Standard Operating Procedure
Research Governance

Title:	**Reporting and Managing Research Related Adverse Events**		
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Revision Log

Previous Version number	Date of Review/Modification	Reason for Review/Modification	New Version Number

1. Purpose

This Standard Operating Procedure (SOP) sets out the procedure for reporting and managing adverse events in research studies in the UK, where Queen's University Belfast is the Sponsor, or Co-Sponsor.

Where the adverse event relates to Human Tissue, then the Human Tissue Standard Operating Procedure (QUB-HTA-004) should be followed.

2. Scope

This SOP applies to all studies where the University is acting in the capacity of Sponsor, or Co-Sponsor. It applies to all members of University staff; both academic and support staff as defined by Statute 1, including honorary staff and students.

2.1 Definitions

2.1.1 Adverse Event (AE)
An adverse event is an untoward medical occurrence (regardless of seriousness, causality or expectedness) in a study participant. An AE does not necessarily have a causal relationship with this treatment.

2.1.2 Serious Adverse Event (SAE)
A serious adverse event is one that:

- Results in death;
- Is life-threatening i.e. it is the opinion of the investigator that the subject was at risk of death at the time of the event;
- Requires hospitalisation, or the period of hospitalisation is prolonged – regardless of the length of stay;
- Results in persistent or significant disability or incapacity;
- Is a congenital anomaly or birth defect;
- Requires medical or surgical intervention in order to prevent permanent damage or impairment of a body function.

2.1.3 Near Miss
An unplanned event that does not cause injury, damage or ill health but could do so.

2.1.4 Urgent Safety Measure
An emergency measure taken by the Sponsor/Chief Investigator/Site Principal Investigator to protect a research participant from immediate harm or risk to health and safety without prior authorisation from a regulatory body.

3. Responsibilities

3.1 Chief Investigator

The Chief Investigator (CI) has overall responsibility for the conduct of the study. He/she must:

- Review all AEs to identify any trends or patterns
- Report all serious adverse events immediately to the Sponsor;
- Supply the Sponsor and the Research Ethics Committee (REC) with any additional information requested;
- Adhere to the Host Organisation's accident/incident policy and report near misses to the Host Organization in accordance with local reporting requirements.

3.2 Site Principal Investigator(s)

In the case of a multi-centre study the CI should delegate to the Site Principal Investigator (SPI) the appropriate responsibilities for managing and reporting adverse incidents on a given site. The Study Delegation Log (SOP-QUB-RGEI-005) should be completed as necessary.

3.3 All Researchers

On discovery of an adverse event, the research team member must record and notify the SPI or CI, whichever appropriate, of all adverse events.

At each trial visit the researcher in contact with the research participant must seek information to ascertain if any serious and/or non-serious adverse events have occurred since their last visit.

3.4 Sponsor

The University as Sponsor will ensure that processes are in place for each study. These functions are delegated to the CI and could involve the use of external organisations. Therefore the process may vary slightly between studies, but oversight will be maintained by the Sponsor with at least:

- Reporting of all related and unexpected Serious Adverse Events to the main REC in an expedited manner;
- Provision of an annual progress report to the main REC.

4. Procedure

4.1 Protocol Development

Before initiating a study, the CI should ensure that the protocol lists known side effects and adverse reactions. Then careful consideration should be given to the following:

- The process for collecting, recording, assessing and reporting AEs;
- Which AEs should be recorded (see paragraph 4.2);
- Which SAEs should be reported (see paragraph 4.2).

The CI may decide that all, or only some, non-serious AEs are to be recorded. The reporting requirements should be appropriate to the nature of the study.

4.2 Collecting, recording, assessing and reporting AEs and SAEs

The procedures for collecting, recording, assessing and reporting AEs and SAEs should be detailed in the study protocol. There should be agreement as to which are defined as disease-related and are therefore not subject to expedited reporting. In addition, the protocol should specify which AE data will be recorded on a Case Report Form (CRF (SOP QUB-RGEI-007)) and when a specific SAE form will be used.

4.2.1 Collecting

Collecting information from all research participants should be undertaken at each study visit to identify if any serious and/or non-serious adverse events have occurred since their last visit. Researchers should also consider other potential sources of information about AEs:

- Information on source documents;
- Information in data collection forms (e.g. diary cards, quality of life forms etc);
- Missed and/or unscheduled visits, dropouts or withdrawals;
- Use of concomitant medications/devices;
- Abnormal clinical laboratory data.

4.2.2 Recording

All AEs (serious and non-serious) must be recorded by the researcher, unless the protocol states otherwise.

The AE record should include a description, the start date, duration and outcome. It should also contain an assessment of its seriousness, relatedness, expectedness, severity, actions and be legibly signed.

The AE should be recorded in the research participant's medical notes (or other relevant source data if not medical notes).

The researcher must also comply with the accident/incident/near miss recording system of the Host Organisation, as appropriate.

4.2.3 Assessing

Each AE should be assessed to determine the seriousness, as outlined in 2.1.2.

4.2.4 Reporting

If the SAE is considered serious, not disease-related and has been specified in the protocol as not requiring recording, the researcher must report the event to the CI immediately, or within 24 hours of being made aware of it. This initial report may be verbal but it must be followed up promptly with a detailed, written report taking into consideration his/her assessment of the seriousness, along with causality, expectedness and severity on a SAE form. Guidance for the reporting of SAEs is provided by the Health Research Authority: http://www.hra.nhs.uk/research-community/during-your-research-project/safety-reporting/

The immediate and follow-up reports should identify participants by unique code numbers assigned to participants rather than by the participants' names, personal identification numbers, and/or addresses.

The CI for all QUB sponsored studies is responsible for ensuring that SAEs are reported to the Sponsor, to the REC, or to other relevant organisations.

A SAE occurring to a research participant should be reported to the REC where in the opinion 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.

These should be emailed to the REC using the Non-CTIMP safety report to REC form within 15 days of the chief investigator becoming aware of the event. Reports of SAEs in double-blind trials should be unblinded. The email to the REC should

be copied to the Sponsor (researchgovernance@qub.ac.uk). There is no requirement for annual safety reports in addition to the information provided through the annual progress report.

The CI, or in the case of a site specific study the SPI, is responsible for ensuring that all adverse incidents/near misses which involve study participants, staff or facilities, are reported in accordance with the relevant Host Organisation's incident reporting procedure. If the adverse incident or near miss occurs on QUB premises, then the IRIS reporting system should be used.

4.3 Urgent Safety Measures

A 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.

The CI should notify the Sponsor (researchgovernance@qub.ac.uk) of the urgent safety measure within 24 hours of becoming aware of it.

The CI must notify the main Research Ethics Committee (REC) immediately by telephone. A substantial amendment should be submitted to the REC within three calendar days, advising that such measures have been taken and the reasons why. This should also be disseminated to PIs at all study sites.

5. References

Health Research Authority, Safety Reporting (last accessed September 2021); https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/

UK Health Departments Research Ethics Service, Standard Operating Procedures for Research Ethics Committees v7.5.1, August 2021 (last accessed September 2021) https://www.hra.nhs.uk/about-us/committees-and-services/res-and-recs/research-ethics-committee-standard-operating-procedures/