Southern Health
NHS Foundation Trust

SH NCP 33

Research Related Adverse Event Reporting Policy

Version: 3

Summary:	This Policy provides a framework to address research related adverse events. The Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments require that organisations which take on the role of Sponsor of Clinical Trials of Investigational Medicinal Products (CTIMPs) must have systems in place to record adverse events relating to such trials.	
Keywords:	Adverse events, research	
Target Audience:	All staff involved in research	
Next Review Date:	October 2021	
Approved & Ratified by:	Clinical Effectiveness Group	**Date of meeting:** 10 December 2018
Date issued:	December 2018	
Author:	Dr Shanaya Rathod, Director of Research Dr Peter Phiri, Research Manager	
Accountable Executive Lead:	Dr Karl Marlowe, Medical Director	

Version Control

Change Record

Date	Author	Version	Page	Reason for Change
July 2014	Shanaya Rathod	2	All	Policy review
Oct – Nov 2018	Andrew Trousdale Prof Shanaya Rathod Dr Peter Phiri	3	All	Policy Review

Reviewers/contributors

Name	Position	Version Reviewed & Date
Dr Shanaya Rathod	Interim Director of Research	V1
Zita Barham	Research Facilitator	V1
Research & Outcomes Committee	Membership	V1
Gill Lambert	R&D Consultant	V1 April 2012
Shanaya Rathod	Interim Director of R & D	V1 May 2012
Research and Outcomes Committee	Membership	V1 May 2012
Shanaya Rathod	Interim Director R & D	V1 August 2012
Shanaya Rathod	Director of R&D	V2. July 2014
Rasha De Marco	R&D Manager	V2. July 2014
Peter Phiri	Interim R&D Manager	V2. July 2014
Andrew Trousdale	Research Portfolio Delivery Lead	V3 October 2018
Marek Czeladzki	Research Portfolio Delivery Lead	V3 October 2018
Dr Peter Phiri	R&D Manager	V3 October 2018
Prof Shanaya Rathod	Director of Research	V3 November 2018

Quick reference guide

This policy sets out the definitions of adverse events related to research, the responsibilities of Investigators and the R&D Department with regard to managing, documenting, and reporting these in an effective and timely manner. The Policy aims to ensure the safety and well-being of research participants, research staff and those visiting the research premises.

Contents

Adapted with kind permission from:

University Hospitals Southampton NHS Foundation Trust

Research Related Adverse Event Reporting Policy

1. Introduction

Southern Health NHS Foundation Trust is committed to supporting the effective and timely reporting and investigation of any adverse incident/accident that occurs; involving patients, employees or other persons on the Trust premises or business, including visitors and contractors. To this end the Trust has put in place the 'Policy for Managing Incidents and Serious Incidents (SI) (NCP 16).

1.1 Overview

The Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments require that organisations which take on the role of Sponsor of Clinical Trials of Investigational Medicinal Products must have systems in place to record adverse events relating to those trials.

The UK Policy Framework for Health and Social Care Research 2017 requests that the safety and well-being of the individual prevail over the interests of science and society. The Policy pays particular attention to clarifying responsibilities and accountabilities with the aim of forestalling research related adverse incidents.

2. Scope

Recording and reporting of Research Related Adverse Events, including Adverse Reactions, Adverse Device Effects, Serious Adverse Events, Serious Adverse Reactions, Serious Adverse Device Effects, Suspected Unexpected Serious Adverse Reactions and Unanticipated Serious Adverse Device Effects will be managed in line with the reporting policy of the Sponsor of a research study.

Where Southern Health is the Sponsor or Co-Sponsor, or where no Sponsor policy exists, this Southern Health policy must be followed.

3. Purpose (objectives and intended outcomes)

In accordance with the UK Policy Framework for Health and Social Care Research (2017), clinical research teams are responsible for reporting adverse events where expected or required.

Research Sponsors and Chief Investigators are responsible for adhering to the agreed procedures and arrangements for reporting (e.g. progress reports, safety reports) and for monitoring the research, including its conduct, the participants' safety and well-being and the ongoing suitability of the approved proposal or protocol in light of adverse events or other developments. Research Sponsors are responsible for ensuring that effective procedures and arrangements for reposting are kept in place

For these reasons Southern Health has implemented this policy in addition to the 'Policy for Managing Incidents and Serious Incidents (SI) (NCP 16)' to record, investigate and report adverse incidents arising specifically from any research undertaken within the Trust.

This policy seeks to:

- define adverse events and levels of severity (AE, SAE, SUSAR, SSAR, SADE, USADE)
- define roles and responsibilities in managing an adverse event

- set time frames for immediate and periodical reporting of adverse events
- define the assessment criteria for adverse events (intensity, causality, expectedness, seriousness)
- define the responsibilities of Southern Health R&D Department

4. Definitions

AE	**Adverse Event** An adverse event (AE) is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. *Comment: An adverse event can therefore be any unfavourable and unintended sign (including abnormal lab results, traffic accident), symptom or disease temporally associated with the use of the medicinal product/medical device/intervention, whether or not considered to be related to the medicinal product/medical device/intervention.*
AR	**Adverse Reaction** An adverse reaction (AR) is any untoward and unintended response in a patient or clinical investigation subject to an investigational medicinal product/medical device/intervention which is related to any dose administered to that subject. *Comment: Any adverse event judged by either the reporting Investigator or the Sponsor as having reasonable causal relationship to a medicinal product/medical device/intervention qualifies as an adverse reaction; there is evidence or argument to suggest a causal relationship.*
ADE	**Adverse Device Effect** An adverse device effect (ADE) is any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or the instructions for use which might lead to or might have led to endangering the health of a patient or the device user.
Causality	The relationship between the drug/device/procedure and the occurrence of each adverse event will be assessed and categorised as 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 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 related, probably related, and or definitely related*** the event is an ***adverse reaction***.
CTIMP	**Clinical Trial of an Investigational Medicinal Product** A study looking at the safety and efficacy of an IMP in a controlled way.
Expectedness of an Adverse Reaction	Adverse reactions must be considered as unexpected if they add significant information on the specificity or severity of an expected adverse reaction. 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 marketing information). • **Expected:** Reaction previously identified and described in protocol and/or reference documents • **Unexpected:** Reaction not previously described in the protocol or reference documents. *NB The protocol must identify the reference documentation used*.
HRA	The **Health Research Authority (HRA)** is an executive non-departmental public body of the Health. The HRA exists to provide a unified national system for the governance of health research. Research projects, before they commence, must receive an HRA Approval.
IB	**Investigator's Brochure (IB)** A document containing a summary of the clinical and non-clinical data relating to an Investigational Medical Product (IMP) that is relevant to the study of the product in human subjects.
IMP	**Investigational Medicinal Product** An Investigational Medicinal Product (IMP) is a pharmaceutical form of 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 approved form or being used for an unapproved indication or when used to gain further information about an approved use.
Intensity	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 participant, 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. *Comment: The term **severity** is often used to describe the intensity (severity) of a specific event. This is not the same as 'seriousness', which is based on participant/event outcome or action criteria which are clearly stated in the Medicines for Human Use Clinical Trials Regulations, details of this are listed under Serious(ness) definition in this section.*
MD	**Medical Device** A Medical Device means any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application intended by the manufacturer to be used for human beings for the purpose of: a) diagnosis, prevention, monitoring, treatment or alleviation of disease, b) diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap, c) investigation, replacement or modification of the anatomy or of a physiological process, d) control of conception,

	and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.
MDCI	**Medical Device Clinical Investigation** (acronyms not commonly used) An investigation of • A non-CE marked medical device; • A CE marked device which has been modified; or • A CE marked device, which is being used outside its intended purpose.
MHRA	**Medicines and Healthcare products Regulatory Agency** The competent authority responsible for the approval of CTIMPS and Medical Device Clinical Investigations.
Other Safety Report requiring expedited reporting	Other safety issues also qualify for expedited reporting where they might materially alter the current benefit-risk assessment of an IMP or that would be sufficient to consider changes in the IMPs administration or in the overall conduct of the trial for instance: • an increase in the rate of occurrence of or a qualitative change of an expected SAR, which is judged to be clinically important • post-study SUSARs that occur after the patient has completed a trial and are reported by the Investigator to the sponsor • a new event, related to the conduct of the trial or the development of the IMP, that is likely to affect the safety of subjects, such as: o an SAE which could be associated with the trial procedures and which could modify the conduct of the trial; o a significant hazard to the subject population such as lack of efficacy of an IMP used for the treatment of a life-threatening disease o a major safety finding from a newly completed animal study (e.g. carcinogenicity) • any anticipated end or temporary halt of a trial for safety reasons and conducted with the same IMP in another country by the same sponsor • a pregnancy that results in an abnormal outcome, which the healthcare professional considers might be due to the drug. • recommendations of the DMC, if any, where relevant for the safety of the subjects
R&D	**Research and Development Department** The Department responsible for the governance review and provision of NHS permission of all research undertaken within Southern Health
REC	**Research Ethics Committee** A Research Ethics Committee (REC) must be authorised under the Governance Arrangement for Research Ethics Committees (GAfREC). RECs conducting ethical reviews of clinical trials of investigational medicinal products (CTIMPs) must in addition be recognised by the United Kingdom Ethics Committee Authority (UKECA).
RSI	**Reference Safety Information (RSI)** The information used for assessing whether an adverse reaction is expected. This is contained in either the Investigator's Brochure (IB) or in the Summary of Product Characteristics (SmPC)
SAE	**Serious Adverse Event** Any untoward medical occurrence that at any dose: • results in death, • is life threatening, • requires inpatient hospitalisation or prolongation of existing

	hospitalisation; • results in persistent or significant disability/incapacity; and • consists of a congenital anomaly or birth defect • is otherwise considered medically significant by the investigator
SADE	**Serious Adverse Device Effect** An adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event
SAR	**Serious Adverse Reaction** An adverse reaction that: • results in death, • is life threatening, • requires inpatient hospitalisation or prolongation of existing hospitalisation; • results in persistent or significant disability/incapacity; and • consists of a congenital anomaly or birth defect • is otherwise considered medically significant by the investigator
SmPC	**Summary of Product Characteristics (SmPC)** A document describing the properties and conditions for use of a particular licensed medical product, which is the basis of information for health professionals on how to use the medicinal product safely and effectively.
SSAR	**Suspected Serious Adverse Reaction.** An 'adverse reaction' is any untoward and unintended response in a subject to an investigational medical product which is related to any dose administered to that subject.
SUSAR	**Suspected Unexpected Serious Adverse Reaction.** An Suspected unexpected adverse reaction is an adverse reaction where the nature and severity is not consistent with the information about the medicinal product or intervention in question set out: (a) in the case of a product with a marketing authorisation, in the Summary of Product Characteristics (SmPC) for that product, (b) in the case of any other investigational medicinal product, in the Investigator's Brochure (IB). *<u>Comment:</u> When the outcome of the adverse reaction is not consistent with the applicable product safety information this adverse reaction should be considered as unexpected.*
Urgent Safety Measure	An Urgent Safety Measure is undertaken to protect clinical trial subjects from any immediate hazard to their health and safety and should be implemented without waiting for approval from REC / MHRA although they should be notified immediately by telephone and in writing **within 3 days.**
USADE	**Unanticipated Serious Adverse Device Effect** An Unanticipated Serious Adverse Device Effect (USADE) is an untoward medical occurrence that happens in a subject or other person; which is related to the investigational device, device procedure, or comparator; which is serious and was unanticipated.

5. Related Trust Policies

Policy for Managing Incidents and Serious Incidents (SI) (NCP 16)

6. Duties and Responsibilities

6.1 All Staff

All staff are responsible for ensuring that all adverse incidents, whether or not related to research, are reported in accordance with the Southern Health 'Policy for Managing Incidents and Serious Incidents (SI) (NCP 16)'

6.2 Chief Investigator (SHFT Sponsored)

- Adhering to the agreed procedures and arrangements for reporting (e.g. progress reports, safety reports) and for monitoring the research, including its conduct, the participants' safety and well-being and the ongoing suitability of the approved proposal or protocol in light of adverse events or other developments

- Ensure that all SAEs, other than those specified in the protocol as not requiring immediate reporting, are promptly assessed in keeping with the requirement for expedited reporting to the regulatory authority and relevant ethics committee.
- Ensure that SAEs, which require immediate reporting, are reviewed by an appropriate safety review committee for the monitoring of trial safety.
- Ensure that all SUSARs are identified and reported in full to the regulatory authority and relevant ethics committee within the required timelines.

- Ensuring the Sponsor, the REC and MHRA (where applicable) informed of any significant findings and recommendations by an independent Data Monitoring Committee or equivalent body where one has been established for the trial.

- Promptly (within 3 calendar days) inform regulatory authorities, ethics committees and investigators of any urgent safety measures taken to protect participants in the study.

6.3 Principal Investigator or delegated team (hosted trials)

- In the event of an **adverse event/reaction**, the PI (or delegated member of research team) 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 subject's **medical notes** (or source data where this is not the medical notes). When adverse event is due to the research participation, the participant and care team will be notified.

- Except where the protocol states otherwise and has exempted certain events from recording or expedited reporting, all **adverse event/reactions** must be recorded in detail on a case report form or equivalent to allow analysis at a later stage. A template for recording adverse events is provided in the forms that accompany this policy. This template should be used where Southern Health is the sponsor for the study or the sponsor has not provided a template for use by Investigators at host organisations.

- For all **adverse event/reactions** the PI will make an **assessment of intensity, causality, expectedness and seriousness**. Detailed guidance on making this assessment is given in the above section.

- **Adverse events** and/or **laboratory abnormalities identified in the protocol as critical** to the evaluations of the safety of the study shall be reported to the Sponsor in accordance with the reporting requirements documented in the trial protocol.

- Ensure that all SAEs, which require immediate reporting, are reported to the Sponsor and the Trust R&D Department (where required to do so) within the timelines required in the protocol.

Event Reporting Process

The Trust Investigator (or delegated person) will report all the information available to the sponsor:

- Using the forms and process specified in the protocol
- Immediately upon knowledge of the event

The initial report will include as much information as is available at the time. This should be copied to the Trust R&D Office.

The Investigator will provide information missing from the initial report **within five working days** of the initial report. Where no reporting form is provided by the sponsor, the Southern Health form should be used (APPENDIX).

The following steps should be followed:

1. The PI (or delegated individual) assesses causality. If related to the trial procedures it is classified as Adverse Reaction (AR). If unrelated it is an Adverse Event (AE).

2. The PI assesses seriousness. If not serious, the PI records and notifies sponsor as per protocol. If serious the PI notifies the sponsor of the SAE/R **within 24 hours.**

3. The sponsor assesses the causality. If unrelated to the IMP, therefore a SAE, the sponsor keeps records and follows up until resolution. If it is related to the IMP, therefore, a SAR, the sponsor assess the expectedness using the Reference Safety Information (RSI) or Investigator Brochure (IB) or Summary of Product Characteristics (SmPC).

4. If unexpected (SUSAR), the sponsor reports to the MHRA and Ethics Committee:
   - Fatal or life threatening SUSARs **within 7 days**
   - All other SUSARs **within 15 days**

5. If Expected SAR, the sponsor keeps records and follows up until resolution

Southern Health R&D will expect to receive copies of the forms submitted to the sponsor. The R&D office will confirm with the PI that the appropriate Trust clinical team has been notified of any serious AD/AR.

See Appendix 1 for Safety reporting flowchart

For all studies the Chief Investigator will inform all Principal Investigators of relevant information about SAEs/SADEs that could adversely affect the safety of subjects.

The Chief Investigator will provide the main REC with copies of all reports and recommendations of any independent Data Safety Monitoring Board established for a trial as part of the SUSAR. Where Southern Health is a host site only these documents will be requested from the sponsor.

For IMP/Medical Device studies, on request of the MHRA the Chief Investigator will submit detailed records of all adverse events that have been reported. Where Southern Health is a site only these documents may also be requested from the sponsor.

Periodic Safety Reporting

Copies of all annual and end of study reports should be provided to the SHFT R&D Office at the time of submission to the REC and the MHRA as applicable.

Type	Reporting	Further Actions
Annual Safety Reports for CTIMPs	• Chief Investigator, Sponsor or Sponsor's legal representative will report to REC that granted approval. All forms for safety reporting are available on the HRA website: https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/	Chief Investigator, Sponsor or Sponsor's legal representative provides a copy of the safety report to Southern health NHS R&D Department
Six monthly Safety Reports for CTIMPs	• Chief Investigator, or Sponsor will report to REC that granted approval • Six monthly safety reports are only required for CTIMPs where a commercial Sponsor is responsible for trials on the IMP at non-UK sites. CTIMPs falling outside these two criteria only need to report annually.	Chief Investigator prepares the Six monthly report to the commercial Sponsor on the safety of subjects in all CTIMPs for which the Sponsor is responsible worldwide, summarising any issues affecting safety or participants, including a global line listing of SUSARs occurring in these trials in the reporting period
Urgent Safety Measures	Sponsor, sponsor's legal representative or Chief Investigator. • *Or exceptionally by local Principal Investigator (PI).* Informs REC immediately as to why Urgent Safety Measure(s) need to be put in place. Information immediately by telephone and in writing within 3 days.	SHFT R&D Department to be informed immediately and copies of any relevant correspondence provided.
Development Safety Update Reports (DSUR)	Chief Investigator or Sponsor will report to : • the MHRA • the REC that granted approval • the hosting R&D Department at yearly intervals on the international birthdate of the Clinical Trials Agreement (CTA) in any member state	Each submission of an DSUR to the main REC must be accompanied by the Safety Report Form for CTIMPs available at: https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/ DSURs should be prepared in line with ICH E2F available at: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2010/09/WC500097061.pdf Further information can be found at: https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#submit-development-safety-

		update-reports-dsurs
Annual Progress Reports for all research studies	**Chief Investigator, Sponsor or Sponsor's legal representative will** submit an annual progress report to: • the REC that granted approval • the Sponsor (if not initiated by them) • the hosting R&D Departments at yearly intervals on the anniversary of the REC Approval *The REC may exceptionally request more frequent reports.*	For CTIMPs, Chief Investigator, Sponsor or Sponsor's legal representative to submit the Annual Progress Report in addition to the Development Safety Update Report, using the specific "CTIMP Annual Progress Report Form" Non-CTIMPs include any safety information, and SAE line listing within the Annual Progress Report using the specific "Annual Progress Report form for all other research" Both forms are available at: http://www.nres.nhs.uk/applications/after-ethical-review/annual-progress-reports/
End of Study Notification all research	**The CI/Sponsor Within 90 days** from conclusion (or **15 days** in case of early termination) will submit an end of study report to: • the Sponsor (where not initiated) • the MHRA (where applicable) • the REC that granted approval • the hosting R&D Department	Study has HRA and REC approvals – notification of the study send only to REC using the forms from the HRA website: https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project/ Study has HRA approval, but no REC approval -a notification by email to hra.approval@nhs.net including IRAS ID and contact information (phone and email).
Summary of final report	**Chief Investigator, Sponsor or Sponsor's legal representative** will submit a summary of final report within one year of declaration of end of study to: • the Sponsor (where not initiated) • MHRA (where applicable) • REC that granted Approval • the hosting R&D Department •	No standard format. The summary should include information on whether the study achieved its objectives, the main findings and arrangements for publication or dissemination, including feedback to participants.

6.3 R&D Department Responsibilities

The R & D department will maintain records of safety reports for all Southern Health approved research and provide quarterly reports to the R & D Committee.

Where there is university (e.g. students research) involvement the R&D Department will inform the relevant University Research Governance Office.

The R&D Department will consider whether any further actions, in addition to those already taken by the investigator, are required and will discuss these with the Investigator in case of a SUSAR/USADE. The R&D Department will ensure that the Southern Health Patient Safety team have also been notified where appropriate.

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, where the safety and wellbeing of research subjects or staff are considered to be at risk.

7. Implementation

The most up-to-date version of this policy is available on the Trust's website as well as the Research Website. The core aspects of this policy form part of the Trust's Research Governance and Good Clinical Practice training for researchers.

8. Monitoring Compliance/Effectiveness

The compliance and effectiveness of this policy will be monitored by the R&D department in accordance with the R&D monitoring standard operating procedure (SOP), also available on the Research website.

9. Policy Review

This policy is to be reviewed at least every 4 years in line with the Southern Health policy review schedule or sooner upon notification of changes to adverse event reporting on a National level. The review will be conducted by the R&D Department.

10. References

COUNCIL DIRECTIVE 93/42/EEC of 14 June 1993 concerning medical devices;
http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31993L0042:en:HTML
and
http://ec.europa.eu/enterprise/sectors/medical-devices/regulatoryframework/legislation/

EudraLex - Volume 10 Clinical trials guidelines, Chapter II: Monitoring and Pharmacovigilance;
http://ec.europa.eu/enterprise/sectors/pharmaceuticals/documents/eudralex/vol-10/index_en.htm#h2-chapter-ii:-monitoring-and-pharmacovigilance

Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use [87 KB]

(Revision 2 of April 2006)

Detailed guidance on the European database of Suspected Unexpected Serious Adverse Reactions (Eudravigilance - Clinical Trial Module) [114 KB] (revision 1 of April 2004)

Questions & Answers specific to adverse reaction reporting in clinical trials [102 KB] (December 2009)

ICH E2F – EMA Guidance Note for Guidance of Development Safety Update Reports EMA/CHMP/ICH/309348/2008
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2010/09/WC500097061.pdf

ISO 14155-2:2003 Clinical investigation of medical devices for human subjects -- Part 2: Clinical investigation plans;
http://www.iso.org/iso/catalogue_detail?csnumber=32217

Medicines for Human Use (Clinical Trials) Regulations 2004, Statutory Instrument 2004
No.1031; http://www.opsi.gov.uk/si/si2004/20041031.htm#33

Medical Devices Regulations 2002, Statutory Instrument 2002:0618;
http://www.opsi.gov.uk/si/si2002/20020618.htm

National Research Ethics Service: (website) Safety Reports
http://www.nres.nhs.uk/applications/after-ethical-review/annual-progress-reports/ (accessed 16 May 2010)

Stark, Nancy J.: “Can you handle the truth?” A New Standard for Medical Device Adverse Event Classification, *Journal of Clinical Research Best Practices*, vol. 5, no. 12, December 2009;
http://firstclinical.com/journal/2009/0912_ISO_14155.pdf

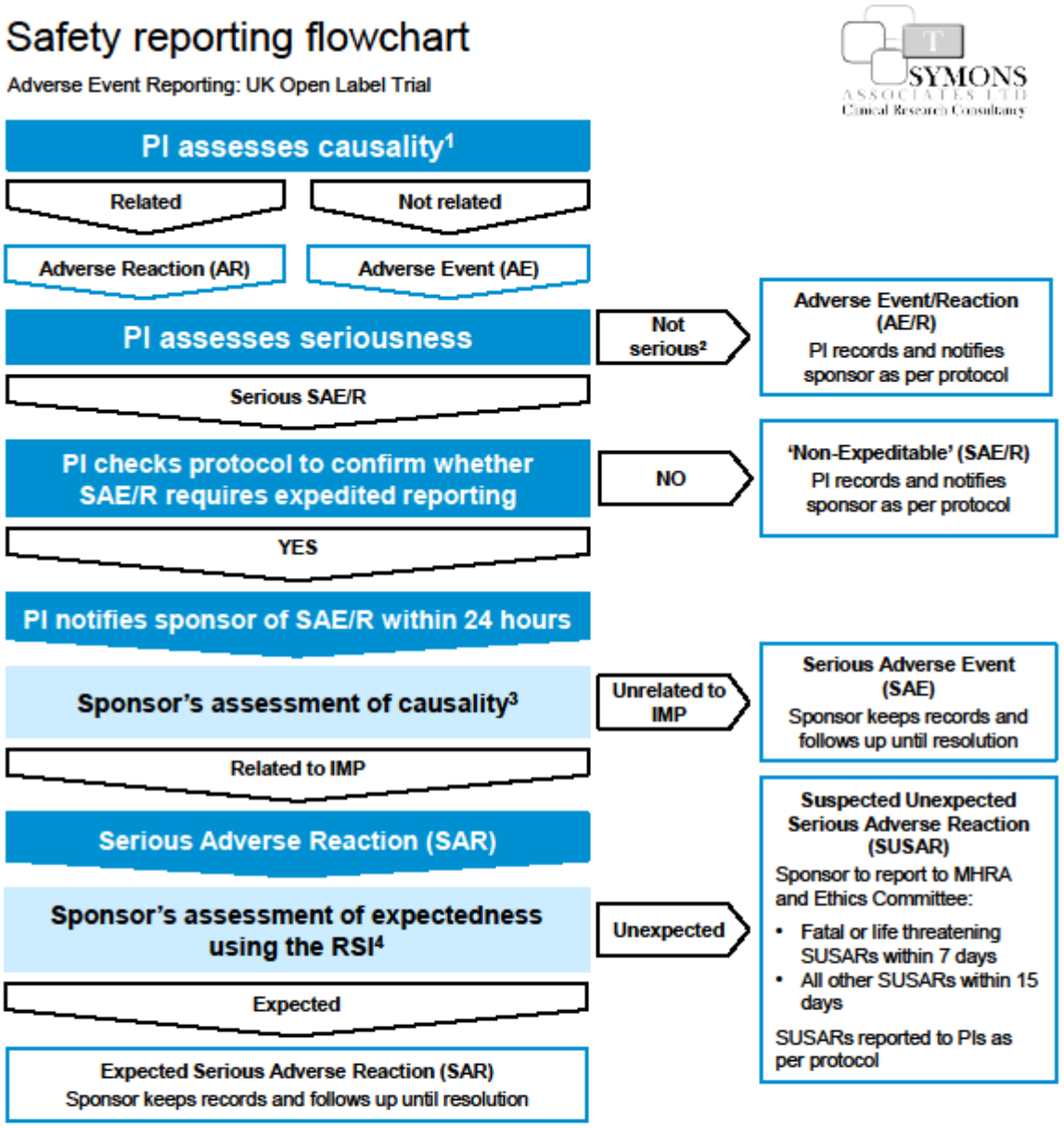
UK Policy Framework for Health and Social Care Research Version 3.3 07/11/17
https://www.hra.nhs.uk/documents/1068/uk-policy-framework-health-social-care-research.pdf

11. Acknowledgements

R&D Department
Southampton University Hospitals NHS Trust

Ms Tanya Symons
T Symons Associates Ltd. 154 Tivoli Crescent North, Brighton, East Sussex.

Appendix 1 Safety Reporting Flowchart



Adverse Event (AE):
Any untoward medical occurrence in a clinical trial subject administered a medicinal product and which does not necessarily have a causal relationship with this treatment.

Adverse Reaction (AR):
Any untoward and unintended response to an IMP which is related (a reasonable causal relationship) to any dose administered.

Serious Adverse Event/Reaction (SAE/R):
- Results in death,
- is life-threatening,
- requires hospitalisation or prolongation of existing hospitalisation,
- results in persistent or significant disability or incapacity,
- is a congenital anomaly or birth defect,
- any other safety issues considered medically important.

PI should actively seek follow-up information on reported SAE/Rs.

Footnotes
[1] PI or delegate.
[2] Notable or safety critical events must be reported as per protocol.
[3] Sponsor cannot downgrade the PI's causality assessment, but can upgrade it.
[4] Reference Safety Information (RSI) in IB or SmPC.

Appendix 2 Safety Report Form for Non-CTIMPs

For all studies except clinical trials of investigational medicinal products, only Serious Adverse Events (SAEs) that are:

- *related to the study (i.e. they resulted from administration of any of the research procedures) and*
- *unexpected (i.e. not listed in the protocol as an expected occurrence)*

Should be submitted to REC

REPORT OF SERIOUS ADVERSE EVENT (SAE)

The Chief Investigator should report any SAE that is both related to the research procedures and is unexpected. Send the report to the Research Ethics Committee that gave a favourable opinion of the research within 15 days of the CI becoming aware of the event.

1. Details of Chief Investigator

Name:	
Address:	
Telephone:	
Email:	
Fax:	

2. Details of study

Full title of study:	
Name of main REC:	
Main REC reference number:	
Research sponsor:	
Sponsor's reference for this report: (if applicable)	

3. Type of event

Please categorise this event, ticking all appropriate options:

Death ☐	Life threatening ☐	Hospitalisation or prolongation of existing hospitalization ☐

Persistent or significant disability or incapacity ☐	Congenital anomaly or birth defect ☐	Other ☐

4. Circumstances of event

Date of SAE:	
Location:	
Describe the circumstances of the event: *(Attach copy of detailed report if necessary)*	
What is your assessment of the implications, if any, for the safety of study participants and how will these be addressed?	

5. Declaration

Signature of Chief Investigator:	
Print name:	
Date of submission:	

6. Acknowledgement of receipt by main REC (please insert name):

The [ ] Research Ethics Committee acknowledges receipt of the above.

Signed:	
Name:	
Position on REC:	
Date:	

Signed original to be sent back to Chief Investigator (or other person submitting report)
Copy to be kept for information by main REC.

Appendix 3 Safety Report Form for CTIMPs

CLINICAL TRIALS OF INVESTIGATIONAL MEDICINAL PRODUCTS

SAFETY REPORT TO RESEARCH ETHICS COMMITTEE

Please indicate which type(s) of safety report you wish to notify with this cover sheet (tick all that apply). Use a separate sheet for notifications relating to different trials. Please send by email to the main REC for the trial concerned together with enclosures. For further guidance see:
http://www.nres.npsa.nhs.uk/applicants/after-ethical-review/safetyreports/safety-reports-for-ctimps/

1. **Expedited report(s) of SUSAR in the UK** ☐
   Notify only Suspected Unexpected Serious Adverse Reactions occurring in the concerned trial at a UK site. SUSAR reports must follow the ICH E2B format.

2. **Annual safety report / DSUR**

- **ASRs must follow the ICH E2F format for Development Safety Update Reports** ☐
- **(DSUR). Include a global list of all SSARs (Suspected Serious Adverse Reactions) related to the IMP and occurring in the reporting period.**

3. **Other** ☐
   For example, report of Data Monitoring Committee or other safety review.

Full title of study:	
EudraCT number:	
Research sponsor:	
Name of Chief Investigator:	
Name of main REC:	
Main REC reference number:	

Contact details for person making this notification

Name:	
Address:	
Telephone:	
Fax:	

Email:	
Date of this notification:	

List of enclosed documents
Please list each report submitted with this notification (insert extra rows in table as required).

1. Expedited SUSARs (UK only)

Sponsor's report no. / reference	Trial site	Date SUSAR first reported to sponsor	Is this a 7 or 15 day report?

2. Other reports

Type of report	Date of report

Acknowledgement of receipt by main REC (please insert name):

The [ ] Research Ethics Committee acknowledges receipt of the above.

Signed:	
Name:	
Position on REC:	
Date:	

Signed original to be sent back <u>only</u> to the sponsor (or other person submitting the report).

Copy to be kept for information by main REC.

Appendix 4: LEAD (Leadership, Education & Development) Training Needs Analysis

If there are any training implications in your policy, please make an appointment with the LEaD department (Louise Hartland, Quality, Governance and Compliance Manager on 02380 874091) to complete the TNA **before** the policy goes through the Trust policy approval process.

Training Programme	Frequency	Course Length	Delivery Method	Facilitators	Recording Attendance	Strategic & Operational Responsibility
Good Clinical Practice (GCP)	2 years	Face to face (Introductory) one day Face to face (Refresher) half a day E-Learning 2hrs	Face to face (Introductory) one day Face to face (Refresher) half a day E-Learning 2hrs	NIHR facilitators	NIHR facilitators Certificate	R&D Department
Directorate	**Service**	**Target Audience**				
MH/LD	Adult Mental Health	Those conducting clinical trials of investigational medicinal products (CTIMPs) must comply with the high level conditions and principles of GCP, but there is no legal requirement for other types of research to do so.				
	Specialised Services	Those conducting clinical trials of investigational medicinal products (CTIMPs) must comply with the high level conditions and principles of GCP, but there is no legal requirement for other types of research to do so.				
	Learning Disabilities	Those conducting clinical trials of investigational medicinal products (CTIMPs) must comply with the high level conditions and principles of GCP, but there is no legal requirement for other types of research to do so.				
ISD's	Older Persons Mental Health	Those conducting clinical trials of investigational medicinal products (CTIMPs) must comply with the high level conditions and principles of GCP, but there is no legal requirement for other types of research to do so.				
ISD's	Adults	Those conducting clinical trials of investigational medicinal products (CTIMPs) must comply with the high level conditions and principles of GCP, but there is no legal requirement for other types of research to do so.				
ISD's	Children's Services	Those conducting clinical trials of investigational medicinal products (CTIMPs) must comply with the high level conditions and principles of GCP, but there is no legal requirement for other types of research to do so.				
Corporate	All	Those conducting clinical trials of investigational medicinal products (CTIMPs) must comply with the high level conditions and principles of GCP, but there is no legal requirement for other types of research to do so.				

Appendix 5: Southern Health NHS Foundation Trust Equality Impact Analysis Screening Tool

Equality Impact Assessment (or 'Equality Analysis') is a process of systematically analysing a new or existing policy/practice or service to identify what impact or likely impact it will have on protected groups.

It involves using equality information, and the results of engagement with protected groups and others, to understand the actual effect or the potential effect of your functions, policies or decisions. The form is a written record that demonstrates that you have shown *due regard* to the need to **eliminate unlawful discrimination**, **advance equality of opportunity** and **foster good relations** with respect to the characteristics protected by equality law.

For guidance and support in completing this form please contact a member of the Equality and Diversity team

Name of policy/service/project/plan:	General Policy on Conducting Research and Development within Southern Health NHS Foundation Trust
Policy Number:	SH CP 8
Department:	Research and Development Department
Lead officer for assessment:	Prof Shanaya Rathod
Date Assessment Carried Out:	14th August 2018

1. Identify the aims of the policy and how it is implemented.	
Key Questions	**Answers / Notes**
Briefly describe purpose of the policy including: - How the policy is delivered and by whom - Intended outcomes	The vision of Southern health NHS Foundation Trust is integration of a comprehensive research strategy into day to day practice as part of the culture, policies and procedures of the organisation. Trust vision: to provide high quality, safe services which improve the health, wellbeing and independence of the people we serve. The R&D vision: Enabling every patient the opportunity to participate in research. The organisation aims to maximise patient and clinician participation in research. High quality clinical and non-clinical research is essential to providing sound, evidenced based health and social care. Clinical research is defined as any research involving human subjects or tissues, including healthy volunteers. Following a number of high-profile problems, clinical research became subject to the Research Governance

	Framework, first written in 2001 and the second edition appearing in 2005. The research governance frameworks were subsequently replaced by the UK Policy Framework For Health And Social Care Research in November 2017. This new policy framework aims to help make the UK an even better place to do research. It is aimed at all those responsible for health and social care research in the UK.

2. Consideration of available data, research and information

Monitoring data and other information involves using equality information, and the results of engagement with protected groups and others, to understand the actual effect or the potential effect of your functions, policies or decisions. It can help you to identify practical steps to tackle any negative effects or discrimination, to advance equality and to foster good relations.

Please consider the availability of the following as potential sources:

- Demographic data and other statistics, including census findings
- Recent research findings (local and national)
- Results from consultation or engagement you have undertaken
- Service user monitoring data
- Information from relevant groups or agencies, for example trade unions and voluntary/community organisations
- Analysis of records of enquiries about your service, or complaints or compliments about them
- Recommendations of external inspections or audit reports

Key questions		**Data, research and information that you can refer to**
2.1	What is the equalities profile of the team delivering the service/policy?	This policy provides a framework for research- active staff that it complies with good practice: The Trust Equality and Diversity team report on equality data profiling
2.2	What equalities training has staff received?	SHFT provides a range of E&D training that includes: Induction training, Respect and Values and E- Learning/Assessments
2.3	What is the equalities profile of service users?	The Trust Equality and Diversity team report on equality data profiling
2.4	What other data do you have in terms of service users or staff? (E.g. results of customer satisfaction surveys, consultation findings). Are there any gaps? **Cultural Competency** A necessary overarching theme among research and human services is cultural competency. In terms of human services is cultural competency. In terms of research; cultural	There a number of ethical principles that should underpin the conduct of all research undertaken by SHFT: - No harm to individuals - Confidentiality and

	competency is broadly defined as "Involving the recognition and understanding of the diverse values, norms, and needs of a community and integrating the knowledge about service [and research] that are accessible and relevant to that community"(Prado & DeRoche, 2008, p.20). **General equality considerations:** - Explore a variety of research methodologies, seeking to identify approaches that are most likely to yield accurate, in-depth outcomes related to all target audiences. Consider a blend of qualitative and quantitative approaches. - Use sampling techniques that provide for adequate representation among all targeted audiences, and address appropriate subpopulations, not merely broad racial or ethnic categories. - Researchers should endeavour to ensure that research participants are protected from undue intrusion, distress, indignity, physical discomfort, personal embarrassment, or psychological or other harm.	Anonymity - Informed Consent - Culturally sensitive methodologies - Language requirements - Remuneration
2.5	What internal engagement or consultation has been undertaken as part of this EIA and with whom? What were the results? Service users/carers/Staff	
2.6	What external engagement or consultation has been undertaken as part of this EIA and with whom? What were the results? General Public/Commissioners/Local Authority/Voluntary Organisations	

In the table below, please describe how the proposals will have a positive impact on service users or staff. Please also record any potential negative impact on equality of opportunity for the target:
In the case of negative impact, please indicate any measures planned to mitigate against this:

	Positive impact (including examples of what the policy/service has done to promote equality)	**Negative Impact**	**Action Plan to address negative impact**			
			Actions to overcome problem/barrier	**Resources required**	**Responsibility**	**Target date**
Age	**Informed Consent:** is a vital aspect of research regardless of age of participants. Southern Health will ensure that all participants understand the negative as well as positive consequences of consenting to participation in the research process		It is the Sponsors responsibility to ensure that Consent sheets comply with GCP and all be approved by an appropriate Research Ethics Committee	None	Sponsor and Chief Investigators	
Disability	**Minimising Risk:** The Trust will provide reasonable adjustments to ensure the full participation of disabled people where appropriate	Not making the research accessible to people with disabilities:- eg, Not providing information in alternative formats for participants: Easy read, BSL, Braille	It is the Sponsors responsibility to review: • The design of research protocols • Inclusion/ exclusion criterion For compliance with Research governance framework, GCP and review by NHS Research Ethics Committee	None	Sponsor and Chief Investigators	
Gender Reassignment	The Trust will take appropriate measures to ensure that the privacy of participants is not invaded. Researchers should be aware of the potential impact of sensitive topics on the community being researched. Researchers should be non-judgemental and objective at	Research studies in coding sex conventionally allow only for the options of male and female. This may exclude people who are "intersex" (born with elements of both M&F sexual organs and biology), transgendered (people engaged in	It is the Sponsors responsibility to review: • The design of research protocol • Inclusion/ exclusion criterion • Data protection. For compliance with Research governance framework, GCP and review by NHS Research Ethics Committee	None	Sponsor and Chief Investigators	

	all times	identity, physical or behavioural changes to what was their gender assignment at birth) or transsexuals (people who have undergone sex change surgery and other forms of treatment)				
Marriage and Civil Partnership	A World Health Organization (WHO) report: "Putting Women First: Ethical and Safety Recommendations for Research on Domestic Violence against Women" highlights the need for specific precautions in undertaking research		It is the Sponsors responsibility to review: • The design of research protocols • Inclusion/ exclusion criterion • Data protection. For compliance with Research governance framework, GCP and review by NHS Research Ethics Committee Research governance Framework Trust policies on lone working			
Pregnancy and Maternity	The Trust will ensure equality of opportunity by supporting researchers during maternity, paternity or adoption leave. Note that maternity leave may have an impact on an individual's ability to conduct research in addition the defined period of maternity leave itself.	Impacts related to pregnancy or maternity may include but are not limited to: medical issues associated with pregnancy or maternity, health and safety restrictions in field work during pregnancy or breastfeeding. Constraints on the ability to travel to undertake fieldwork	Research Governance Framework Trust Policies on Maternity, Paternity or Adoption leave	None	Chief Investigator/ Principal Investigator	
Race	The Trust provides	Providing information	It is the Sponsors			

	interpreting and Translation services Researchers must have an understanding of the culture of the BME community being studied. The Trust E&D team will provide support, advice and signposting to relevant agencies to promote understanding and awareness. Appropriate Representation of BME community and different groups in research	in a format that the participant will not understand Specific consideration should be given when using interpreters in BME communities as some of these communities tend to be small and sensitive to issues of confidentiality Researchers should be aware that some groups may be sensitive to certain issues and should therefore ensure that the research experience is not a distressing one. Particular research methodologies that discriminate against people from different racial, ethnic, religious and cultural backgrounds.	responsibility to review: • The design of research protocols • Inclusion/ exclusion criterion • Data protection. For compliance with Research governance framework, GCP and review by NHS Research Ethics Committee Trust policies on E&D			
Religion or Belief	The Trust will engage and ensure that the religious requirements of participants will be respected (for example prayer facilities, dietary requirements) as appropriate	Research events planned and schedules on days that may exclude certain groups	It is the Sponsors responsibility to review: • The design of research protocols • Inclusion/ exclusion criterion • Data protection. For compliance with Research governance framework, GCP and review	None	Sponsor, CI/PI	

			by NHS Research Ethics Committee Trust policies on E&D			
Sex	Researchers must pay attention to, and respect gender differences, attention must be paid to the use of gender language and the impact of methodologies on men and women	Research methodologies that discriminate against men or women inappropriately to the research question	It is the Sponsors responsibility to review: • The design of research protocols • Inclusion/ exclusion criterion • Data protection. For compliance with Research governance framework, GCP and review by NHS Research Ethics Committee	None	Sponsor, PI/CI	
Sexual Orientation	The Trust will ensure the privacy, dignity and respect of all research participants and avoid using terms that may cause offence	It is recognised that lesbian, gay and bisexual (LGB) people experience various forms of discrimination and harassment because of their sexual discrimination	It is the Sponsors responsibility to review: • The design of research protocols • Inclusion/ exclusion criterion • Data protection. For compliance with Research governance framework, GCP and review by NHS Research Ethics Committee Trust policies on E&D			

Appendix 6: Record of Serious Adverse Event (SAE) Form

STUDY NAME

Protocol Number:_____

Site Name:_____

Pt ID:_____

Date Participant Reported:

__ __ / __ __ __ / __ __ __ __
d d m m m y y y y

1. SAE onset date: ___ ___ / ___ ___ ___ / ___ ___ ___ ___
   d d m m m y y y y

2. SAE stop date: ___ ___ / ___ ___ ___ / ___ ___ ___ ___
   d d m m m y y y y

3. Location of SAE:_____

4. Was this an unexpected adverse event? ☐ Yes ☐ No

5. Brief description of participants with no personal identifiers:
   Sex: ☐ F ☐ M Age: _____
   Diagnosis for study participation:_____
   _____

6. Brief description of the nature of the SAE (attach description if more space is needed):
   _____
   _____
   _____
   _____
   _____
   _____

7. Category of the SAE:
   - ☐ Date of death ___/_____/_____ (dd/mmm/yyyy)
   - ☐ Life threatening
   - ☐ Hospitalization – initial or prolonged
   - ☐ Disability/incapacity
   - ☐ Congenital anomaly/birth defect
   - ☐ Required intervention to prevent permanent impairment
   - ☐ Other:_____

8. Intervention type:
   - ☐ Medication or nutritional supplement (specify):_____
   - ☐ Device (specify):_____
   - ☐ Surgery (specify):_____
   - ☐ Behavioral/lifestyle (specify):_____

9. Relationship of event to intervention:
   - ☐ Unrelated (clearly not related to the intervention)
   - ☐ Possible (may be related to intervention)
   - ☐ Definite (clearly related to intervention)

10. Was study intervention discontinued due to event? ☐ Yes ☐ No

11. What medications or other steps were taken to treat the SAE?

    _____

12. List any relevant tests, laboratory data, and history, including preexisting medical conditions:

    _____

13. Type of report:
    - ☐ Initial
    - ☐ Follow-up
    - ☐ Final

Signature of principal investigator: _____ Date: _____