Gloucestershire Hospitals
NHS Foundation Trust

SOP 23: Urgent Safety Measures

SOP reference:	SOP 23	
Version:	1.0	
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	23/05/2024	
Implementation date of current version:		27/06/2024
Date of Review:		27/06/2026

IT IS THE RESPONSIBILITY OF ALL USERS OF THIS SOP TO ENSURE THAT THE CORRECT VERSION IS BEING USED

All staff should regularly check the Research & Development Webpage for information relating to the implementation of new or revised versions. Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded version are promptly withdrawn from use unless notified otherwise by the SOP Controller.

The definitive version of all Gloucestershire Hospitals NHS Foundation Trust SOPs appear online. If you are reading this in printed form, check that the version number and date below is the most recent one as shown on the R&D website:

https://www.gloshospitals.nhs.uk/about-us/research-our-hospitals

The Gloucestershire Hospitals NHS Foundation Trust wishes to acknowledge York Hospitals NHS Foundation Trust and University Hospitals Bristol NHS Foundation Trust who gave permission to use their templates in the development of these SOPs.

Version History Log

This area will be updated with details of all changes made to the SOP whether due for full review or not.

Version	Details of Change	Date Implemented
1.0	Original SOP	

This SOP will be reviewed every two years unless changes to any relevant legislation require otherwise

Related Documents:

SOPs
SOP 04 Consent
SOP 19 Periodic Safety reporting to Regulatory Authorities
SOP 20 Adverse events and reaction safety reporting
SOP 22 Non-compliance and serious breaches

Glossary

CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational Medicinal Product
GHNHSFT	Gloucestershire Hospitals NHS Foundation Trust
HRA	Health Research Authority
IMP	Investigational Medicinal Product
ISF	Investigator Site File
MHRA	Medicines and Healthcare products Regulatory Agency
PI	Principal Investigator
REC	Research Ethics Committee
TMF	Trial Master File
USM	Urgent Safety Measure

Definition

Combined review	Combined review is the way research teams seek approval for new Clinical Trials of Investigational Medicinal Products (CTIMPs) and combined medicine and device trials. Research teams make a single application using a new part of IRAS, which goes to both the Medicines and Healthcare products Regulatory Agency (MHRA) and a research ethics committee (REC) at the same time. The application also goes for study wide review, such as HRA and HCRW approval, if the study is to take place in the NHS or Northern Ireland HSC.

Contents

1. Introduction, Background and Purpose

The Medicines for Human Use (Clinical Trials) Regulations 2004, Regulation 30 specifies that a Sponsor or Investigator may take appropriate urgent safety measures (USM) in order to protect against any immediate harm to the health or safety of research study participants.

This measure can be put into action before seeking approval from competent authorities and ethics committees. If any USM is implemented, this must be reported to the Sponsor as soon as practically possible. The Sponsor will, following a reported USM, make immediate contact with the relevant regulatory authorities; the MHRA for CTIMPs and MHRA notifiable trials and REC.

This SOP explains the process for GHNHSFT sponsored and hosted research studies.

2. Who should use this SOP?

- All Members of the Research & Innovation Team
- Any individuals involved in research studies hosted by GHNHSFT
- Any individuals involved in research studies sponsored by GHNHSFT

3. When this SOP should be used

This SOP should be followed if an immediate hazard to health, or safety, of a research participant/s is identified, and urgent changes in study delivery or conduct are taken, or need to be implemented, before approval from the competent authorities can be obtained.

Examples of situations requiring an USM might include:

- A series of adverse reactions or a single case of an unexpected serious adverse reaction.
- An increase in the intensity or frequency of expected events and reactions.
- Study devices producing erroneous measures.
- An expected Serious Adverse Reaction (SAR) with an unexpected outcome, e.g. death

- Serious omissions in the approved protocol.

Urgent safety measures might include the following;

- A temporary halt to the study at one site or study-wide.
- An urgent change to study procedures.
- The addition of “unapproved” study procedures

4. Procedure

4.1 GHNHSFT Hosted Studies

In the event that an USM for a hosted study is implemented by the sponsor, the study team should follow instruction received from the sponsor. PI, all members of the research team and all relevant supporting departments, e.g. Pharmacy, should be informed of the USM as soon as possible. Pertinent correspondence should be copied to R&I using the generic email account ghn-tr.glos.rdsu@nhs.net.

In the event that a hazard is identified at site, research teams should follow protocol guidance and liaise with the sponsor or medical liaisons as required. Usual protocol safety reporting guidance should also be followed.

All correspondence relating to the USM should be filed in the ISF. A GHNHSFT Datix incident report should be made if applicable.

4.2 GHNHSFT Sponsored Studies

Where the CI, or a PI, implements, a USM, responsibility for notifying MHRA and/or the REC is delegated to the CI. In exceptional circumstances this may be done by a PI.

For a sponsor implemented USM, notification will be done by the R&I Department as sponsor representative.

After implementation of USMs the following must be notified:

- MHRA (CTIMP and MHRA notifiable studies only)
- REC (CTIMP and non-CTIMP studies)

- R&I Department (CTIMP and non-CTIMP studies)
- CI (if PI is making notification).

Any other research sites (if applicable) and all the local study team, including supporting departments, must be notified immediately when a USM is implemented.

4.2.1 Notifying MHRA

The CI, or Sponsor representative, should discuss the issue with an MHRA medical assessor by telephone (MHRA Clinical Trials Unit: 020 3080 6456), ideally within 24 hours of the USM being taken.
Information requested will include:

- The IRAS ID and/or the EudraCT number of;
  - The trials for which USM action has been taken,
  - Other ongoing trials with the same Investigational Medicinal Product(s) (IMP(s))
  - Trials run by a different Sponsor affected by the USM action
- The affected IMP(s) - commercial or developmental names
- Nature of the safety concern and whether it has been reported as a SUSAR
- Which USMs have been taken and when
- The number of UK subjects who are currently receiving the IMP, the number of subjects who received it and the number affected by the USM
- Contact details in case of further questions

Following the discussion with the medical assessor, the MHRA must be provided with written notification of the measures taken and discussed with the medical assessor, within three days from the date the measures were taken. Details of how to make the written notification are found on the MHRA website (https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#urgent-safety-measures)

4.2.2 Notifying REC

For studies not submitted via combined review

The research ethics committee (REC) must be notified by email within three days. The notice should set out that such measures have been taken and the reasons why. A copy of the USM notification should be submitted with the study amendment, if being made (see below).

The information should be provided to the REC that approved the study using the appropriate REC safety reporting cover sheet (the current CTIMP and non-CTIMP safety report to REC forms are found on the HRA website: https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/).

For CTIMPs submitted via combined review

An urgent safety measure (USM) notification should be submitted in IRAS (Integrated Research Application System (myresearchproject.org.uk). No additional notification is required to the REC.

4.2.3 Notifying Sponsor

The CI or PI must notify the sponsor immediately following implementation of a USM using the Notification of Urgent Safety Measure Reporting Form (See Appendix 1) sent via email to the GHNHSFT R&I Department (ghn-tr.glos.rdsu@nhs.net). The R&I Department will acknowledge receipt of the email by noon of the next working day. It is the responsibility of the Investigator reporting the USM to ensure a receipt is received and to contact the R&I Department immediately by telephone (Tel: 0300 422 5463) if a receipt is not received within this timescale.

The R&I Department will contact the Investigator reporting the USM on the next working day. The reporting Investigator should make him/herself available to discuss the matter. In exceptional circumstances, if the reporting Investigator will be unavailable, s/he must discuss the matter fully with a delegated individual and give that person's contact details on the USM report form.

The Notification of USM report must be filed in the ISF and TMF. The R&I department will ensure the R&I study folders and EDGE are updated with all documentation connected to the USM.

4.2.4 Notification of sites in multi-centre studies

Not currently applicable to the Trust, as no multi-site studies are sponsored. Should this change in the future the following guidance should be followed.

The CI, or delegate, must inform all PIs at all collaborating sites of the USM immediately, or within 3 days from the date the measures were taken. Notification must be in writing (email) and must detail the required actions to be taken by the PIs at each site.

The PI at each collaborating site must acknowledge, and confirm implementation, of the USM within 3 calendar days of notification via email and alert their local R&D/I offices as per their local processes.

Details of collaborating sites notification and acknowledgement must be documented on the USM Reporting Form (Appendix 1). Sponsor (ghn-tr.glos.rdsu@nhs.net) should be copied in to all correspondence.

4.2.5 Submitting a Substantial Amendment

A substantial amendment covering the changes made as part of the USM, and any relevant changes to study documents, must be submitted to the MHRA/REC within 2 weeks of the first notification to the Competent Authorities. The USM related substantial amendment must only include changes required as part of USM; unrelated changes may result in the rejection of the amendment.

For studies which were submitted via the combined review process or for non-MHRA notifiable studies, the substantial amendment should be made through IRAS. (myresearchproject.org.uk)

If the study was submitted prior to the combined review process, the substantial amendment should be submitted using MHRA submissions.

4.3 Notifying participants

For both hosted and sponsored studies, study participants must be informed of the USM and given the option to continue in the study with the modified study procedures or to withdraw from the study.

Following sponsor guidance, study participants may be contacted initially by phone and then informed in writing of the rationale for the USM and the steps taken, or new procedures required, to minimise the risk. This may take the form of an updated Patient Information Sheet, once the substantial amendment has been processed. Participants who are willing to continue in the study, must be re-consented, using the updated study documentation.

All communication and correspondence with participants must be fully documented in the participant medical notes and in the Case Report Form, if applicable.

4.4 Temporary Halt to a Research Study

If the CI and Sponsor decide that the hazard necessitates a temporary halt to the study, the CI must notify the R&I Office, MHRA and REC within 15 days of the halt. A substantial amendment must be submitted, and this may be included on the same substantial amendment form as the notification of the USM (as per details above). Notice of a temporary halt should make clear what specifically has been halted, (i.e. recruitment, or an interruption of the treatment of patients currently on the study) and the reasons for all decisions made.

To restart a study that has been temporarily hated, another substantial amendment is required. The application should include evidence that it is safe to restart the study.

If the Sponsor and CI decide not to recommence a temporarily halted study, the CI should submit an End of Trial Declaration form to REC and MHRA, if applicable within 15 days of this decision. This form can be found on the HRA Website.

Trust R&I should be made aware of a temporary halt to study for any hosted research studies.

References

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

Safety reporting - Health Research Authority (hra.nhs.uk)

IRAS User Guide - Reporting during research (myresearchproject.org.uk)

Register to make submissions to the MHRA - GOV.UK (www.gov.uk)

https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project/

Appendix 1.

Notification of Urgent Safety Measure Reporting Form

Email to R&I department immediately on implementing an Urgent Safety Measure (USM):
ghn-tr.glos.rdsu@nhs.net
A receipt will be sent by noon of next working day – if this is not received, reporting Investigator must contact R&I by telephone: 0300 422 5463

1. Details of Chief Investigator

Name:		**Telephone:**	
Address:		**Email:**	
Contact details for Investigator to be contacted to discuss the USM *(if different to above):*			

2. Details of Study

Full title of study:			
Sponsor:		**Local Project Ref:**	
Name of REC:		**EudraCT number:**	
IRAS ID:			

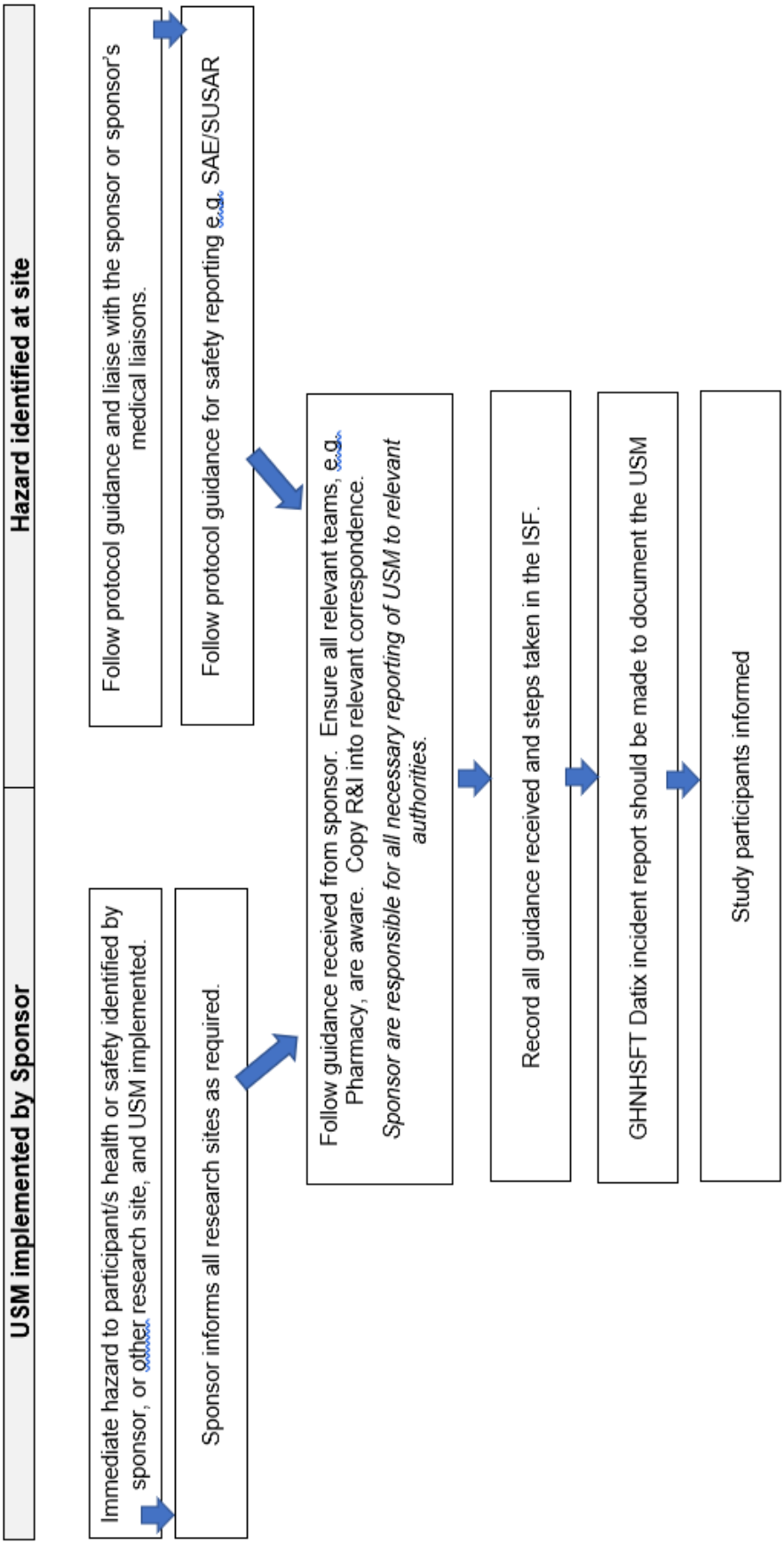
3. Details of Urgent Safety Measure

Date USM implemented:	
Details of USM implemented:	

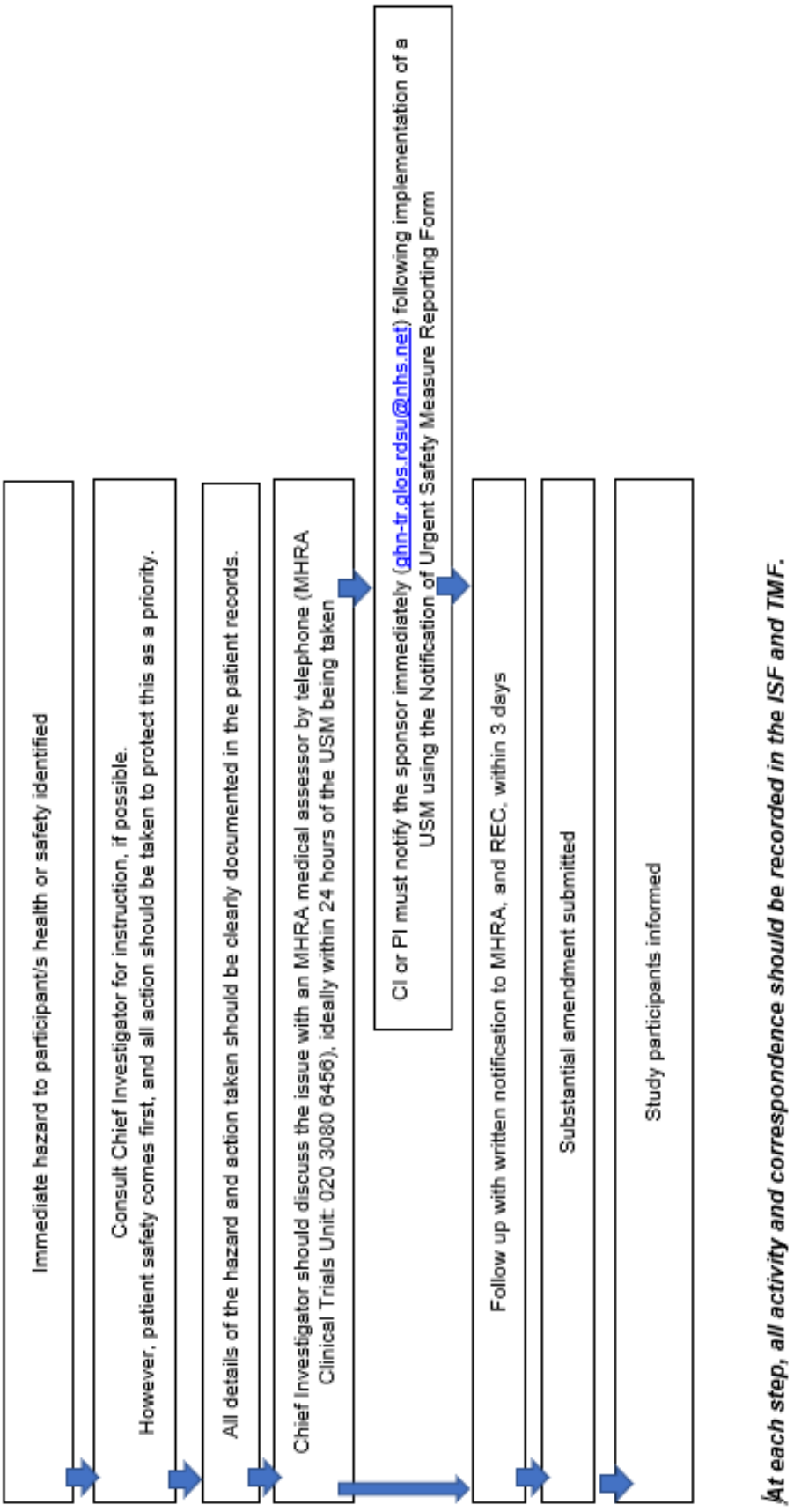
Circumstances giving rise to USM:	
Measures taken:	
Name of MHRA assessor contacted:	
Date MHRA contacted:	
Additional notes:	

Name of person making report:	
Date	
Signature:	

Appendix 2: Hosted Study USM Flowchart



Appendix 3: GHNHSFT Sponsored Study USM Flowchart



At each step, all activity and correspondence should be recorded in the ISF and TMF.