Safety Reporting and Pharmacovigilance in the King's Clinical Research Facility

Document Detail	
Document type	Standard Operating Procedure
Document name	CRF-QA-SOP-5: Safety Reporting and Pharmacovigilance in the King's CRF
Document location	Q-Pulse \ CRF Documents
Version	6.0
Effective from	09 November 2022
Review date	09 November 2024
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Related documents	KHP CTO Pharmacovigilance Policy CRF-STU-FRM-9: AE Workbook CRF-STU-FRM-10: Adverse Event Log KCH Policy for the Management, Reporting, & Investigation of Adverse Incidents (including Serious Incidents)
Keywords	Pharmacovigilance, Adverse Event, Serious Adverse Event, reporting, Safety
Supporting references	See Section 6.0

Change History		
Date	Change details, since approval	Approved by
18th December 2013	1. Amended text in SOP title from "Clinical Research Facilities" to "King's Clinical Research Facility" 2. Amended name of Director to reflect new Director 3. Amended logos to update to current CRF letterhead template 4. Amended document number from CRF SOP003 to CRF-QA-SOP-4 to comply with QPulse document numbering system 5. Amended numbers of documents referred to throughout the text to reflect revised QPulse/CRF numbers	E. Giemza
January 2016	1. Administrative changes to the text for clarification and to reflect current practice and to incorporate all types of studies 2. Updated related documents, including new CRF forms, and references	E. Giemza

February 2018	1. Section 6.0: updated references and links 2. Minor amendments to the text for clarity 3. No changes to the procedure are required	E.Giemza
July 2020	1. Section 5.2: Addition of 'for their intensity and relationship to study treatments or procedures 2. Section 5.6: Addition of ' the outcome of event must be completed by the PI or delegated physician 3. Change to Author	E. Giemza
Nov 2022	1. Change to author	E Giemza

Review History		
Date	Review details	Approved by
18th December 2013	Review of v1.0 conducted by Lara Edwards, CRF QA Manager, superseded by v2.0 (effective date 03rd January 2014)	E. Giemza
January 2016	Review of v2.0 conducted by Georgia Bullock, CRF QA Manager, as per the review date. Changes made as per 'Change History' and re-issued as v3.0.	E. Giemza
January 2018	Review of v3.0 conducted by Georgia Bullock, CRF QA Manager, as per the review date. Changes made as per 'Change History' and re-issued as v4.0.	E. Giemza
July 2020	Review of v4.0 conducted by Angelina Twumasi, CRF QA Manager, as per the review date. Changes made as per 'Change History' and re-issued as v5.0	E. Giemza
Nov 2022	Review of v5.0 conducted by Bidisha Chakraborty, CRF QA Manager, as per the review date. Changes made as per 'Change History' and re-issued as v6.0	E Giemza

1.0 Background

1.1 Pharmacovigilance is the science relating to the collection, monitoring, assessment and evaluation of information on the adverse effects of medicinal products. It is important in clinical trials to ensure the safety of the trial subjects and the safety of current and future patients.

1.2 All Investigators and Sponsors involved in clinical trials have responsibilities for safety reporting, including the recording, assessing and reporting of adverse events. The safety data collected in a clinical trial allows the Sponsor to provide updated information on the medicinal product to investigators and subjects and to assess whether it is safe to continue the trial.

1.3 An 'Adverse Event' (AE) 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'. An AE can therefore be any unfavourable and unintended sign (e.g. an abnormal laboratory finding).

An ‘Adverse Drug Reaction’ (ADR) is any untoward and unintended response in a subject to a medicinal product which is related to any dose administered to that subject.

1.4 A ‘Serious Adverse Event’ (SAE) or Serious Adverse Reaction (SAR) is any adverse event which falls into any of these categories:

- Results in death
- Is life-threatening (the subject is at immediate risk of death)
- Requires hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability or incapacity
- Consists of a congenital anomaly or birth defect

1.5 A ‘Suspected Unexpected Serious Adverse Reaction’ (SUSAR) is any SAE/SAR which is both RELATED to the Investigational Medicinal Product (IMP) and UNEXPECTED. This means that the event is not documented in the trial protocol, Summary of Product Characteristics (SmPC) or Investigator Brochure (IB) as an expected reaction to the IMP.

1.6 An ‘Important Medical Event’ (IME) is an event which may not be immediately life-threatening or result in death or hospitalisation, but may jeopardise the subject or may require intervention to prevent any of the outcomes in the SAE definition. These events should be considered serious.

2.0 Purpose

2.1 The purpose of this Standard Operating Procedure (SOP) is to describe the regulatory and local requirements for adverse event recording and reporting for all trials and studies conducted within the King’s Clinical Research Facility (CRF).

3.0 Scope

3.1 The CRF encompasses the Clinical Trials Facility (CTF), the Experimental Medicine Facility (EMF) and the Cell Therapy Unit (CTU). CRF SOPs will apply to the CTF and EMF only and staff working in those areas should work to all relevant CRF SOPs. The CTU will continue to control and use its own policies and SOPs to ensure compliance with Good Manufacturing Practice (GMP).

3.2 This SOP applies to all core CRF staff involved in the conduct of clinical trials/studies and all external personnel conducting studies in the CRF (users of the CRF). Each staff member must be aware of their specific responsibilities with regards to safety reporting.

3.3 Clinical trials involving IMPs which are sponsored or co-sponsored by any of the King's Health Partners should follow the procedures in the KHP CTO Pharmacovigilance Policy.

4.0 Responsibilities

4.1 The **Chief Investigator** (CI) has overall responsibility for the conduct of a study/trial. The **Principal Investigator** (PI) is responsible for the research at each research site. For single-site studies, the CI and PI will normally be the same individual. For multi-site studies/trials, the PI is responsible for informing the CI, or the coordinating research team, of all SAEs that occur on their study in the CRF, by following the procedure documented in the study protocol and any relevant Sponsor SOPs/policies. The CI has coordinating responsibility for reporting SAEs to the Sponsor by following the procedure documented in the study protocol and any relevant Sponsor SOPs/policies.

4.2 The **Sponsor** of the study/trial is responsible for ensuring that all information about a SUSAR is reported to the relevant authorities, e.g.: the Medicines and Healthcare products Regulatory Agency (MHRA) and the Research Ethics Committee (REC), within the required timelines. The Sponsor is also responsible for submitting an annual safety report for each trial to the REC and MHRA.

5.0 Procedure

Adverse Events (AEs)

5.1 All related and unrelated AEs should be recorded in the study's Case Report Form and patient medical records at each study visit, as per the study protocol and Sponsor requirements. If no AE form is provided by the Sponsor, the CRF's Adverse Event Log (*CRF-STU-FRM-10*) can be used. The CRF also has an AE Workbook (*CRF-STU-FRM-9*) available for studies if necessary.

5.2 All AEs must be assessed by the PI or delegated physician for their intensity and relationship to study treatments or procedures. If the AE does not meet the criteria for a Serious Adverse Event, it should be recorded and followed up until the event or reaction has resolved or as per the study protocol, by appropriately medically trained personnel.

Serious Adverse Events (SAEs) and Suspected Unexpected Serious Adverse Reactions (SUSARs)

5.3 If an AE has been classed as serious by an appropriately medically trained member of the research team, it must be recorded in the study's Case Report Form and patient medical records. It must be reported to the CI and Sponsor using the relevant SAE reporting form, in compliance with the study protocol and Sponsor requirements and usually within **24 hours** of notification of the event. SAEs on trials sponsored by any of the King's Health Partners should be reported using the KHP CTO SAE reporting form. Only SAEs listed in the study protocol as not requiring reporting do not need to be reported.

5.4 SUSARs must be reported in the same manner and as per the Sponsor and protocol requirements, to ensure that the Sponsor, or their delegate, can report them to the relevant authorities within the required timelines (7 days for death and life-threatening SUSARs and 15 days for all others).

5.5 The participant's General Practitioner should be contacted by the PI or delegate if it is medically indicated to do so.

5.6 The participant should be followed up until the event or reaction has resolved, by an appropriately medically trained member of the research team. The 'Outcome of Event', must be completed by the PI or delegated Physician as per protocol.

Pregnancy Reporting

5.7 Pregnancy is not considered an adverse event. However, the PI or delegate must collect pregnancy information for female trial participants or female partners of male trial participants who become pregnant while participating in a study/trial. The PI or delegate must follow the Sponsor's guidance and the study

protocol, and should complete the pregnancy reporting form provided by the Sponsor.

Documentation

5.8 All documents relating to safety reporting (e.g.: completed SAE and SUSAR reports, pregnancy reporting forms, follow-up documentation and all correspondence between the PI/CI/Sponsor) must be filed appropriately in the Investigator Site File (ISF).

King's College Hospital (KCH) Incident Reporting

5.9 Any SAE or SUSAR occurring in the CRF that meets the definition of an adverse incident, as defined in the KCH Policy for the Management, Reporting, & Investigation of Adverse Incidents (including Serious Incidents) must be reported using the KCH Incident Reporting Form on Datix http://datix/datix/live/index.php**.** Where appropriate, a note of the incident should also be made in the patient's medical notes.

6.0 Related documents and References

6.1 KHP CTO Pharmacovigilance Policy and SAE form:
http://khpcto.co.uk/SOPs/PVPolicy.php

6.2 CRF-STU-FRM-9: AE Workbook

6.3 CRF-STU-FRM-10: Adverse Event Log

6.4 HRA Safety Information:
http://www.hra.nhs.uk/research-community/during-your-research-project/safety-reporting/

6.5 EudraLex - Volume 10 Clinical trials guidelines (Chapter II, Safety Reporting):
http://ec.europa.eu/health/documents/eudralex/vol-10/index_en.htm

6.6 KCH Adverse Incidents:
http://kweb/kwiki/Adverse_incidents
http://datix/datix/live/index.php

7.0 List of Appendices

N/A

8.0 Approval and sign off

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