University Hospitals Plymouth NHS Trust

STANDARD OPERATING PROCEDURE

DO NOT USE THIS SOP IN PRINTED FORM WITHOUT FIRST CHECKING IT IS THE LATEST VERSION

The definitive versions of all UHPNT RD&I Dept. SOPs appear online, not in printed form, to ensure that up to date versions are used. 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 Trust's website: https://www.plymouthhospitals.nhs.uk/researchers

Reporting of Suspected Unexpected Serious Adverse Reactions (SUSARs) in Clinical trials of Medicinal Products for UHPNT UK Sponsored Studies.

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Date 08th Nov 2018

1 Purpose and Scope

To describe the procedure within the RD&I Department, for recording and reporting of SUSARs to designated bodies in University Hospitals Plymouth NHS Trust (UHPNT) sponsored studies.

It is a requirement of the Medicines for Human Use (Clinical Trials) Amended Regulations 2006 that all research related Suspected Unexpected Serious Adverse Reactions (SUSARs) in Clinical Trials of Investigational Medicinal Products (CTIMPs) are reported to appropriate bodies (Medicines and Healthcare products Regulatory Agency [MHRA], Research Ethics Committee [REC] and the Data Management Committee [DMC]) within stipulated timelines.

The Research Governance Manager or their delegate is responsible for the reporting of SUSARs to the regulatory authority (MHRA).

In scope: Clinical Trials of an Investigational Medicinal Product (CTIMP) research sponsored by UHPNT.

Definitions

CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational Medicinal Product
DMC	Data Monitoring Committee
GCP	Good Clinical Practice
HCA	Health Care Assistants
HRA	Health Research Authority
MHRA	Medicines and Healthcare products Regulatory Agency
UHPNT	University Hospitals Plymouth NHS Trust
PI	Principal Investigators
RD&I	Research, Development and Innovation
REC	Research Ethics Committee
RO	Research Office

SOP Standard Operating Procedure

SUSAR Suspected Unexpected Serious Adverse Reaction:

Means an adverse reaction that is classed in nature as serious and which is not consistent with the information about the medical product in question as set out:

- In the case of a licensed product, in the Summary of Product Characteristics (SmPC) for that product
- In the case of any other investigational medicinal product, in the Investigators Brochure (IB) relating to the trial in question.

2 Who should read this document?

The Research Governance Manager, RD&I Senior Managers and the Senior Research Facilitators.

3 Procedure to Follow

3.1 Researchers will report SUSARs to the RD&I Dept. by telephone or e-mail within 24 hours of becoming aware of the event.

3.2 When the RD&I administrative staff receive a SUSAR notification, they will alert the Research Governance Manager or in their absence the RD&I Manager and or the Deputy Research Manager.

- On receipt of notification of the SUSAR the Research Governance Manager will e-mail the reporting researcher and the study's Chief Investigator (CI) to confirm the receipt of the documentation of the SUSAR report. At this point they will also request any follow-up details which are available in order to complete the MHRA web base e-SUSAR report.

- For blinded clinical trials, the blind should be broken for individual concerned in the interest of the subject safety. It is recommended that the blind is broken by the sponsor (normally the Research Governance Manager or delegate acting on behalf of UHPNT) for all SUSARs judged reportable on an expedited basis, before they are reported to the MHRA for that specific subject (even if the CI/PI remains blinded).
- To break a blind for an individual on a clinical trial during normal office hours (09.00-17.00), the Pharmacy Clinical Trials Manager will be contacted with the study and patient details. This can be done over the telephone and will be confirmed by e-mail to the RD&I office by the Pharmacy Clinical Trials Manager. Out of office hours, the "on call" Pharmacist should be contacted if the blind has

to be broken urgently due to patient safety. The Pharmacy Clinical Trials Manager will confirm details of the blind break by e-mail the on arrival at work.

- Care should be taken at all times not to disclose to researchers on the study the outcome of the blind break unless it is requested by the study's CI. All SUSARs should be referred to as potential SUSARs whether they are reported or not to maintain the researchers' blind.

- The Research Governance Manager or delegate will complete the MHRA e-SUSAR report and the Clinical Trials of Investigational Medical Products Safety Report to main Research Ethics Committee form (http://www.hra.nhs.uk/documents/2016/06/safety-report-form-ctimps.docx).

- **Creating and Submitting MHRA e-SUSAR Reports**

  Submitting SUSAR reports using the MHRAs e-SUSAR form is a straight forward and logical process. You will need to log onto the MHRA's eSUSAR website (https://esusar.mhra.gov.uk/). The Trial details are automatically populated in the report by first selecting the trial for which the report is to be made. The form then guides the user through a series of steps collecting information on the Trial Subject, the Reaction and the IMP (Suspect Drug). The Reporter details are also automatically populated into the report and are defined by the account information of the logged in user.

  Prior to submission, a summary of the data collected is presented and the user has the option to amend any details prior to submission. The user also has the option to download a full report in either PDF format or as XML. Institutions may find these reports useful for informing Ethics Committees of SUSARs.

  As well as creating and submitting new reports, users can submit follow-up reports, edit previously created but as yet not submitted reports and create and submit copy reports based on previous reports.

  Phone the MHRA's Clinical Trial Unit on 020 3080 6456 to discuss the issue with a safety scientist, ideally within 24 hours.

3.3 Within 7 days of becoming aware of the event.

The RD&I Dept will report all SUSARs that are fatal or life threatening to:

- The MHRA
- The REC that grant approval.
- Ensure that the CI has informed all Principal Investigators (PIs) of a multicentre trial which UHPNT is the sponsor.
- The RD&I Dept. will report further information within a further 8 days of the initial report to the MHRA and REC.

3.4 Within 15 days of becoming aware of the event.

The RD&I Dept. will report all SUSARs that are **NOT** fatal or life threatening to:

- The MHRA
- The REC that grant approval.
- Ensure that the CI has informed all Principal Investigators (PIs) of a multicentre trial which UHPNT is the sponsor.

3.5 e-SUSAR reports will be made via the MHRA website *via* https://esusar.mhra.gov.uk/ by the nominated RD&I staff.

3.6 The Research Governance Manager or delgate who submits the initial report is responsible for ensuring the required follow-up data is sent within the required timeframes.

3.7 The Research Governance Manager is the Trust's nominated administrator for the e-SUSAR site.

3.8 Copies of the SUSAR notification may also be required the Data Monitoring Committee (DMC) and IMP supplier.

3.9 In addition to expedited reporting required for SUSARs, annual safety reports to the MHRA and REC are required for all CTIMP studies.

4 Document Ratification Process

The review period for this document is set as ***default of three*** years from the date it was last ratified, or earlier if developments within or external to the Trust indicate the need for a significant revision to the procedures described.

This document will be approved by the ***a Senior RD&I manager or their Deputy***.

Non-significant amendments to this document may be made, under delegated authority from ***a Senior RD&I manager***, by the nominated author. These must be ratified by ***a Senior RD&I manager***.

Significant reviews and revisions to this document will include a consultation with ***appropriately knowledgeable staff***. For non-significant amendments, informal consultation will be restricted to ***staff*** who are directly affected by the proposed changes.

Dissemination and implementation

4.1. Dissemination of this SOP

4.1.1. New SOPs and new versions of existing SOPs: The Research Governance Manager will be responsible for ensuring authorised SOPs are uploaded on the RD&I internet site. Internal Trust Staff are expected to use the RD&I internet site to access latest versions of SOPs and to check the website regularly for updates.

Notice of new or amended procedural documents that have undergone a major amendment will be given *via* the following routes:

- Inclusion in the Trust weekly e-bulletin Vital Signs
- Direct email to Trust Researchers and or teams

4.2. Training in this SOP

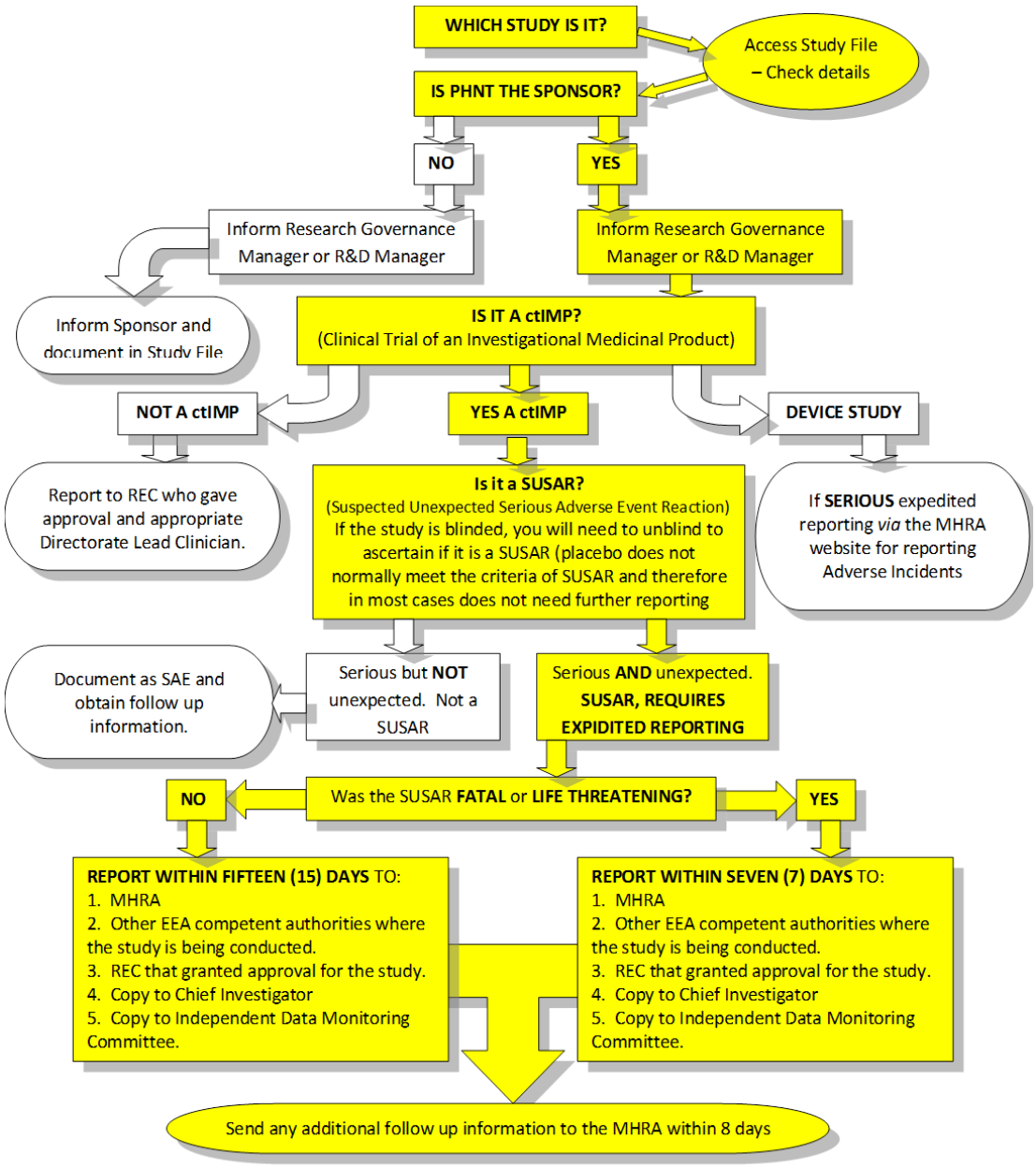
4.2.1. All staff whose activities are subject to this SOP should ensure that they read and understand the content of the SOP.

5 Reference material

MHRA's eSUSAR website: https://esusar.mhra.gov.uk/

Further information and guidance regarding monitoring and pharmacovigilance in clinical trials can be found in Chapter II of EudraLex - Volume 10 Clinical trials guidelines. https://ec.europa.eu/health/documents/eudralex/vol-10/

Appendix: RD&I Dept onward SUSAR — Appendix 1



SUSAR reported *via* the MHRA online e-SUSAR site (http://esusar.mhra.gov.uk/). All Trust Sponsor ctIMP studies will have been pre registered onto the MHRA e-SUSAR database when they are approve by the R&D Dept. This will be done by the Research Governance Manager.

Appendix: e-SUSAR Reporting Form (MHRA) — Appendix 2

Institution Registration

Institutions will need to register their details with the MHRA before using the e-SUSAR website for the first time. This process registers the Institution and a representative of the institution as an Administrator. In order to commence the registration process, the representative should complete the e-SUSAR Registration Form (available on the MHRA website) and email it to **esusar@mhra.gsi.gov.uk** with the subject line e-SUSAR Registration. UHPNT are already register and the Research Governance Manager is the administrator.

Using the form

The e-SUSAR form was designed to be intuitive, with clear instructions and an easy to use format. It is hoped that users will quickly understand the administrative aspects of registering new members and creating new trials as well as being able to navigate through the steps involved in creating and submitting a SUSAR report to the MHRA.

Help icons have been included to provide hints and advice at key stages throughout the website. To view the help information simply hold the mouse over the relevant icon and the text will be displayed.

Administration

Institution Management: Following the initial registration process, changes to Institution details can only be made by the MHRA's e-SUSAR administrator. Any requests to change these details should be made by sending an email to the **esusar@mhra.gsi.gov.uk** with the subject line e-SUSAR Administration.

Member/Administrator Management: Following completion of the registration process, new Members and Administrators (collectively referred to from hereon in as users) of an Institution can be added, and existing Member details can be edited, by any Administrator of that Institution. There is no limit to the number of users that can be added for each Institution.

Users can be flagged as either active or inactive; only active users have the ability to login.

When a new user is created, an email notification is sent to the new user's registered email address that will include their login details. The new user will be prompted to change their password at first login.

Trial Management: Administrators of an Institution have the responsibility to add and edit Trials. It is recommended that, as soon the sponsor receives the Notice of Acceptance from the MHRA for a clinical trial, the trial is created by each Institution that has a

responsibility for safety reporting in that Trial to avoid any unnecessary delays at the time of submission of the first SUSAR report.

As for users, trials can also be flagged as either active or inactive; SUSAR reports can only be submitted for active trials.

There is no limit to the number of trials that can be created for each Institution and there is no restriction on the number of Institutions that can submit SUSAR reports for a particular trial. However, each Institution will have to create and maintain its own record of the Trial and will only be able to view reports created and submitted by its own users.

Administrators also have the responsibility to associate users with each trial; only users associated with a particular trial will have the ability to submit SUSAR reports for that trial. There is no limit to the number of users that can be associated with each trial.

Comments or Question?
If you have any questions or comments regarding the e-SUSAR form, please send an email to esusar@mhra.gsi.gov.uk with the subject line e-SUSAR Reporting Form.

6 Amendment History

Version Number:	5.1
Date Of Amendment:	Nov 2018
Details Of Amendment:	SOP reviewed; format updated. Changed Trust and Dept. names.
Version Number:	5.0
Date Of Amendment:	Aug 2017
Details Of Amendment:	Updated SOP template and numbering system. Reviewed and updated SOP.
Version Number:	4.1 (minor amendment)
Date Of Amendment:	Mar 2012
Details Of Amendment:	Cover page - Change of SOP location address.
Version Number:	4.0
Date Of Amendment:	September, 2010
Details Of Amendment:	Added more detail on breaking study blinds. Updated to include procedure for report SUSARs electronically *via* the MHRA website.