need to be submitted to the MHRA.

4.3 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/

4.4 Reporting local trust incidents

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 local Trust's Incident and Accident reporting policy.

5. 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. This must be documented on the study Delegation of Authority and Signature Log. Please see device event categorisation flow chart (T1007).

Each AE must be assessed for seriousness, causality and expectedness.

Assessment of Seriousness

The assessor should make an assessment of seriousness, whether the event is classes as serious as detailed in the definitions.

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.

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.

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. Quarantine of Devices

If the device needs quarantining, it 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
- Removed from the site / organisation premises without previous agreement from the Sponsor

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.

The Investigator and the Sponsor will undertake any requirements outlined in the MHRA investigation and follow-up as instructed.

7. 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 T1023 (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 (T1024).

All SAE/SADE/USADE/Device Deficiencies reported to the Sponsor will be reviewed by the Director of R&I, or nominated delegate.

8. Documentation

The following documentation, where applicable, 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 record (T1021**)**
- Device Deficiency Report Form (T1025)
- Evidence of submission and receipt of SAE/SADEs/Device Deficiency reports 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**.**

12. 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

13. Supporting Documents and Key References

T1007

T1021-T1026

Medical Device Regulations 2002

14. Key Words

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

This line signifies the end of the document

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

DEVELOPMENT AND APPROVAL RECORD FOR THIS DOCUMENT		
Author / Lead Officer:	Jen Boston	**Job Title:** R&I Deputy Director of Operations
Reviewed by:	R&I Governance Meeting	
Approved by:	Professor Nigel Brunskill	**Date Approved:** 3rd February 2025

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
Sep 2024	3	Jen Boston	Review of SOP due.

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