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Safety Reporting in Research Other than Clinical Trials of Investigational Medicinal Products (non-CTIMPs)

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Version	Date	Reason for Change
2.0	**24/05/2016**	Title of SOP changed to reflect more accurately the SOP Introduction section updated Definitions updated Responsibilities updated Addition of expectedness definitions Clarification on reporting requirements BSUH R&D safety reporting team contact details have changed from fax number 01273 664741 to email address safety@bsuh.nhs.uk Content changed to reflect HRA guidelines HRA website link changed Addition of appendices

1.0 Purpose

This SOP describes the processes for the management of Safety Events or (Serious) Adverse Events S(AEs) in research other than CTIMPs for studies sponsored by BSUH (Brighton and Sussex University Hospital NHS Trust). This SOP does not apply to clinical investigations of medical devices or CTIMPs.

2.0 Introduction

The Department of Health's Research Governance Framework states that researchers have a responsibility for the reporting of any adverse drug reactions or other adverse events; (section 3.5.1) and the Sponsor has to be satisfied there is an agreement on the appropriate arrangement to record, report and review significant developments as the research proceeds, particularly those which put the safety of individuals at risk[1]. The Health Research Authority (HRA) requires that The Chief Investigator should report any Serious Adverse Event that is both related to the research procedures and is unexpected to the Ethics Committee that gave a favourable opinion within 15 days of the CI becoming aware of the event[2].

3.0 Definitions

3.1 Adverse Event (AE)

An AE can be defined as any untoward medical occurrence in a research participant whilst they are taking part in a research study. An adverse event (AE) can therefore be any unfavourable and unintended sign, symptom, or disease temporally associated with participation in the research study, whether or not considered related to the administration of any study procedures.

3.2 Serious Adverse Event (SAE)

Any untoward medical occurrence that:-

- results in death
- is life-threatening
- requires hospitalisation or prolongation of existing inpatients' hospitalisation
- results in persistent or significant disability or incapacity
- is a congenital anomaly or birth defect
- is otherwise considered medically significant by the investigator

3.3 Urgent Safety Measures (USMs)

The sponsor or investigator may take appropriate urgent safety measures in order to protect research participants against any immediate hazard to their health or safety, without prior authorisation from a regulatory body. However, the main REC must be informed immediately and in any event within three days, in the form of a substantial

amendment, that such measures have been taken and the reasons why. The sponsor must also be informed.

4.0 Responsibilities

Chief Investigator (CI): The CI is responsible for ensuring the protocol contains a list of expected adverse events in relation to the administration of study procedures. The protocol should outline what adverse events require reporting and documenting in the source documents. The CI is responsible for reporting SAEs to the Sponsor immediately they become aware of it and to the ethics committee, if unexpected and related to the study procedure, within 15 days of becoming aware of the event.

Principal Investigator (if multi-centred): The PI delegated individual must assess each AE for causality, seriousness and expectedness and document accordingly in the participants notes and data collection form, if appropriate. The PI or delegated individual at site is responsible for reporting SAEs to the CI and sponsor immediately they become aware of the event.

Sponsor: The Sponsor is responsible for ensuring any related and unexpected SAEs are reported to the REC (Research Ethics Committee) that gave the favourable opinion within 15 days of the CI becoming aware of the event. The Sponsor is responsible for creating and maintaining a database of reported SAEs. The Sponsor is responsible for ensuring there are written systems in place to ensure quality standards are met for a non CTIMP study

5.0 Procedure

Once the participant has consented to take part in a research study, all AEs should be evaluated for causality, seriousness and expectedness, unless specified otherwise in the protocol.

Causality	Description
Unrelated	No evidence of any causal relationship to administration of study procedures
Unlikely	Little evidence to suggest a causal relationship (e.g. the event did not occur within a reasonable time after administration of study procedures). There is another reasonable explanation for the event (e.g. the patient's clinical condition, other concomitant treatment)
Possible	Some evidence to suggest a causal relationship
Probable	Evidence to suggest a causal relationship and the influence of other factors is unlikely
Definite	Clear evidence to suggest a causal relationship and other possible contributing factors can be ruled out
Not Assessable	Insufficient or incomplete evidence to make a clinical judgement of the causal relationship.

Expectedness	Description
Expected	The nature, seriousness, severity or outcome of the event is consistent with the expected events specified in the protocol
Unexpected	The nature, seriousness, severity or outcome of the event is not consistent with the expected events specified in the protocol

If the event is recorded as **Serious** (see section 3.2), is **Related** to the research procedure and is **Unexpected (not listed in the protocol as an expected event)** then this should be submitted to the Sponsor and Ethics committee as soon as the researcher is made aware of the event and definitely within 15days of the CI becoming aware of the event.

5.1 SAE Reporting Procedure

The SAE reporting requirements and procedures must be included in the protocol for all non-CTIMPs studies. Procedures should detail any exemptions to reporting if applicable. If SAEs are not required to be reported to the sponsor according to the protocol, it should be clearly documented in the source notes that the PI has reviewed and confirmed the event as not reportable. If an event is reportable to the sponsor according to the protocol, the site must notify the sponsor immediately by sending a copy of the BSUH Non-CTIMP SAE report (appendix 1) to

safety@bsuh.nhs.uk

A database of SAEs will be maintained by the Sponsor R&D Quality Assurance team.

5.2 Reporting to Ethics Committee

The ethics committee that gave the initial approval for the study must be informed within 15 days of the CI becoming aware of the event using the HRA Report of Serious Adverse Event form for Non-CTIMPs (appendix 2). The CI must complete the form and email a copy to the EC and send a copy to safety@bsuh.nhs.uk

5.3 Sponsor oversight

All reported SAEs will be reviewed by the Research Governance & Quality Assurance Committee and any further actions required will be documented in the meeting minutes.

6.0 Training

This is a 'read and understand' SOP. All research staff involved in non-CTIMP studies sponsored by BSUH should read and understand this SOP. Evidence of this

training should be provided by completion of a Training Record. For BSUH staff, a copy of the completed training record should be forwarded on to the R&D administrator. Please note that the R&D department discourages the retention of hard copies of SOPs and can only guarantee that the most up-to-date version is on the Trust website.

7.0 References

1. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/139565/dh_4122427.pdf (accessed 20th May 2016)
2. http://www.hra.nhs.uk/resources/during-and-after-your-study/progress-and-safety-reporting/ (accessed 20th May 2016)

Appendix 1: BSUH AE in Non-CTIMP study pro-forma

Appendix 2: HRA SAE report

Brighton and Sussex University Hospitals NHS Trust

Study Title:	IRAS number:
FOR BSUH USE ONLY	SAE ID : ☐☐ — ☐☐☐

NON-CTIMPS SERIOUS ADVERSE EVENT (SAE) REPORT

Please email this form as soon as becoming aware of the SAE to safety@bsuh.nhs.uk

Patient details

Patient Study Number: ☐

Patient initials: ☐☐☐

Sex: ☐ Male ☐ Female

Year of birth: ☐☐☐☐ (y y y y)

Site name: _____

Date site notified of SAE: ☐☐ ☐☐ ☐☐☐☐ (d d m m y y y y)

Type of report: ☐ Initial ☐ Follow Up, number .....

Date of report: ☐☐ ☐☐ ☐☐☐☐ (d d m m y y y y)

Serious Events

Event Term	Dates of Onset & Resolution (dd/mm/yyyy)	Outcome of Event[1]	Causal relation of study procedure to event[2]:	Expectedness (tick one)
	Onset ☐☐ ☐☐ ☐☐☐☐	☐	☐	Expected ☐
	Resolution ☐☐ ☐☐ ☐☐☐☐			Unexpected ☐

Codes: **(1) Outcome of Event** (enter one code per event): **1 = Fatal 2 = Not Resolved 3 = Resolved 4 = Resolved with Sequelae**

(2) Causal Relationship (enter <u>one</u> code): **0 = "Related (reasonable possibility)" 1 = "Not related (no reasonable possibility)"**

Why was the SAE serious? *(tick one only – please refer to the safety section of the protocol for details)*

Resulted in death	☐	Date of death: ☐☐ ☐☐ ☐☐☐☐ (d d m m y y y y)
Life threatening	☐	
Required new or prolonged hospitalisation	☐	
Resulted in persistent or significant disability/incapacity	☐	
Resulted in congenital anomaly or birth defect	☐	
Other medically significant *(e.g. non-serious adverse events of special interest)*	☐	*specify* _____

Case narrative

(Give a concise medical description of the events including all relevant signs and symptoms, body systems, and any additional information deemed relevant to the case. State the rationale for causal relationship between the event and study procedure include medical judgement considering all relevant factors.)

Assessment of safety implications *(CI to complete)*

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

Continued on a separate sheet? ☐ Y

Form(s) completed by: *(must be authorised on staff delegation log to complete CRFs and report SAEs)*

Print Name: _____ Signature: _____ Date of Completion: d d m m y y y y

Chief Investigator sign off

Print Name: _____ Signature: _____ Date of Completion: d d m m y y y y

Research Governance & Quality Assurance sign off

Print Name: _____ Signature: _____ Date of Completion: d d m m y y y y

Sponsor Comments:

SAE Reporting form non-CTIMP form sent to Ethics Committee

Print Name: _____ Signature: _____ Date form sent: d d m m y y y y

Signed original to be sent back to Chief Investigator (or other person submitting report).
Copy to be kept by R&D department

APPENDIX 2

NHS
Health Research Authority

REPORT OF SERIOUS ADVERSE EVENT (SAE)
(For all studies except clinical trials of investigational medicinal products)

The Chief Investigator should report any SAE that is both related to the research procedures and is unexpected. Send the report to the Research Ethics Committee that gave a favourable opinion of the research within 15 days of the CI becoming aware of the event.

1. Details of Chief Investigator

Name:	
Address:	
Telephone:	
Email:	
Fax:	

2. Details of study

Full title of study:	
Name of main REC:	
Main REC reference number:	
Research sponsor:	
Sponsor's reference for this report: (if applicable)	

3. Type of event

Please categorise this event, ticking all appropriate options:

Death ☐	Life threatening ☐	Hospitalisation or prolongation of existing hospitalization ☐
Persistent or significant disability or incapacity ☐	Congenital anomaly or birth defect ☐	Other ☐

4. Circumstances of event

Date of SAE:	
Location:	
Describe the circumstances of the event: *(Attach copy of detailed report if necessary)*	
What is your assessment of the implications, if any, for the safety of study participants and how will these be addressed?	

5. Declaration

Signature of Chief Investigator:	
Print name:	
Date of submission:	

6. Acknowledgement of receipt by main REC (please insert name):

The [ ] Research Ethics Committee acknowledges receipt of the above.

Signed:	
Name:	
Position on REC:	
Date:	

Signed original to be sent back to Chief Investigator (or other person submitting report)
Copy to be kept for information by main REC.