Portsmouth Hospitals NHS
NHS Trust

CLINICAL RESEARCH SAFETY MONITORING

POLICY

For Completion by SOP Author	
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The definitive versions of all Portsmouth Hospitals Trust SOPs, Templates and Forms for Research are online at http://www.porthosp.nhs.uk/research-department

If you are reading this Policy in printed form you are reading an uncontrolled document.

You must therefore verify that the version number and date are the most recent, by cross-checking with the Trust research website before proceeding with implementation.

CONTENTS

Portsmouth Hospitals NHS Trust is committed to ensuring that, as far as is reasonably practicable, the way we provide services to the public and the way we treat our staff reflects their individual needs and does not discriminate against individuals or groups on any grounds. This SOP has been assessed accordingly

1. INTRODUCTION

Portsmouth Hospitals NHS Trust is a research and innovation-based organisation, acting as both host and Sponsor to high quality research activity. This document has been produced to ensure the Trust meets UK clinical trial regulatory requirements [(1)]; as well as Health Research Authority and National Research Ethics Service (NRES) reporting procedures [(2)], and standards of good practice for the management and reporting of Adverse Events during clinical research studies [(3)(4)]

Adverse Events and clinical incidents which occur during any research study should be recorded and monitored because they can indicate when things are going wrong; for example when the safety profile of an investigational product has changed, or when a study protocol or procedure may be causing harm. It is therefore important that we know when an event or incident is serious, unexpected, occurring at an unexpected frequency or an escalation of events; and when an event may be caused by a research intervention, investigation, procedure, or due to the study design. This information will help us to make decisions and take action where necessary to mitigate any risk to our research participants and our patients

Pharmacovigilence and research safety monitoring is the responsibility of the Research Sponsor, and as a Sponsor organisation the Trust must have systems in place to oversee those studies for which it is accountable. In addition the Trust should have oversight over participant safety during all research for which it is a host site.

The Medicines for Human Use (Clinical Trials) Regulations 2004 in conjunction with the Amendment Regulations [(1)] (collectively referred to hereafter as "the Regulations") stipulates the reporting requirements for Clinical Trials of Investigational Medicinal Products (CTIMPS) and these are incorporated into this procedure. A serious breach of these regulations may constitute a breach in criminal law.

2. PURPOSE

The purpose of this document is to set out the Trust's policy on the management of adverse events and safety reporting procedures during clinical research for which the Trust is responsible.

This Policy should be read in conjunction with the Trust's Standard Operating Procedure for the management of adverse events in clinical research, PHT/RDSOP/007.and the Trust's Policy for the Management of Adverse Incidents and Near Misses [(6).]

3. SCOPE

This policy applies to:

- All clinical research activity conducted at Portsmouth Hospitals NHS Trust
- All clinical research activity for which PHT is responsible as Sponsor (including external sites),
- All clinical research for which the Trust has been delegated Pharmacovigilance monitoring responsibilities

The Trust recognises that some external sponsors, networks, funders and employers may require the use of their own SOPs for the good governance of research. In such cases it is the responsibility of the Portsmouth Hospitals Trust user (including those individuals contracted to work on behalf of the Trust), to ensure that the external SOP does not conflict the SOP outlined below

In the event of an infection outbreak, flu pandemic or major incident, the Trust recognises that it may not be possible to adhere to all aspects of this document. In such circumstances, staff should take advice from their manager and all possible action must be taken to maintain ongoing patient and staff safety

4. ABBREVIATIONS AND DEFINITIONS

Adverse Events (AE) can be any unfavourable and unintended sign (including abnormal lab results), symptom or disease temporally associated with a clinical research protocol [(7).] **In CTIMPS**, The Regulations define an adverse event to be 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

Comment: An adverse event can be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease in any subject in a clinical trial (including those in an untreated control group), whether or not considered related to the intervention investigational medicinal product

Adverse Incident (AI) is defined as an event or omission, which caused physical or psychological injury to a patient, visitor or staff member or any event of circumstances arising during NHS care that could have or did lead to unintended or unexpected harm, loss or damage.

Comment: An AI might be for example, a lack of essential or life saving equipment available in a research setting during an interventional clinical study

Adverse Reaction (AR) is any untoward and unintended response in a subject to an investigational medicinal product, which is related to any dose administered to that subject. Note: Any adverse event judged by either the reporting investigator or the sponsor as having reasonable causal relationship to an IMP qualifies as an AR as there is evidence or argument to suggest a causal relationship. All adverse reactions are adverse events.

Clinical Trial of an IMP (CTIMP) means any investigation in human subjects, other than a non-interventional trial, intended:

- To discover or verify the clinical, pharmacological or other pharmaco-dynamic effects of one or more medicinal products
- To identify any adverse reactions to one or more such products, or
- To study absorption, distribution, metabolism and excretion of one or more such products, with the objective of ascertaining the safety or efficacy of those products.

Investigational Medicinal Product (IMP) (CTIMPS Only) 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.

Non-Investigational Medicinal Products (NIMP) applies to **CTIMPs ONLY.** NIMPS are medicinal products that are not the object of an investigation (i.e. other than the tested product, placebo or active comparator), which may be supplied to subjects participating in a clinical research study and used in accordance with the protocol. This might be, for example, medicinal products such as support/rescue medication given for preventative, diagnostic or therapeutic reasons and/or to ensure that adequate medical care is provided for the subject. These medicinal products do not fall within the definition of investigational medicinal products (IMPs) and are called non-investigational medicinal products (NIMPs) [8]

Non-CTIMP SUSAR is defined as any Serious Adverse Event judged to be:

- Related to the administration of any intervention or any study procedure of interest to the study i.e. having a reasonable causal relationship to that procedure or intervention
- Unexpected, i.e. not listed in the protocol (or product information) as an expected occurrence for those specified procedures/intervention, and
- Unrelated to the administration of an IMP i.e., having no reasonable causal relationship to an IMP

**For Medical Device Trials this may be classified as an Unanticipated Serious Adverse Device Effect (USADE).*

Pharmaco-vigilence (drug safety) is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problems.

Serious Adverse Event (SAE): an adverse event, adverse reaction or unexpected adverse reaction that:

- results in death
- is life-threatening*****
- requires hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability or incapacity
- consists of a congenital anomaly or birth defect
- other - any other safety concern

Comment: Medical judgment should be exercised in deciding whether an adverse event/reaction should be classified as serious in other situations. Important adverse events/reactions that are not immediately life-threatening or do not result in death or hospitalisation, but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, should also be considered serious.

*****Life-threatening in the definition of a serious adverse event or serious adverse reaction refers to an event in which the subject was at risk of death at the time of the event. It does not refer to an event which hypothetically might have caused death if it were more severe.

SAE ALERT Notice: is a sticker to be inserted in the health record where SAE reporting is required by the Sponsor.

Suspected Serious Adverse Reaction (SSAR) is any Serious Adverse Reaction that is suspected (*possibly*, *probably or definitely*) to be related to an Investigational Medicinal Product

Suspected Unexpected Serious Adverse Reaction (SUSAR) is a Suspected Unexpected Serious Adverse Reaction.

Comment: All adverse events that are suspected to be related to an investigational medicinal product and are both unexpected and serious are considered to be SUSARs.

Source Documents are original documents, data and records (e.g. hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subjects files, and records kept at the pharmacy, at the laboratory and at medico-technical departments involved in the clinical research [(4)]

Unexpected Adverse Reaction is an adverse reaction the nature and severity of which is not consistent with the information about the medicinal product in question set out:

- In the case of a product with a marketing authorisation, in the Summary of Product Characteristics (SPC) for that product
- In the case of other IMPs, in the investigator's brochure (IB) relating to the trial in question.

Comment: Reports which add significant information on the specificity, increase of occurrence, or severity of a known, already documented adverse reactions constitute unexpected events

5. POLICY STATEMENTS

5.1. The following policy statements should be taken **in conjunction with** the responsibilities of a Sponsor and host organisation, as defined in the Dept. of Health's Research Governance Framework [(3)] and in the Regulations *(CTIMPS)*

All Clinical Studies

- The **Sponsor** should put in place adequate and appropriate safety-monitoring procedures that are proportionate to the study's risk safety profile.

- The Sponsor should ensure study procedures are reviewed or halted, and any urgent safety measures [(15)] implemented across sites as appropriate, should the risk-benefit ratio or safety profile of a study change to the detriment of its participants.

- The **host** should ensure study-relevant safety incidents, hazards or concerns are monitored and reported to the Sponsor.

- The host should respond immediately to any safety measures implemented by the Sponsor

For all CTIMPS and Studies of Additional Safety Risk (*defined in 5.2 below*)

- The **Sponsor** should clearly specify in the study protocol or supporting documentation, all procedures for safety monitoring; across all participating sites.

- The Sponsor should ensure there is in-depth statistical analysis of safety data and that this is accurately reflected in the study's final publication

- The Sponsor should ensure that all expedited reporting requirements to the MHRA and REC are met within the timescales required.

- The Sponsor should monitor all events of interest to the study, across all sites for which it is responsible.

- The **Host** organisation should ensure that safety reporting procedures are in place and clearly specified by the Sponsor **prior to NHS permission.**

- The host should ensure the expedited reporting to the Sponsor of all Serious Adverse Events, SUSARS and Non-CTIMP SUSARS unless otherwise explicitly excluded in the agreed protocol or supporting documentation.

- The host should monitor any local Serious Adverse Events that are assessed by an investigator to be both related *and* unexpected to study procedures (SUSARS and Non-CTIMP SUSARS); 'local' meaning the event has occurred at PHT

- The host should ensure best practice and regulatory compliance in the recording, assessment and reporting of Adverse Events

5.2. DEFINING STUDIES OF ADDITIONAL SAFETY RISK

- The Trust considers the following studies to be of a safety risk that is additional to normal patient care or routine practice; and therefore require detailed safety reporting procedures to be set out in the protocol or supporting documents:

  (a) All Clinical Trials of IMP (CTIMPs)*

  (b) All interventional studies of a novel procedure or device without/used outside of its CE mark, (including Regulated Device trials*)

  (c) All studies, where the study procedures are considered to be of an additional safety risk to participants, compared with routine clinical practice.

  For PHT sponsored studies this will be judged by independent peer review or by the Research Quality Committee.

  For PHT hosted studies this will be judged by the clinical team at site study set-up and captured during the site risk assessment.

- **In addition** the Trust will ensure safety reporting procedures are in place and followed for any study with specified safety objectives (this includes observational studies).

  **Means there is also a regulatory requirement to report SAEs*

5.3. MEETING OUR RESPONSIBILITIES

- In order to meet our responsibilities as both a host and sponsor organisation, the Trust shall:

  - Implement Standard Operating Procedures (SOPs) for Investigators and Research Office staff in the recording, assessment, and reporting of adverse events in clinical research (See PHT/RDSOP/007[14]; the Reporting of Urgent Safety Measures (See PHT/RDSOP/006 [15]); and the Reporting of Clinical Incidents[6]

  - Centrally record and monitor all SUSARS, Non-CTIMP SUSARS, and any safety concerns, via the PHT Research Office, for all studies.

  - Centrally record and monitor all clinical incidents via the Trust's incident reporting procedures

  - Centrally monitor and audit compliance with safety reporting via research quality assurance and control procedures.

  - Check that all studies of 'additional safety risk' as defined in *5.2* above, are clearly identified in the protocol or supporting documentation, before issuing NHS permission at PHT.

    For PHT Sponsored studies procedures to be included are outlined in *Section 7.1.*

    For PHT hosted studies further discussions with the Sponsor shall be instigated should there be any concerns about the quality of the planned safety procedures (e.g. inaccurate definitions, no procedure in place or procedure is unlikely to be delivered or responsive).

Additional safety reporting procedures may be introduced or NHS permission refused as a result.

- Conduct the statistical analysis and safety monitoring of adverse event data centrally reported to the Research Office for apparent trends that may indicate a safety concern related to the research. Establish study-specific Data Safety Monitoring Committees (DSMCs) to conduct independent interim analysis on behalf of the Research Office where appropriate.

PHT-sponsored studies only

- The Trust will centrally analyse and monitor the following in all PHT Sponsored CTIMPs and studies of additional safety risk:

  (a) All SAES, unless otherwise agreed to be excluded from expedited reporting

  (b) All periodic line-listings of adverse events and excluded SAES

  (c) All annual Developmental Safety Update Reports (DSURS)

  (d) All DSMC safety findings and recommendations, where appropriate

- The Trust shall ensure there is a second independent medical assessment of any adverse event in a Trust Sponsored study, reported to be Serious by the investigator.

6. RESPONSIBLE PERSONS

Investigators (including Chief Investigators and delegated persons) are responsible for**:**

- The roles and responsibilities outlined in *PHT/RDSOP/007*
- The complete and accurate recording, assessment and reporting of Adverse Events as specified in the protocol and in accordance with *PHT/RDSOP/007*

The Research Department is responsible for:

- Ensuring that departmental mailboxes and fax machines designated to receive SAE reports are checked daily.
- The timely recording and assessment of SAE forms reported to the Research Office.
- Activating the appropriate tracking procedure for the assessment and management of SAES, SSARs, SUSARs and Non-IMP SUSARS; including ensuring the timely expedited reporting of events to the MHRA and the REC as appropriate.
- Maintaining a database of all reported SAES/SSAR, SUSARs and Non-CTIMP SUSARS, for central monitoring; providing safety reports to the Research Quality Committee.
- Forming study-specific DSMC where appropriate; coordinating transfer of safety data to the DSMC and convening meetings, for studies where PHT is the Sponsor.
- The review of all protocols at study set up to ensure appropriate safety reporting processes are in place prior to NHS Permissions.
- Suspending or withdrawing approval for a study if appropriate. This may happen (but is not limited to), where public health and safety is considered to be at risk or where the safety and well being of research subjects or staff are considered to be at risk.
- Providing SAE Alert templates to research staff who are involved in studies with SAE reporting requirements.

The Research Quality Committee is responsible for the oversight of:

- All research safety procedures,
- Monitoring safety, in particular:
    - SAE/SSAR, SUSAR and Non-CTIMP SUSAR reports for possible trends
    - Findings and minutes from Trust sponsored Data Safety Monitoring Committees and Annual Developmental Safety Update Reports for Trust Sponsored studies.
    - Study publications, to ensure that all Adverse Events and reactions, which were recorded during the research study are subject to a statistical analysis, and that any subsequent conclusions are included in the study's final report
- All study safety procedures established for PHT Sponsored studies of additional safety risk, This includes:
    - Confirming which Adverse Events/ Serious Adverse Events should be recorded and subject to expedited reporting to the Research Office.

7. PROCESS

7.1. DEFINING SAFETY PROCEDURES IN THE PROTOCOL

PHT Sponsored CTIMPS and Studies of Additional Safety Risk Only:

- For Trust sponsored studies assessed to be of additional safety risk, the following should be clearly documented in the protocol or supporting procedures, and agreed before NHS permission.

    - The definitions of Adverse Events as given in *Section 4* of this policy
    - Those adverse events of interest to the study that are to be recorded in the CRF and Source data (where an event is not defined as Serious then instructions in the protocol should aide investigators to decide if the Adverse Event must be recorded)
    - A statement that all adverse events defined as Serious should be recorded.
    - A statement that all Serious Adverse Events (whether they are events of interest to the study or not) must be reported to the Research Office unless defined as 'exempt' from this expedited reporting.
    - Any serious adverse events which have been agreed to be 'exempt' from expedited reporting to the Research Office. This should include a rationale for the exemption
    - SAE reporting procedures to be followed for the study
    - The procedures for analysing all recorded AES and SAES required by the protocol that are not immediately expedited to the Research Office
    - Details of any product suppliers and Marketing Authority licence holders.
    - Details of any contractual requirements that specify additional safety reporting requirements, for example to the supplier or manufacturer
    - The SAE reporting period is usually defined as the point in time from which participant-related trial procedures commence *(*including screening procedures), until the end of the SAE observation period to be defined in the protocol,
    - All known side effects and adverse reactions of any investigational interventions or procedures, to support the assessment of expectedness. This includes information contained within (manufacturer's) product information (IB or SmPC) and should be written in agreement with the relevant drug/device company where applicable. Rare/very rare events may or may not be included depending on individual study requirements. This should be clearly referenced as the 'Reference Safety Information' in the study Protocol and approved by the MHRA for CTIMPs.

- **Guidance for Defining AEs to be Recorded:**

The following guidance is useful in defining which AEs should be recorded:

> *"The need to collect data on other Adverse Events (those that do not meet the criteria of a Serious Adverse Event), depends completely on whether the data is likely to be relevant to the consideration of the trial results and whether it is feasible to collect. For some studies, no data on Adverse Events is recorded (besides data on SAEs).*
>
> *For other studies, data is laboriously collected on every single Adverse Event occurring during the trial. A plan to collect extensive data on every single adverse event should not be included in a protocol, if it is not feasible to collect any reliable data on the adverse events occurring during the study and if there is no rationale for the collection of this data. Likewise, a study protocol should not neglect to include a plan for collecting data on adverse events, if such data will be important for monitoring the safety of the participants, or analysing and reporting on the relative safety of the study treatment/s under investigation.*
>
> *For most investigator-driven trials, data is collected on a set of Adverse Events that may be considered relevant in the consideration of the trial results. These adverse events are sometimes referred to in protocols as* ***'adverse events of interest'****, and are pre-defined during the development of the protocol. The type and amount of data that will be collected on each of these events is also considered early by the research team and used to plan fields on the data collection forms.*
>
> *The data collected may simply be limited to the date of adverse event occurrence, so that the incidence can be compared between the study groups. Alternatively, the data on each event may be more extensive, such as: the duration of the event, the outcome of the event, a description of the event (e.g. signs and symptoms), the likelihood of the event being related to the study treatment, the severity of the event and any action taken to manage the event (e.g. therapy)."*
>
> http://www.rch.org.au/crdo/advice.cfm?doc_id=13588.
>
> (Ref: The Royal Children's Hospital Melbourne, Clinical Research Development Office, Questions and Answers Page)

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7.2. EXCLUDING SERIOUS ADVERSE EVENTS FROM EXPEDITED REPORTING TO THE RESEARCH OFFICE

- Agreement for Serious Adverse Events to be excluded from expedited reporting to the Research Office must be made at the beginning of the study and clearly documented in the protocol.

- The decision to exclude an SAE from central reporting will usually be made on the basis that:

    - The events are primary endpoints of the trial

    - The events are well established events for the disease condition, intervention or Investigational Medicinal Product

    - Their occurrence does not materially affect the risk/benefit profile of the Investigational Medicinal Product or intervention

- Where events are excluded from being reported to the Research Office in an expedited manner, these SAEs must nevertheless be recorded and a safety analysis performed, in order to detect any safety trends such as the increase in frequency of an expected event.

- Periodic Line listings of excluded SAEs should be reported to the Research Quality Committee along with all Adverse Event data.

7.3. RECORDING and ANALYSING ADVERSE EVENT DATA

7.3.1. Recording Data

- A minimum set of information should be recorded for each adverse event. Please refer to PHT/RDSOP/007 for further definitions and guidance

    - A verbatim description of the event
    - The date of onset
    - Intensity (mild, moderate, severe)*
    - Relatedness (unrelated, unlikely, possibly, probably, definitely)
    - Serious adverse event (yes, no)
    - Action taken (including whether or not the intervention was ceased, and any information on rechallenge)
    - Outcome of the event (resolved, ongoing, died)
    - The date of resolution (if resolved)

- This minimum dataset will be entered into the Trust's safety database for events which have been expedited to the Research Office for central analysis. For Trust Sponsored studies Chief Investigators will also record this minimum dataset for all recordable events.

- Additional data may be collected to characterise the adverse event and permit causality assessment, for example:
    - Dose at time of event (if CTIMP)
    - Concomitant medications
    - Duration of event
    - Indication
    - Batch
    - Route
    - Form
    - Regimen

7.3.2. Analysing Data

- Analysis of adverse event data will be performed according to DMC requirements for studies with a DMC, and according to Research Quality Committee specifications for all other studies requiring safety monitoring.

- Analysis may include the following as appropriate, preferably defined in the safety section of the protocol:

    - Summary data of number of patients experiencing an adverse event by study arm (also stratified where relevant by other factors, for example disease severity, time interval) (frequency, %)

    - Aggregate tables of all adverse events by study arm, organised according to dictionary hierarchy (frequency, %)

- Aggregate tables of SAEs, including various denominators (number of patients, number of adverse events in that dictionary group) (frequency, %)

- Shift tables of laboratory value sets at predefined follow-up visits (for example, n, % of haemoglobins at baseline in various ranges – normal, mild anaemia, moderate anaemia, severe anaemia), 14 days, 30 days etc)

- Line list of SAE reports
- Line list of all events considered to be related to the intervention or study procedures of interest

- Additional methods may be used to report data, including graphics; time to onset analysis, relative risks etc, as per protocol specifications.

- For further information and guidance are available from references [10] and [11]

7.3.3. Data Monitoring Committees (DMC):

The following guidance on DMCs, is taken directly from the MRC/DH Joint Project, Work stream 6: Pharmacovigilence [(12)]

"A committee that is usually independent of the investigators, funders and sponsors of a trial. A DMC reviews the accruing trial data on a regular basis to assess whether there are any safety issues that investigators or participants should be aware of. The DMC is the only body that routinely has access to semi-blinded or unblinded data (competent authorities might request unblinded data and, in emergency situations, unblinding might occur for an individual subject). It is recommended that appropriate reporting channels (normally via the sponsor) be established for each trial; for example, the sponsor should ensure that the DMC receives any information that may be relevant to their assessments, such as urgent safety measures (see Section 8.0).

The decision whether or not a DMC is required depends on the trial's design and the potential risks and benefits to participants associated with the trial. A number of different titles are used for DMCs, for example: Independent Data Monitoring Committee (IDMC), Data and Safety Monitoring Board (DSMB), Independent Safety Monitoring Committee (ISMC) and Data Monitoring and Ethics Committee (DMEC). The DAMOCLES project considered the role and function of DMCs. The following publications may be of interest: DAMOCLES study group. A proposed charter for clinical trial Data Monitoring Committees: helping them to do their job well. The Lancet 365:711-722, 2005.

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AM Grant, DG Altman, A. B. Babiker, MK Campbell, FJ Clemens, JH Darbyshire, DR Elbourne, SK McLeer, MKB Parmar, SJ Pocock, DJ Spiegelhalter, MR Sydes, AE Walker, SA Wallace, and the DAMOCLES group. Issues in data monitoring and interim analysis of trials. Health Technology Assessment monograph series 9 (7), 2005.
EMA Guidelines On Data Monitoring Committees"

8. TRAINING REQUIREMENTS

- All research staff should have access to this policy. Evidence of training shall be required for Chief Investigators of PHT sponsored CTIMP studies and other high risk PHT Sponsored studies; and for Research Office staff.

- The Research Dept will endeavour to notify staff of Policy and SOP developments that may be relevant to them. Updates on Policies and SOPs will feature in research bulletins and communications. It is the responsibility of all research active staff to ensure that they read the Issued updates that may be relevant to them.

- When a new Policy or SOP is authorised, or when an existing document is revised, self directed training must be carried out by all staff to which the Policy/SOP is relevant and this training documented in their training record. A study specific SOP training plan will be developed for investigators on high risk PHT Sponsored studies.

- Staff should take time to read and fully understand the Policy and relevant documents, ensuring that they are able to implement the SOP when required. If clarification is needed then the trainee should approach their line manager and the SOP Controller who will arrange additional training. All staff should complete their training prior to the published implementation date.

9 REFERENCES AND ASSOCIATED DOCUMENTATION

(1) The Medicines for Human Use (Clinical Trial) Regulations 2004 and the Medicines for Human Use (Clinical Trial) Amendment Regulations 2006, the Medicines for Human Use (Clinical Trials) Amendment (No.2) Regulations 2006, the Medicines for Human Use (Clinical Trials) and Blood Safety and Quality (Amendment) Regulations 2008, and the Medicines for Human Use (Miscellaneous Amendments) Regulations 2009.

(2) National Research Ethics Service *(Last accessed July 2012)* http://www.nres.nhs.uk/applications/after-ethical-review/safetyreports/

(3) Research Governance Framework for Health & Social Care, *Dept. Health*. 2005. *(Last accessed July 2012)* http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4108962

(4) ICH Harmonised Tripartite Guideline for Good Clinical Practice E6 (R1), Key Requirements Affecting Clinical Trials in Europe, *Canary,* 2010

(5) Policy for the Management of Adverse Incidents and Near Misses, *Portsmouth Hospitals NHS Trust.*

(6) MRC http://www.dt-toolkit.ac.uk/glossary.cfm?cit_id=0&startLetter=A

(7) Definition of IMPS and NIMPS. Vol., 10 Clinical Trials, Chapter V. European Commission. *(Last accessed July 2012)* *http://ec.europa.eu/health/files/pharmacos/docs/doc2006/07_2006/def_imp_2006_07_27_en.pdf*

(8) http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/Safetyreporting-SUSARsandASRs/index.htm *(Last accessed July 2012)*

(9) http://www.cdisc.org/stuff/contentmgr/files/0/5aee16f59e8d6bd2083dbb5c1639f224/misc/adam_ae_v1.0.pdf

(10) http://www.nidcr.nih.gov/Research/ToolsforResearchers/Toolkit/DataandSafetyMonitoring.htm

(11) MRC/DH Joint Project Work stream 6: Pharmacovigilence, Draft Document *Updated July 2012* by T Symons (T Symons Associates Ltd)

(12) 'Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use CT-3 2011'

(13) PHT/RDSOP/007: Standard Operating Procedure for Investigators, Recording, Reporting and Assessing Adverse Events in Clinical Research http://www.porthosp.nhs.uk/Research-Department/policies--sops.htm

(14) PHT/RDSOP/006 Reporting of Urgent Safety Measures http://www.porthosp.nhs.uk/Research-Department/policies--sops.htm

9. VERSION HISTORY LOG

This area should detail the version history for this document. It should detail the key elements of the changes to the versions.

Version	Date Implemented	Details of Significant Changes
1.0	31/01/2013	N/A
2.0	07/04/2016	Removal of references, addition of 'other' category for SAE, clarification of where RSI information should be included, additional information regarding SOP training added and minor typographic changes

10. APPENDICES

Portsmouth Hospitals NHS
NHS Trust

CONFIRMATION OF POLICY TRAINING RECORD

A copy of this record may be kept in your personal training file to confirm your training in a specific Policy. The research department or your line manager may request copies to verify your training. If required by a study Sponsor a record may also need to be kept in the Trial Master Files (TMF) or Investigator Site Files (ISF).

Policy Details: To be completed by the SOP Controller	
Title of Policy	Clinical Research Safety Monitoring Policy
Reference Number	PHT/RDPOLICY/002
Version	V2.0
Issue Date	07 April 2016
Implementation Date	07 June 2016

Personnel Details	
Name	
Job Title & Research Role	
Date of Training	
Nature of Training	Self Directed/Delivered by etc
Records of any meetings to clarify details in Policy	

Signatures
I confirm that I have read and consider myself to be sufficiently trained in the above Policy with regards to my individual roles and responsibilities Signature of Trainee …… Date ……
I confirm training in the above Policy was delivered as recorded above and that the trainee may be considered sufficiently trained in their roles and responsibilities Signature of Trainer …… Date ……

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Additional Notes & Signatures

Signature of Trainer (where appropriate)

I confirm training in the above Policy was delivered as recorded above and that the trainee may be considered sufficiently trained in their roles and responsibilities

Signature of Trainer …… Date ……..