POLICY ON RESEARCH RELATED ADVERSE EVENT REPORTING

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V10		Updated references to new guidelines and legislation, along with new job titles	Sarah Dawe
V11		Repetitions deleted	Sarah Dawe

Policy Summary / Key Information

Whilst the Chief Investigator/Principal Investigator retains overall responsibility for a study, responsibility for raising adverse events lies with the individual who becomes aware of the incident.

Chief investigator/Principal Investigator responsibilities:

- Accurately recording and reporting all adverse events in the medical records (or source data where this is not the medical records)
- Following the Sponsor's policy for reporting of Adverse Events as per the protocol
- Where QVH is the Sponsor, accurately recording all Serious Adverse Events on the Trust's Datix system
- Reporting all Serious Adverse Events immediately to:
    - Sponsor
    - Any other body defined in the protocol
- Submitting a detailed written report of SAEs to the Sponsor and the Medical Director within 24 hours and providing follow-up reports to the Sponsor and the Medical Director until event resolution
- Providing the Sponsor with details of all Adverse Events identified in the protocol as critical to the evaluation of the safety of the Investigational Medicinal Product as specified in the protocol
- Assessing each event for causality, expectedness and seriousness
- Supplying the Sponsor, the R&I Dept and the Medical Director with any supplementary information they request
- Ensuring the safety of study participants

Contents

1. Introduction

The UK Policy Framework for Health and Social Research 2017 pays particular attention to clarifying responsibilities and accountabilities with the aim of forestalling **research related** adverse incidents. QVH must therefore have systems in place to record, investigate and report adverse incidents arising from any research undertaken within the Trust.

The Medicines for Human Use (Clinical Trials) Regulations 2004 apply to Clinical Trials of Investigational Medicinal Products (CTIMPs) and specify the management and reporting requirements for this sub-set of trials.

2. Scope

This policy defines the requirements for reporting adverse events in studies where QVH is the Sponsor or where the Sponsor has not provided safety reporting documentation. For externally-sponsored research, QVH's policy will be to accept and enact the safety rules embedded in the contractual agreement.

This document outlines the responsibilities of both the Investigator and the Sponsor. If (as is commonplace) the Sponsor delegates duties to the Chief Investigator (CI) or Principal Investigator (PI) the CI/PI must understand and be able to fulfil the duties and responsibilities they have agreed to undertake. The Sponsor will still remain ultimately responsible for any delegated duties

3. Duties

Summary of Investigator and Sponsor responsibilities in CTIMPs

Any Chief Investigator (CI) of a Clinical Trial of an Investigational Medicinal Product (CTIMP) will be delegated responsibility for Part 5 of the Medicines for Human Use (Clinical Trials) Regulations by the Sponsor. Below is a summary list of the responsibilities of the Investigator and Sponsor. Any Chief Investigator/ Principal Investigator who has agreed to undertake duties for pharmacovigilance delegated by the Sponsor must undertake both Investigator's and Sponsor's responsibilities as described throughout this document.

Investigator's responsibilities:

1) Accurately recording and reporting all adverse events in the medical records (or source data where this is not the medical records)
2) Reporting all Serious Adverse Events immediately (orally or in writing) to:

    a. Sponsor
    b. Any other body defined in the protocol

3) Submitting a detailed written report to the Sponsor and the Medical Director within 24 hours and providing follow-up reports to the Sponsor and the Medical Director until event resolution
4) Providing the Sponsor with details of all Adverse Events identified in the protocol as critical to the evaluation of the safety of the Investigational Medicinal Product as specified in the protocol
5) Assessing each event for causality, expectedness and seriousness

6) Supplying the Sponsor, the Competent Authority(ies)[1], the Research Ethics Committee and the Medical Director with any supplementary information they request

Sponsor's Responsibilities:

The Sponsor allocated to undertake Part 5 of the UK regulations (pharmacovigilance) is ultimately responsible for the following. When necessary in order to carry out drug-related responsibilities, the Chief Investigator/ Principal Investigator may delegate responsibilities to the funder/drug manufacturer, provided this is clearly documented:

1) Ongoing safety and evaluation of any Investigational Medicinal Product(s) being investigated
2) Promptly notifying any investigators, Competent Authority(ies)[1] and Research Ethics Committee of any findings that may affect the health of subjects
3) Ensuring written procedures and systems are in place so that safety reporting is conducted according to regulatory requirements and that personnel are suitably trained for the purposes of data submission, validation, entry and review
4) Keeping detailed written reports of all Adverse Events reported by Investigators and performing an evaluation with respect to seriousness, causality and expectedness
5) Reporting all relevant safety information to the relevant Competent Authority(ies)[1] and Research Ethics Committee
6) Reporting, within expedited timeframes, all Suspected Unexpected Serious Adverse Reactions (SUSARs - tested Investigational Medicinal Product and comparators) to:

    a. The relevant Competent Authority(ies)
    b. The Research Ethics Committee
    c. The Medical Director
    d. QVH R&I department (both when QVH is sponsoring and when QVH is not the sponsor but the Suspected Unexpected Serious Adverse Reaction originated in the Trust)
    e. Comparator product Suspected Unexpected Serious Adverse Reactions to the marketing authorisation holder

7) Breaking treatment codes before submitting expedited reports (e.g. Suspected Unexpected Serious Adverse Reactions) to Competent Authority(ies) and the Research Ethics Committee for specific subjects, even if the Chief Investigator/Principal Investigator has not broken the code[2]
8) Ensuring that for blinded studies, emergency procedures for unblinding are in place
9) Submitting the annual safety report to the Competent Authority(ies) and the Research Ethics Committee[4]
10) Submitting periodic (blinded) line listings of all Suspected Unexpected Serious Adverse Reactions that have occurred to all participating investigators.

4. Abbreviations and definitions

[1]Competent Authorities in all member States in which the trial is conducted. If the trial is conducted in the UK alone, then the MHRA will be the only CA requiring notification.

[2] A system for maintaining the blind for any researcher (including the chief investigator) involved in data reporting and interpretation should be agreed in advance and documented

4.1 Abbreviations

AI	Adverse Incident
AE	Adverse Event
AR	Adverse Reaction
CA	Competent Authority (MHRA in the UK and the equivalent of the MHRA in other countries)
CI	Chief Investigator
CRF	Case Report Form
CTIMP	Clinical Trial of an Investigational Medicinal Product
DMC	Data Monitoring Committee
IMP	Investigational Medicinal Product
MHRA	Medicines and Healthcare products Regulatory Agency
PI	Principal Investigator
REC	Research Ethics Committee (main REC giving favourable opinion)
SAE	Serious Adverse Event
SmPC	Summary of Product Characteristics
SSAR	Suspected Serious Adverse Reaction
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File

4.2 Definitions

The following definitions are taken from the Medicines for Human Use (Clinical Trials) Regulations 2004 and refer to Clinical Trials of Investigational Medicinal Products.

Investigational Medicinal Product (IMP)

An ***Investigational Medicinal Product*** is an active substance or placebo being tested or used as a reference in a clinical trial including a medicinal product which has a marketing authorisation but is, for the purposes of the trial being used or assembled (formulated or packaged) in a way different from the authorised form or being used for an unauthorised indication or when used to gain further information on an authorised form.

Adverse Event (AE)

An *adverse event* is any untoward medical occurrence in a subject to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product.

Note: An adverse event can therefore be any unfavourable and unintended sign (including abnormal lab results), symptom or disease temporally associated with the use of the medicinal product, whether or not considered to be related to the medicinal product.

Adverse Reaction (AR)

An *adverse reaction* is any untoward and unintended response in a subject to an investigational medicinal product which is related to any dose administered to that subject.

Note: Any adverse event judged by either the reporting investigator or the Sponsor as having a reasonable causal relationship to an Investigational Medicinal Product qualifies as an AR; there is evidence or argument to suggest a causal relationship.

All adverse reactions are adverse events.

Unexpected Adverse Reaction

An *unexpected adverse reaction* is an adverse reaction, the nature and severity of which is not consistent with the applicable product information:

(a) the summary of product characteristics for that product (for an approved investigational medicinal product) *or*
(b) the investigator's brochure (for an unapproved investigational product)

Note: Reports which add significant information on specificity or severity of a known, already documented serious adverse reaction constitute unexpected events. For example, when the outcome of an expected adverse reaction is not consistent with the relevant product information, the event may be considered unexpected.

Serious Adverse Event (SAE) or Serious Adverse Reaction (SAR)

An adverse event, adverse reaction or is defined as **serious** if it:

(a) results in death
(b) is life-threatening[1]
(c) requires hospitalisation
(d) prolongs a current hospitalisation
(e) results in persistent or significant disability or incapacity
(f) consists of a congenital anomaly or birth defect
(g) other (please specify)[2]

[1] *Life threatening in the definition of a Serious Adverse Event (SAE) or Serious Adverse Reaction (SAR)*
refers to an event in which the subject was at risk of death at the time of the event; not an event that hypothetically might have caused death if it were more severe.

[2] *Medical judgement should be exercised in deciding whether other Adverse Events may be considered serious because they jeopardize the patient or may require intervention to prevent one of the other outcomes. Examples include blood dyscrasias or convulsions that do not result in hospitalisation, or development of drug dependency or cancer.*

Suspected Serious Adverse Reaction (SSAR)

A *serious adverse reaction,* the nature and severity of which is consistent with information about the Investigational Medicinal Product in question presented in either:

(a) the summary of product characteristics for that product (in the case of a product with a marketing authorisation)
or
(b) the investigator's brochure relating to the Investigational Medicinal Product in question (in the case of any other IMP)

Suspected Unexpected Serious Adverse Reaction (SUSAR)

All adverse events that are suspected to be related to an investigational medicinal product and that are both unexpected and serious are considered to be Suspected Unexpected Serious Adverse Reactions (SUSARs).

Not all adverse events are adverse reactions but all adverse reactions (including those that are unexpected) are adverse events.

Sequelae

Sequelae refers to any abnormal bodily condition related to or arising from a pre-existing disease or a complication of a disease.

5. Procedures

5.1 Trial Planning and Protocol Writing

The Sponsor should decide which Adverse Events/Serious Adverse Events are recorded in the Case Report Form (CRF). This decision should be consistent with the purpose of the trial and any toxicity and efficacy endpoints. In trials where new Investigational Medicinal Products are being tested or where Investigational Medicinal Products are being used for an unauthorised indication or in new patient groups where the safety profile of the Investigational Medicinal Product has not been fully established, it is strongly suggested that the Case Report Form (CRF) is designed to record all Adverse Events.

5.2 SAE Definition and Reporting Procedures in the Protocol

The safety section of the protocol should clarify all adverse event definitions, responsibilities and requirements. The protocol should also define any Serious Adverse Events/Reactions that do not require expedited reporting, for example, because they are primary endpoints of the trial or are well established events for the disease condition or Investigational Medicinal Product and their occurrence do not materially affect the risk/benefit profile of the Investigational Medicinal Product. Even though these events are not reported in an expedited manner, the Sponsor should ensure an integrated safety analysis is performed on all events in order to detect any safety trends such as the increase in frequency of an expected event. In addition, all Suspected Serious Adverse Reactions (whether unexpected or not) should be reported to the Sponsor for submission on the annual safety report (as well as the Medical Director).

5.3 Trial Termination/Suspension & Requirement for an Independent Data Monitoring Committee

Ultimately, the R&I Dept will have the authority to suspend or terminate a trial, through its own deliberations or upon the recommendation of an appropriate ethics committee.

The Sponsor may appoint an Independent Data Monitoring Committee in trials with high morbidity or mortality to review safety data regularly and when necessary, recommend to the Sponsor whether to continue, modify or terminate the trial. This procedure should be defined in the protocol

5.4 Evaluation of Adverse Events Reported During the Trial

Each Adverse Event should be evaluated for seriousness, causality, expectedness and intensity. This evaluation may be performed by both the Principal Investigator and the Sponsor.

It is most appropriate for the treating Principal Investigator at each centre to evaluate each event before reporting it to the Sponsor. The Principal Investigator's causality assessment should not be downgraded by the Sponsor. If a Sponsor disagrees with the Principal Investigator's assessment, both the opinion of the Principal Investigator and the Sponsor should be provided if the report requires expedited reporting to the Competent Authority and Research Ethics Committee.

5.5 Blinded Trials

In blinded trials, the Adverse Event should be assessed for seriousness, causality and expectedness as if it were the tested Investigational Medicinal Product. If the case appears to be a Suspected Unexpected Serious Adverse Reaction then it should be

unblinded. Prior to initiation of the study, blinded trials must put in emergency unblinding procedures.

5.6 Criteria for the Evaluation of Adverse Events

5.6.1 Intensity (severity)

The assessment of intensity will be based on the investigator's clinical judgement using the following definitions:

- **Mild:** An event that is easily tolerated by the patient, causing minimal discomfort and not interfering with everyday activities.
- **Moderate:** An event that is sufficiently discomforting to interfere with normal everyday activities.
- **Severe:** An event that prevents normal everyday activities.

*Note: **severity** is often used to describe the intensity of a specific event. This is not the same as 'seriousness', which is based on patient/event outcome or action criteria.*

5.6.2 Seriousness

The assessment of the seriousness of the event should be based on the definition in section 4.2 of this policy.

5.6.3 Causality

The relationship between the drug and the occurrence of each adverse event will be assessed and categorised (as detailed below). The investigator will use clinical judgement to determine the relationship. Alternative causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors etc. will also be considered. The Investigator will also consult the Investigator Brochure or other product information.

- **Not related:** Temporal relationship of the onset of the event, relative to administration of the product, is not reasonable or another cause can by itself explain the occurrence of the event.
- **Unlikely:** Temporal relationship of the onset of the event, relative to administration of the product, is likely to have another cause which can by itself explain the occurrence of the event.
- **Possibly related:** Temporal relationship of the onset of the event, relative to administration of the product, is reasonable but the event could have been due to another, equally likely cause.
- **Probably related:** Temporal relationship of the onset of the event, relative to administration of the product, is reasonable and the event is more likely explained by the product than any other cause.
- **Definitely related:** Temporal relationship of the onset of the event, relative to administration of the product, is reasonable and there is no other cause to explain the event, or a re-challenge (if feasible) is positive.

*Where an event is assessed as **possibly, probably, or definitely related,** the event is an **adverse reaction**.*

5.6.4 Expectedness

The expectedness of an adverse reaction shall be determined according to the reference documents as defined in the study protocol (e.g. investigator brochure or summary of product characteristics - SmPC).

- **Expected:** Reaction previously identified and described in protocol and/or reference documents e.g. Investigator Brochure, summary of product characteristics (SmPC).
- **Unexpected:** Reaction not previously described in the protocol or reference documents.

N.B. Adverse reactions must also be considered as unexpected if they add significant information on the specificity or severity of an expected adverse reaction.

5.7 Recording/Documentation of Adverse Events

When a research related *adverse event/reaction* occurs, the investigator must review all documentation (e.g., hospital notes, laboratory and diagnostic reports) relevant to the event. The event and relevant comments must then be recorded in the source data (subject medical notes or worksheet).

If a Serious Adverse Event is reported by the Principal Investigator, the reports (along with all follow-up reports) should be filed in the study site trial documentation.

The Sponsor should keep detailed written reports of all Adverse Events reported by Investigators

5.8 Serious Adverse Event Reporting by the Principal Investigator

Initially, researchers should use the Trust's standard incident reporting system (Datix).

Within 24 hours of a member of the research team becoming aware of a serious adverse event, the Sponsor (Principal Investigator/Chief Investigator in QVH sponsored trials) must be notified. The Principal Investigator (or delegated person) will make an initial report, orally or in writing. Oral reports will be followed by detailed written reports within 24 hours of the initial report. Written reports will be made by the Principal Investigator who must complete a Serious Adverse Event Report Form provided by the Sponsor of the research study. The only exception to this would be in cases where the PI is unable to report within the required timeframes, in which case this responsibility can be delegated to another member of the research team or support can be requested from the R&I Department, if necessary.

Where QVH is the Sponsor or where no form has been provided, the investigator will use the QVH *Serious Adverse Event Report Form* (**Appendix 2**) and *Instructions for Completion of Serious Adverse Event Forms* (**Appendix 1**). They should also follow the Trust's separate general incident reporting system (Datix).

If a Data Monitoring Committee (DMC) has been constituted, it is recommended that Serious Adverse Events are reported to the Data Monitoring Committee in a timely fashion.

The only exception to this section is where the protocol or Investigator's Brochure identifies the event as not requiring immediate reporting. However, even if these events are not reported in an expedited manner, the data will still need to be reviewed by the Data Monitoring Committee or Sponsor as part of the integrated safety analysis procedures that have been adopted for the trial.

After the initial report, the Principal investigator is required to actively follow-up the subject. The Principal investigator (or delegated person) will provide missing and follow-up information as soon as it is available until the Serious Adverse Event has resolved or a decision for no further follow-up has been taken. Where QVH is the Sponsor or where no form has been provided, the investigator will use the QVH *Serious Adverse Event Report Form* (Appendix 2) and *Instructions for Completion of Serious Adverse Event Forms* (Appendix 1). Completed Serious Adverse Event Report Forms for both initial and follow-up reporting must be sent to both the Sponsor and the Medical Director.

5.9 Evaluation of the Serious Adverse Events/Adverse Events by the Sponsor

The Sponsor must assess all Adverse Event records and must also perform an evaluation of seriousness, causality and expectedness. Any Serious Adverse Event that the Sponsor assesses as a Suspected Unexpected Serious Adverse Reaction (SUSAR) will require expedited reporting. (See section 6.6: Criteria for evaluation of Adverse Events).

6. Safety analysis & Safety Reporting

6.1 Reporting Other Safety Issues by the Sponsor

In addition, other safety issues also qualify for expedited reporting (15 day timeframe) where they might alter the current risk-benefit assessment of the Investigational Medicinal Product or would be sufficient to consider changes in the Investigational Medicinal Product administration or overall conduct of the trial, for example:

a. single case reports of an expected serious adverse reaction with an unexpected outcome (e.g. death);
b. an increase in the rate of occurrence of an expected serious adverse reaction, which is judged to be clinically important;
c. post-study Suspected Unexpected Serious Adverse Reactions that occur after the patient has completed a trial;
d. a new event, related to the conduct of the trial or the development of the Investigational Medicinal Product (IMP), that is likely to affect the safety of subjects, such as:

- a serious adverse event which could be associated with the trial
- procedures which could modify the conduct of the trial; a significant hazard to the subject population such as lack of efficacy of an Investigational Medicinal Product used for the treatment of a life-threatening disease;
- a major safety finding (e.g. carcinogenicity) from a newly completed animal study.

These safety issues must be reported to the Competent Authority and the main Research Ethics Committee in the format of a letter titled “Safety Report” (copied to the Medical Director).

The Sponsor should retain a copy of the expedited report and associated documentation in the Trial Master File (TMF).

6.2 Pregnancy

In the event that a subject or their partner becomes pregnant whilst taking part in a CTIMP, the pregnancy should be followed up until outcome. This should be done via the patient's healthcare professional ensuring that if the patient leaves the area, the new healthcare professional is informed. If the pregnancy results in an abnormal outcome, which the healthcare professional considers might be due to the drug, this should be treated as an expedited report.

6.3 Safety Trends

The Sponsor should perform an integrated safety analysis of all adverse event information reported and ensure discussions are held and actions undertaken to secure the safety of all subjects. Discussions may result in the expedited reports being submitted and/or the discontinuation of the trial.

6.4 Annual Safety Reporting by the Sponsor

For all Investigational Medicinal Product studies, one year following the granting of a Clinical Trials Authorisation Certificate, and thereafter annually, the Chief Investigator (or nominated body/delegate for blinded trials[3]) must compile an **annual safety report**, consisting of:

- a list of all the suspected serious adverse reactions (including all Suspected Unexpected Serious Adverse Reactions) which have occurred **during that year** in relation to those trials, whether at trial sites in the United Kingdom or elsewhere, including those reactions relating to any investigational medicinal product used as a placebo or as a reference in those trials, and for each investigational medicinal product being tested,
- an aggregate summary tabulation of suspected Serious Adverse Reactions that occurred in the concerned trial.
- a report on the safety of the subjects of those trials.

One year following the granting of a Clinical Trials Authorisation Certificate, and thereafter annually, the Chief Investigator (or nominated body/delegate for blinded trials[6]) must send the annual safety report to the:

- Medicines and Healthcare products Regulatory Agency (MHRA)
- QVH Research and Development Department (where QVH is the sponsor an additional report is not required)
- Deputy Medical Director with responsibility for governance
- The Research Ethics Committee (REC) that granted approval (main REC). Please refer to the NRES web site for requirements for reporting of safety information to the main REC .

In order to produce the annual safety report, the Chief Investigator (or delegate) should refer to the European Commission – Detailed Guidance on the Collection, Verification,

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[3] *Reports are to be sent to the appropriate individuals/organisations **unblinded** (a process that may require an IDMC to be engaged).*

*If the CI is unable to make appropriate arrangements for external reporting of SUSARs within the required timeframes, it is essential that the sponsor is notified **within 24 hours** (for trust-sponsored research contact the R&D office).*

and Presentation of adverse events arising from clinical trials on Medicinal Products for Human Use: Section 6.3.2.1 and Annex 4 and *5*

7. Research and Innovation Department Responsibilities

QVH will defer to the Sponsor of CTIMPs and follow their reporting procedures. Where QVH is the sponsor of a research study, the R&I Department will follow up on adverse events recorded on Datix.

The R&D Department, in liaison with the Medical Director, will consider whether any additional actions (separate to those already taken by the investigator) are required and will discuss these with the Investigator. The R&D Department, in liaison with the Medical Director, will then inform the Investigator, in writing, of any further actions required.

The R&D Department reserves the right to suspend or withdraw approval for a study. This may happen, but is not limited to, where public health and safety is considered to be at risk and/or where the safety and well-being of research subjects or staff are considered to be at risk.

8. Safety Reporting Responsibilities and Requirements for Non-Clinical Trials of Investigational Medicinal Products (Non-CTIMPs)

8.1 Summary of investigator and sponsor responsibilities in non-CTIMPs

8.1.1 Investigator's responsibilities:

1) Accurately recording and reporting all adverse events in the medical records (or source data where this is not the medical records)
2) Logging all adverse events or serious adverse events on Datix.
3) Reporting all Serious Adverse Events immediately to:
    a. Sponsor
    b. Any other body defined in the protocol

If there is a clinical incident, the Investigator is responsible for ensuring that all Serious Adverse Events, whether or not related to research, are reported in accordance with the QVH Risk Management & Incident Reporting Policy.

4) Submitting a detailed written report to the Sponsor and the Medical Director within 24 hours and providing follow-up reports to the Sponsor and the Medical Director until event resolution
5) Assessing each event for causality, expectedness and seriousness
6) Supplying the Sponsor and the main Research Ethics Committee with any supplementary information they request

8.1.2 Sponsor/ Chief Investigator Responsibilities:

1) Ongoing safety and evaluation of any procedure being investigated
2) Promptly notifying any investigators and the main Research Ethics Committee of any findings that may affect the health of subjects
3) Ensuring written procedures and systems are in place so that safety reporting is conducted according to good practice requirements and that personnel are suitably trained for the purposes of data submission, validation, entry and review
4) Keeping detailed written reports of all Adverse Events reported by Investigators and performing an evaluation with respect to seriousness, causality and expectedness
5) Reporting all relevant safety information to the main Research Ethics Committee

6) Breaking treatment codes before submitting expedited the main Research Ethics Committee for specific subjects

8.2 Research Ethics Committee Reporting requirements

Within 15 days of being made aware of the event, the Chief Investigator should report to the main Research Ethics Committee, all Serious Adverse Events that are:

- *Related* – that is, possibly, probably or definitely resulted from administration of the research procedure, and
- *Unexpected* – that is, the type of event is not listed in the protocol as an expected occurrence

Reports should be sent unblinded. In addition, an annual safety report should be sent to the main Research Ethics Committee by the Chief Investigator.

9. Training and Awareness

All staff have access to a copy of the policy on the Trust's intranet site. In addition, staff working on CTIMPs receive validated GCP training, which includes reporting of adverse events.

10. Equality

This policy and protocol has been equality impact assessed in accordance with the Trust's impact assessment toolkit. Completed assessments are available upon request from qvh.eqia@nhs.net.

11. Data Protection

The Data Protection Act 2018 protects personal data which includes information about staff, patients and carers. The NHS relies on maintaining the confidentiality and integrity of its data to maintain the trust of the community. Unlawful or unfair processing of personal data may result in the Trust being in breach of its data protection obligations.

12. Freedom of Information

Any information that belongs to the Trust may be subject to disclosure under the Freedom of Information Act 2000. This act allows anyone, anywhere to ask for information held by the Trust to be disclosed (subject to limited exemptions). Further information is available in the Freedom of Information Act Trust Procedure which can be viewed on the Trust Intranet.

13. Records Management

Records are created or received in the conduct of the business activities of the Trust and provide evidence and information about these activities. All records are also corporate assets as they hold the corporate knowledge about the Trust. The Trust has a Records Management Policy for dealing with records management. Compliance with and the application of this policy will ensure that the Trust's records are complete, accurate and provide evidence of and information about the Trust's activities for as long as is required.

14. Review

This policy will be reviewed in 3 years' time. Earlier review may be required in response to exceptional circumstances, organisational change or relevant changes in legislation or guidance.

14.1 Discipline

Breaches of this policy will be investigated and may result in the matter being treated as a disciplinary offence under the Trust's disciplinary procedure.

15. Monitoring Compliance with this Policy

The process of managing the Policy will be led by specialty research leads and overseen by the Director for R&I, and will be audited by the R&I Dept after each recorded adverse event to ensure that the process and policy has been adhered to. Evidence will be provided from Datix and the separate serious advert event reporting form, as appended below.

Activity being monitored	**Methodology to be used for monitoring**	**Responsibility for monitoring**	**Frequency of monitoring and reporting**	**Process for review and improvement**
Datix reporting	Evidence obtained from Datix and any adverse event reporting form	Head of Research	After any adverse event	In consultation with Director of R&I

16. References

1. UK Policy Framework for Health and Social Care
https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/

2. The Medicines for Human Use (Clinical Trials) Regulations 2004
Statutory Instrument 2004 No. 1031
http://www.legislation.gov.uk/uksi/2004/1031/contents/made

3. EMEA Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use. Revision 1, April 2004.

17. Associated Documentation

Appendix A Instructions for completion of Serious Adverse Events

Appendix B Serious Adverse Event Form

Appendix A: Instructions for completion of Serious Adverse Event (SAE) forms

RESEARCH RELATED SAEs/SUSARs

An event/reaction is serious if it:

- results in death,
- is life threatening,
- results in persistent or significant disability/incapacity,
- requires hospitalisation,
- prolongs a current hospitalisation
- results in a congenital anomaly or birth defect.

(drugs, devices and interventions)

Written reports will be made by the Principal Investigator who must complete a Serious Adverse Event Report Form provided by the Sponsor of the research study. The only exception to this would be in cases where the PI is unable to report within the required timeframes, in which case this responsibility can be delegated to another member of the research team or support can be requested from the R&I Department, if necessary. Where QVH is the Sponsor or where no form has been provided, the investigator will use the form in appendix 2.

*Report forms will be transmitted to the Sponsor and the Medical Director by email. The following instructions and associated SAE form apply **where QVH is the sponsor** of the research study in which the Serious Adverse Event has occurred or where no other form has been provided by the (external) sponsor.*

Instructions for completion of SAE Form (shown in Appendix 2) for Initial and Follow up reporting

1. As soon as possible, and at the latest within 24 hours of becoming aware of event,
   - Complete the SAE Form and send to the Sponsor and the Medical Director.
2. As soon as possible, and at the latest within 5 days of becoming aware of the event,
   - Complete a **further** Serious Adverse Event form with Follow up information and send to the Sponsor and the Medical Director
3. For both initial and follow-up reporting of Suspected Unexpected Serious Adverse Reactions (SUSARs), it is advisable for the Chief Investigator to date and time stamp all reports and to notify both the R&I Office and the Medical Director **within 24 hours**. All SUSARS must be reported to the R&I Office the Medical Director
4. Complete and return (as above) further Follow-up SAE Form(s) for data collected later than 5 days post Serious Adverse Event (SAE) until the SAE has resolved or a decision for no further follow up has been taken.
5. For non-Investigational Medicinal Product studies where the SAE was possibly/probably/definitely related to participation in the research, send a copy of each form to the ethics committee that granted approval.
6. Keep original forms in Investigator Site File (ISF).

Appendix B: Serious Adverse Event Form

SERIOUS ADVERSE EVENT FORM (for initial and follow up reporting)

Written reports will be made by the Principal Investigator (except in cases where this is not possible within the required timeframes), who must complete an SAE Report Form. Where QVH is the Sponsor or where no form has been provided, the investigator will use the following form.

As soon as possible and at the latest within 24 hours of becoming aware of the event (or within 5 days for follow up), send this completed form to the Sponsor and the Medical Director.

1. This serious adverse event is defined as: (please tick "√" all boxes that apply):

1. ☐ Death

2. ☐ Life-threatening

3. ☐ Requiring or prolonging inpatient hospitalisation

4. ☐ Persistent or significant disability or incapacity

5. ☐ Congenital abnormality / birth defect

6. ☐ Other, please specify below
e.g. incapacity for work for more than 3 days

Signature of Ward Manager: _____

Signature of Service Manager: _____ **Date:**

2. Subject Information:

Surname: **Forename:**

Address:

Ward:

Gender:
☐ Male
☐ Female

Date of birth |__|__| |__|__| |__|__|
Day month year

Weight (kg) |__|__|__|

Height (cm) |__|__|__|

Ethnicity:
☐ Caucasian
☐ Black
☐ Other, please specify:

3. Adverse Event date of onset (1st symptom)**:** |__|__| |__|__| |__|__|
Day month year

Onset Time: |__|__| : |__|__|

End Date: **End Time:**

Or Duration:

Location:

Date when AE became serious (if different from onset date): |__|__| |__|__| |__|__|
Day month year

4. INCIDENT DETAILS:

Diagnosis, reporting signs and / or main symptoms(s) – Provide detailed description (attach additional sheets if necessary)

5. Tests:

Yes ☐ No ☐

Specify relevant data and attach all reports with normal ranges (where applicable) and date of result

Laboratory: Yes ☐ No ☐
Date lab / test:

6. Name of Study Drug:

Treatment No. |__|__|__|__|__| **Indication**_____

Batch No:
Therapy Dates: **From: |__|__| |__|__| |__|__|** **To: |__|__| |__|__| |__|__|**
☐ If continuing Day month year Day month year
At the time of the event provide: **Unit Dose:** _____ **Regimen:** _____
Route: _____
Last Dose Date and Time (prior to event): |__|__| |__|__| |__|__| **Time: |__|__| : |__|__|**
Day month year

Was the study drug administered in accordance with the protocol?
YES ☐
No ☐ If no, specify:
Was the study code broken? (code should not be broken, unless necessary or subject treatment decision)
☐ Yes If yes, specify reasons:
☐ No
☐ NA

7. Concomitant Drugs: (exclude those used to treat the event)

Drug	Indication for Use	Daily Dose	Route	Date of Administration	
				From Day Month Year	**To** Day Month Year

8. Relevant Medical History:

☐ No
☐ Yes If yes, specify reasons:

9. Concomitant Diseases

☐ No
☐ Yes If yes, specify reasons:

10. Action Taken With Study Drug:

☐ **Blood sample taken**

Name of person giving treatment: _____ **Status:** _____

Signature: _____

1 ☐ **No change**

2 ☐ **Dosage Changed** **Unit Dose:**_____
Regimen: _____

3 ☐ **Drug temporarily discontinued** **Date of reintroduction:** |__|__| |__|__| |__|__|
Day month year

Did the event reappear after reintroduction? ☐ **Yes** ☐ **No**
Any use of corrective therapies? ☐ **Yes** ☐ **No**
if yes, specify:

4 ☐ **Drug permanently discontinued**

11. Outcome:

1 ☐ **Death** **Date:** |__|__| |__|__| |__|__|
Day month year
Autopsy performed? **No** ☐
Yes ☐ **If yes, attach report**
Specify causes and circumstances of death:

2 ☐ **Ongoing (persistence)**
3 ☐ **Recovered with sequelae** **Date:** |__|__| |__|__| |__|__|
Day month year
Specify sequelae:
4 ☐ **Recovered without sequelae** **Date:** |__|__| |__|__| |__|__|
Day month year

12. Was The Patient Withdrawn From The Study?

☐ **No**
☐ **Yes**

13. Causality and Expectedness (Relationship to Study Drug as assessed by the investigator)

Is the SAE related to the drug / device / intervention?

☐ Not related
☐ Unlikely to be related
☐ Possibly related
☐ Probably related
☐ Definitely related

If possibly, probably or definitely related, was the SAE unexpected?

☐ Yes

☐ No

(Unexpected means not described in the protocol or other product information)

Comment:

14. Documentation

Has this patient been informed? ☐ **Yes** ☐ **No**
Has this incident been documented in patient's medical record? ☐ **Yes** ☐ **No**
Have the relatives been informed (if applicable)? ☐ **Yes** ☐ **No**

15. Additional Comments or Further Information: (if any)

16. Name of Person Making Report:

Chief / Principal Investigator's Name (at QVH site):
(if different from Investigator)
Signature: **Signature:**

I / we confirm that the contents of all pages of this form are accurate and complete

Job title / role in study:
Email address:
Telephone No:

17. Date received by R&I office (initial and follow-up reporting of SUSARs)**:**

18. MANAGERIAL FOLLOW-UP

Date notified of incident / SAE:
Was the location of person authorised? ☐ **Yes** ☐ **No** ☐ **N/A**
Was the activity of the person authorised? ☐ **Yes** ☐ **No** ☐ **N/A**
Action taken to mitigate future risk to research subjects:

Incident severity grading (see matrix below):

Potential Consequences / Impact & Final Outcome (please re-assess & re-grade at follow-up)

Intensity	Insignificant	Minor	Moderate	Major e.g. life-threatening	Catastrophic e.g. Death
MILD					
MODERATE					
SEVERE					

e.g. SAE resolved / no further follow-up required

FOLLOW-UP BY PATIENT SAFETY MANAGER

Name of Patient Safety Manager:

Date:

Follow up

FOLLOW-UP BY HEALTH & SAFETY ADVISOR/PHARMACIST

Is this incident notifiable to HSE / RIDDOR? ☐ **Yes** ☐ **No** **Date:**

Has the MHRA been notified? ☐ **Yes** ☐ **No** **Date:**

Name: **Date:**