LOUGHBOROUGH UNIVERSITY RESEARCH OFFICE
STANDARD OPERATING PROCEDURE

Loughborough University (LU) Research Office
SOP–1009 LU

Processing and Reporting of Serious Adverse Events, Serious Adverse Reactions and Suspected Unexpected Serious Adverse Reactions for NHS Research Sponsored by Loughborough University

Effective Date: January 2016

1.0 Introduction

This Standard Operating Procedure (SOP) describes the requirements of Loughborough University (LU) for identifying, documenting and reporting all Serious Adverse Events.

The outcome is that LU fulfills its requirements to identify, document and report all categories of Serious Adverse Events.

2.0 Definitions

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

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

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

- Results in death

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

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

Suspected Unexpected Serious Adverse Reaction (SUSAR)
Is defined as a serious adverse reaction, the nature and severity of which is **not consistent** with the applicable product information in the Investigator Brochure (IB) or Summary of Product Characteristics (SPC).

3.0 Pregnancy Reporting

Although pregnancy in a trial subject or their partner is not classified as a serious adverse event in itself, it is however an important event and should be reported.

Please contact the Research Governance Officer for a copy of the Pregnancy Notification Form.

Although these are the standard definitions of serious adverse events, the reporting requirements of each trial may differ, dependent on the nature of the trial and the patient population. Specific protocol reporting instructions should be followed.

4.0 SAE/SAR Reporting Procedure

AE (Adverse Events)
There are no requirements to report these events, but they should be documented in the Case Report Form (CRF) and patients' medical records and observed to ensure that they do not escalate to a serious adverse event.

All serious adverse events in studies sponsored by LU must be reported to the Sponsor immediately and within 24 hours of the research team becoming aware of the event.

5.0 Reporting form

For LU sponsored studies the LU Serious Adverse Event Form must be used. This form is available on the Ethics Approvals (Human Participants) Sub-Committee Website.

5.1 LU Sponsored Studies

For LU Sponsored studies, the Chief Investigator (CI) or Principal Investigator (PI) is responsible for the review and sign off of all serious adverse events. After discussion with, and agreement by, the Sponsor it may be possible for additional medically qualified individuals to be delegated the responsibility for reviewing and signing off the SAE form.
This must be recorded on the Delegation of Authority and Signature Log.

5.2 LU Sponsored Multi-Centre Studies

Where the study is a non CTIMP, the SAEs for the lead site must be submitted to the Research Governance Officer. Details of SAEs occurring at collaborating sites must be completed by the Chief Investigator utilising the Multi Centre SAE listings table and submitted to the Research Governance Officer on a quarterly basis.

5.3 Causality

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

The definitions below can be used:

Unrelated - There is **no** evidence of causal relationship

Related - There **is evidence** of causal relationship

Events relating to placebo or reference drugs must also be reported.

5.4 Expectedness

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

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

Events relating to placebo or reference drugs must be reported.

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

6.0 SAR/SUSARs (Serious Adverse Reaction/Suspected Unexpected Serious Adverse Reactions)

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

In an LU sponsored study, the responsibility to evaluate whether or not a reaction is a SUSAR is delegated to the Chief Investigator.

As for all SAEs, a SUSAR must be reported to the Sponsor with immediate effect and within 24 hours of the research team becoming aware of it. The responsibility to report to the MHRA through the eSUSAR system and the main REC is that of the sponsor.

The initial report must be submitted as soon as possible and, in any event, within 7 calendar days for a death or life threatening SUSAR (and submit any follow up information within an additional 8 calendar days) or within 15 calendar days for other SUSARs.

6.1 Blinded Studies

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

6.2 Urgent Safety Measures

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

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

SAEs occur in research that does not involve an Investigational Medicinal Product. These SAEs should be reported as per 5.0 above.

Where in the opinion of the Chief Investigator (CI) the event was **related** (that is, it resulted from administration of any of the research procedures), and **unexpected** (that is, the type of event is not listed in the protocol as an expected occurrence). The SAE report form for non-CTIMPs, available from the National Research Ethics Service (NRES) website should be completed and sent to the main REC within 15 days of the CI or PI becoming aware of the event. A copy of the SAE form must also be submitted to the Research Governance Officer.

8.0 Documentation

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

- SAE, SAR and SUSAR reports and follow-up information
- AE / SAE Logs
- Evidence of submission and receipt of SAEs to the sponsor/ R&D department within the required timeframe.
- Evidence of timely SUSAR submission to the MHRA and main REC

The investigator must ensure that all SAE information is recorded accurately in the study Data Collection Form**.**

9.0 SAE Review Process

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

Each SAE will be registered on the Joint R&D Office SAE database and reviewed by the Sponsor or their delegate. This review may lead to queries being issued by the Research Governance team to request signed documentation, clarify information or complete outcome event. All queries must be responded to within the stated timeframe as per the SAE Amendment Request Form.

10. Responsibilities

	Responsibility	Undertaken by	Activity
1	CI/PI/Delegated individual	CI/PI/Delegated individual	Report all serious adverse events to the sponsor (except those identified as exempt)
2	CI/PI/Delegated	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/PI/Delegated individual	CI/PI/Delegated individual	Identify subjects by trial study number and initials this information should be recorded on all reports. No personal identifiable data should be recorded on the SAE form or supporting documentation
4	CI/PI//Delegated individual	CI/PI//Delegated individual	Supply the Sponsor and the main REC with any additional information requested
6	Sponsor	Sponsor	Ensures that all SUSARs are reported to the MHRA and REC within mandatory timelines
7	Sponsor	Sponsor	Monitor all SAEs reported within the Trust on a monthly basis to identify and if necessary act upon any emerging safety issues

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

DEVELOPMENT AND APPROVAL RECORD FOR THIS DOCUMENT		
Author / Lead Officer:	Jackie Green	**Job Title:** Research Governance Officer
Approved by:	Ethics Committee	**Date Approved: 5/2/16**

REVIEW RECORD			
Date	**Issue Numb**	**Reviewed By**	**Description Of Changes (If Any)**

	er		

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

SERIOUS ADVERSE EVENT REPORT FORM

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

Sponsor Reference Number	
Study Title:	
Patient Study Number and Initials	

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

1.Type of Report (Tick relevant box) ☐ **Initial** ☐ **Follow Up** ☐ **Final**

Date of Report ____/____/_____

Serious Adverse Event:

_____

Date of Onset ____/____/____

Date Study Team Aware ___/____/_____

2.Serious Criteria:

☐ **Resulted in death**

☐ **Life threatening**

☐ **In-patient hospitalisation or prolongation of existing hospitalisation**

☐ **Persistent or significant disability/incapacity**

☐ **Congenital anomaly/birth defect**

☐ **Other**

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

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

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

☐ Yes ☐ No

5) Was the event related to a protocol violation?

☐ Yes ☐ No

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

☐ Yes ☐ No

7) Outcome of the Event

☐ Resolved

☐ Resolved with Sequalae

☐ Ongoing

☐ Unknown at present

☐ Fatal Date of Death:

Cause of

Death .....

Cause of death obtained from (tick one)

Working Diagnosis ☐ Coroners Inquest ☐ Death Certificate ☐

Supporting documentation to be supplied with SAE

Reporting Person:	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 documents to the Research Governance Officer by email to researchpolicy@lboro.ac.uk

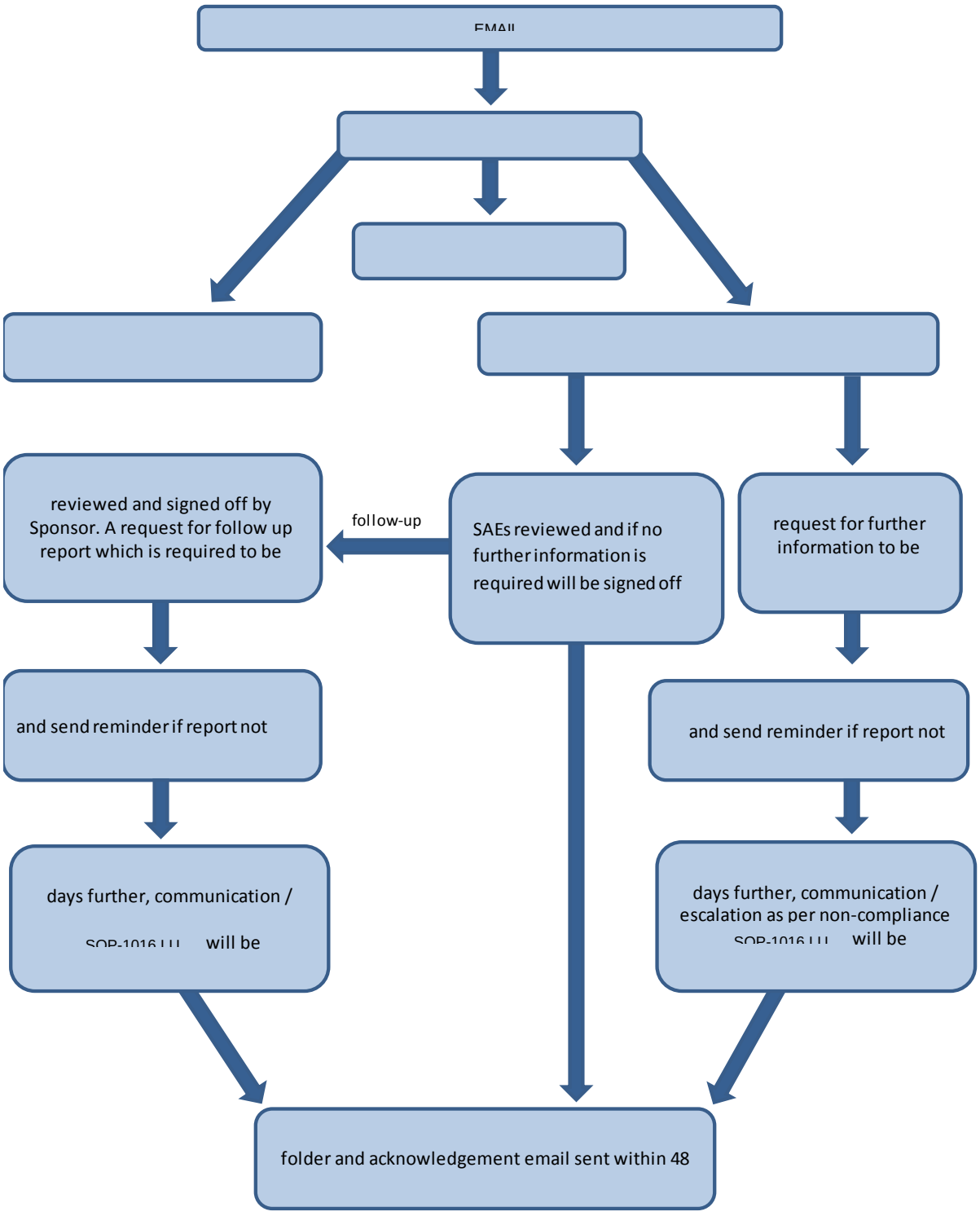
Reporting and completion of SAEs not involving investigational medicinal products must be undertaken in accordance with SOP 1009 LU Processing and Reporting of Serious Adverse Events, Serious Adverse Reactions and Suspected Unexpected Serious Adverse Reactions for all Research Sponsored by Loughborough University

LU Sponsored Multi Centre Non CTIMP
Serious Adverse Event Listing Table

Sponsor Reference Number		**Principal Investigator:**
Study Title		

Study Centre	**Date of SAE**	**Patient Study ID**	**Brief Description of Event**	**Assessment of relationship to procedure/intervention Related/Unrelated**	**Assessment of relationship to Investigational device Related/Unrelated**	**Outcome**	**Date of event resolution**

LU SAE Review Process Flowchart



SAE AMENDMENT REQUEST FORM

The following SAE form(s) have been received by the Research Governance Officer. They require amendment/further information or signature as indicated by X in relevant box below:

Sponsor Reference No:	Patient Study Number /Initials
Study Title:	
SAE Date:	SAE Title:

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

All amendments should be emailed to the Research Governance Officer: researchpolicy@lboro.ac.uk

For Research Governance Office admin use only

Date sent:	Date reply Received :
Date 2nd Reminder sent	Date sent to Sponsor