SOP number	**55.004**	Version	**5.0**
Title	**Safety Reporting Requirements for Research Other Than Clinical Trials of Investigational Medicinal Products and non CE Marked Medical Devices**		

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SOP category	NHS GG&C Sponsor Pharmacovigilance
Staff category	

Staff Category	R	A	C	I
Sponsor Pharmacovigilance Office		X		
Sponsor Research Co-Ordinator				X
Project Managers	X			
Chief Investigators	X			
Principal Investigators	X			

1. Scope

This procedure applies to NHS GGC staff with sponsor responsibilities. Chief Investigators of Non-CTIMP studies may be provided with a copy if safety reporting is managed via the PV Office.

2. Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe the safety reporting requirements for clinical research Sponsored or Co-Sponsored by NHS Greater Glasgow and Clyde which does not fall under the requirements of the Clinical Trials Regulations or the Medical Devices Regulations 2002.

The safety reporting requirements in research involving Medical Devices are described in GCTU SOP 55.007: Safety Reporting Requirements in Medical Device Trials and Studies.

3. Procedures

3.1. Protocol

The proposed safety recording, notification and reporting procedures should be detailed in the trial protocol.

The research protocol should document:

- How adverse events will be identified (e.g. by enquiry at study visits, from lab reports)
- Which adverse events are to be recorded and reported
- How adverse events are to be recorded in the CRF and/or patient records
- For any trial specific procedure a list of any expected complications relating to all trial specific interventions should be included within the protocol. Where this is a drug the SmPC may be referenced, for other trial specific interventions the CI along with other relevant members of the trial management team should provide details of those events considered expected for each trial specific intervention.

3.2. Definition

Serious Adverse Event

In research other than CTIMPs, a Serious Adverse Event (SAE) is defined as an untoward occurrence that:

(a) results in death;

(b) is life-threatening;

(c) requires hospitalisation or prolongation of existing hospitalisation;

(d) results in persistent or significant disability or incapacity;

(e) consists of a congenital anomaly or birth defect; or

(f) is otherwise considered medically significant by the investigator.

3.3. Reporting Requirements

3.3.1. Reporting to the Sponsor

The requirement for reporting adverse events to the sponsor will be agreed on a study specific basis during the study risk assessment and captured in the study protocol. The R&I co-ordinator will engage with the Pharmacovigilance and Safety Manager, when appropriate, during the risk assessment stage of NHS GG&C sponsored non-CTIMPs.

In general; there is no requirement to report SAEs to the Sponsor for non CTIMP trials unless those events are related to the trial specific procedures and are unexpected. This does not mean that events such as hospitalisations, deaths, etc. should not be collected as they may be important for the analysis of the trial but formal reporting via SAE forms is not required. In such cases the relevant information should be collected via the trial CRFs.

The Sponsor may assess a study as high risk at the time of risk assessment and additional requirements for reporting may be required. In such scenarios the reporting requirements must be agreed with PV and safety manager before they are documented within the protocol.

Related and unexpected SAEs must be reported to the sponsor Pharmacovigilance (PV) Office immediately (within 24 hours) via one of two routes:

1. In Non-CTIMPs using a Glasgow Clinical Trials Unit (GCTU) eCRF, reporting procedures may be built into the eCRF application and in such cases report

2. For trials with no reporting functionality built into the eCRF. The SAE form is downloaded from https://www.glasgowctu.org/Home/media/2304/sae_non-ctimpv-1-1.pdf, printed off, completed and signed. A copy of this form will also be included in the investigator site file. The form is then emailed to the PV office. A copy is placed in the Study Site File.

If all of the required information is not available at the time of initial reporting, the investigator must ensure that missing information is forwarded to the PV Office as soon as this becomes available. The report should indicate that this information is follow-up information for a previously reported event.

For related and unexpected SAEs the PV manager will assess this SAE against the list of expected events within the protocol and where required may query the expectedness of the event with the reporting investigator. The PV manager will forward a copy of the SAE to the CI for review if applicable.

3.3.2. Reporting to the Research Ethics Committee (REC)

An SAE occurring in a research participant must be reported to the main REC (i.e. the REC that gave a favourable opinion of the study) where in the opinion of the investigator it is:

- "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.

Reports of related and unexpected SAEs should be submitted **within 15 calendar days** of the PV Office becoming aware of the event, using the 'Non-CTIMP safety report to REC form' published on the NHS Health Research Authority website.

https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/

The form should be completed in typescript and signed by the Chief Investigator. The co-ordinator of the main REC will acknowledge receipt of safety reports within 30 calendar days.

The PV Office can assist in the preparation and submission of the report. This will be agreed on a study specific basis.

3.3.3. Annual progress report

The Chief Investigator is responsible for providing an annual progress report to the REC. A report on the safety of participants is included in this report. The responsibility for preparing and submitting this report may be delegated to a Project Manager or other designee.

A progress report should be submitted to the REC which gave the favourable opinion 12 months after the date on which the favourable opinion was given. Annual progress reports should be submitted thereafter until the end of the study.

The report is submitted on the form available from the Health Research Authority website: https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/

3.3.4. Reporting to the Medicines and Healthcare Products Regulatory Agency (MHRA)

There is no statutory requirement to report serious adverse events in clinical research which does not fall under the requirements of the Clinical Trials Regulations or Medical Devices Regulations to the MHRA.

Events which are "related" and/or "unexpected" to a medicinal product used in a research study can be reported to the MHRA via the Yellow Card Scheme. See MHRA website for details. http://yellowcard.mhra.gov.uk/

Where the study involves the use of a CE marked medical device then any events that are related to the medical device should be reported to the manufacturer where agreements are in place, or via one of the following pathways:

In England and Wales: Reports should be made via the Yellow Card Scheme http://yellowcard.mhra.gov.uk/

In Scotland: Reports should be made via the Incident and Reporting and Investigation Centre (IRIC) https://www.nss.nhs.scot/health-facilities/incidents-and-alerts/report-an-incident/

4. Referenced documents

- https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/
- SOP 55.007 - Safety Reporting in Clinical Trials of Medical Devices of Non CE Marked Medical Devices or CE Marked Devices Used Outside of their Intended Purpose (Sponsored and hosted clinical investigations)
- http://yellowcard.mhra.gov.uk/
- https://www.nss.nhs.scot/health-facilities/incidents-and-alerts/report-an-incident/
- https://www.glasgowctu.org/Home/media/2304/sae_non-ctimpv-1-1.pdf

5. Related documents

- International Conference on Harmonisation and Good Clinical Practice (ICH GCP)
- The Scottish Executive Health Department Research Governance Framework for Health and Community Care (Second Edition, 2006)

6. Document history

Version	Date	Description
1.0	22/11/07	Release of version 1 (for review)
1.1	19/05/08	Released to staff
1.2	11/09/08	Revision of title for clarification. Inclusion of full author/approver names Disclaimer amended to refer to web instead of intranet.
1.3	18/06/09	Minor clarifications
2.0	15/05/13	Change to Title and Scope Addition of requirement to report to sponsor in High Risk studies Exclusion of Devices studies
3.0	15/07/2016	Template updated (v1.4). SOP category changed and renumbered (previously 18.005). Change to Staff Category and Scope. Additional guidance on progress report. References updated.
4.0	09/10/19	Updated reportable events, minor clarifications, amended roles
5.0	09/06/2023	Updated to include CE marked medical devices, minor clarifications.