NIHR | Research Delivery Network

Standard Operating Procedure for Safety Reporting

Reference SOP 05, Version 7

Standard Operating Procedure Title: **Safety Reporting**

Standard Operating Procedure Number: 05

Version Number: **V.7**

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Review History

Version No.	Date	Reviewer	Amendments
2	23.01.13		Minor changes and additional reference documents listed
3		CP	Author title previously PCRN-EoE Network Co-ordinator. Minor changes throughout
4		BD JH	Section 1: UK Policy Framework for Health and Social Care Research (HRA 2017) replaces Research Governance Framework (DH 2005). Minor changes
5	21.05.20	JJ	Minor amendments
6	17.03.22	JJ / KH	Minor amendments
7	Aug 2024	SNEE Team	Minor grammatical changes

1. Introduction, Background and Purpose

"The rights, safety and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society" **ICH GCP Principle 3.**

A **clinical trial of an investigational medicinal product (CTIMP)** is a legal definition and describes those trials which fall within the scope of the Medicines for Human Use (Clinical Trials) Regulations 2004.

These regulations, including subsequent amendments, and the **UK Policy Framework for Health and Social Care Research (HRA 2017)** set out specific requirements for the safeguarding of participants involved in clinical research and the management of Adverse Events (AEs).

Non CTIMP trials, while not governed by law, are governed by the UK Policy Framework for Health and Social Care Research (HRA 2017). All studies therefore require an awareness of safety reporting requirements.

Pharmacovigilance is the continuous process of monitoring, evaluating and improving the safety of medicines, which is ongoing throughout the period of drug development, from animal testing through to post-marketing surveys.

All data concerning adverse events, including Serious Adverse Events (SAEs) and Suspected Unexpected Serious Adverse Reactions (SUSARs) is of paramount importance in the evaluation of the trial and is likely to be a key feature in the study report.

This SOP and the related Work Instructions serve to give clarity to the safety procedures and should be followed if there is no safety reporting information in the protocol for a study hosted by the CRN. Any uncertainty around safety reporting should be checked, in the first instance, with the study sponsor or their representative.

This SOP must be read in conjunction with

- The study specific protocol
- WI 20 Adverse Event Reporting
- WI 21 Serious Adverse Event and SUSAR Reporting
- The Investigator's Brochure (IB) or
- The Summary of Product Characteristics (SmPC)

2. Abbreviations

See Reference Document: CRN Glossary of Terms and Abbreviations.

3. Scope

This SOP applies to all study staff involved in recruitment and management of participants, in interventional studies adopted by the CRN Primary Care.

The safety reporting procedures set out in the study protocol and study specific SOPs take precedence over this SOP.

4. Responsibilities

4.1 Sponsor

The Sponsor is responsible to:

- Ensure that the **study protocol** includes appropriate instruction on safety reporting.
- Provide and update the **Investigator's Brochure** (at least annually).
- Ensure written **SOPs** and systems are in place to ensure safety and quality standards are met.
- Conduct ongoing **safety evaluation** of the investigational products.
- Keep detailed written reports of all **AEs** reported by Principal Investigators (PIs), assess the causality and expectedness of these (as well as those by the Investigator) and request follow up information until all queries are addressed.
- Report: **SUSARs** and any other findings that may:
  - Adversely affect the safety of subjects
  - Impact on the conduct of the trial or
  - Alter the Institutional Review Board (IRB)/Independent Ethics Committees' (IEC) approval/favourable opinion to continue the trial to all concerned investigators, IRB/IEC and regulatory authority(ies) within specified timelines
- Submit safety updates and **periodic reports** to the regulatory authority and IRB/IEC, including documentation of any **protocol deviation** initiated as an urgent safety measure.
- Encourage the set up of **independent data monitoring committees** when necessary, to review trial data.
- Register users for **Pharmacovigilance** data entry with the European Medicines Agency (EMA).

4.2 Chief Investigator (CI)

The CI has overall responsibility for the conduct of the study and will be informed of all SUSAR reports by the sponsor. These are SAEs which are considered to be unexpected and related to treatment or trial procedure.

4.3 Principal Investigator (PI)

The PI reports to the Chief Investigator and has responsibility for the research at a local site. The PI must:

- Ensure that adequate **medical care** is provided to a subject for any adverse events, including clinically significant laboratory values, related to a trial. Any protocol deviation implemented to eliminate immediate hazard to trial subjects, without prior IRB/EC approval, should be documented and immediately submitted to the sponsor, who will in turn notify the IRB/EC and regulatory authority
- Ensure that all staff who are **delegated responsibilities** which impact on subject safety are trained and fully equipped to perform their role. (e.g. access to IB, unblinding procedures, safety reporting systems)
- Report all **Serious Adverse Events** immediately, and definitely within 24 hours of discovery, to the Sponsor, except for those that the protocol or IB identifies as not requiring immediate reporting. The immediate report shall be followed by detailed written reports
- Report **Adverse Events** and/or laboratory abnormalities identified in the Protocol as critical to safety evaluation to the sponsor, according to the reporting requirements and within the time periods specified in the

protocol, having assessed each event for causality, severity and expectedness
- Supply the Sponsor, MHRA, REC and relevant R&D office with any **supplementary information** they request

5. Procedures

In order to assess the safety of an investigational product it is important to:
- Collect baseline information on the health status of trial participants
- Be aware of and record all concomitant medications at every visit
- Ask about the subject's health status at every visit and record all untoward medical occurrences (AEs) as specified in the protocol
- Report AEs and SAEs within the specified time frames, including organisational requirements for Incident Reporting
- Collect all data as accurately as possible

Adverse Events are classified into different categories
- Adverse Event
- Adverse Reaction

The procedure for recording, managing and reporting these is outlined in: **WI 20 Adverse Event Reporting**

Serious Adverse Events are classified into different categories
- Serious Adverse Event/Reaction
- Serious Adverse Device Effects
- Suspected Unexpected Serious Adverse Reaction (SUSAR)
- Unanticipated Serious Adverse Device Effect (USADE)

The procedure for recording, managing and reporting these is outlined in: **WI 21 Serious Adverse Event Reporting**

6. Related SOPs, Work Instructions and Reference Documents

6.1 SOPs
SOP 03 Study Set Up
SOP 04 Study Conduct

6.2 Work Instructions
WI 08 Initiation Visit
WI 09 GCP and Training Records
WI 10 Study Files and Filing
WI 13 CRF Completion
WI 16 Audit and Inspection
WI 20 Adverse Event Reporting
WI 21 Serious Adverse Event Reporting

6.3 Reference Documents
Declaration of Helsinki
EU Clinical trials Directive (EUCTD)
UK Policy Framework for Health and Social Care Research
ICH Good Clinical Practice (GCP)
CRN Glossary of Terms and Abbreviations

7. Appendices

There are no appendices to this Standard Operating Procedure