<table>
<thead>
<tr>
<th>Title:</th>
<th>Research Adverse Event and Safety Reporting Procedures</th>
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<tbody>
<tr>
<td>Outcome Statement:</td>
<td>Research Teams will be able to correctly identify and report Adverse Events and complete Annual Safety Reports for research studies taking place in the Trust.</td>
</tr>
<tr>
<td>Written By:</td>
<td>Bonnie Teague, Research Manager</td>
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</table>
| In Consultation With: | Kim Clipsham, DenDRoN Research Nurse  
Kaye Russell, Clinical Studies Officer |
| Approved By and Date: | Research Governance Committee 29th August 2013 |
| With Reference To: | 1. EU ICH E2F, European Medicines Agency 2010, Sep2010  
EMA/CHMP/ICH/309348/2008 Committee for medicinal products for human use (CHMP)  
2. ICH Topic E 6 (R1): Guideline for Good Clinical Practice  
5. National Research Ethics Service: (website) Safety Reports |
| Associated Trust Policies: | Q11 – Serious Incidents Requiring Investigation Policy.  
R&D005 – Conducting Clinical Trials of Investigational Medicinal Products. |
| Applicable To: | Trust staff working on research studies taking place in NSFT (Norfolk and Suffolk sites). |
| For Use By: | Research Teams, Chief Investigators, Research and Development, Clinical Teams |
| Reference Number: | R&D016 |
| Version: | 2.0 |
| Published Date: | 30th August 2013 |
| Review Date: | September 2014 |
| Impact Assessment: | |
| Reason for Review: | An increase in Trust research activity and the introduction of Trust-sponsored research studies has highlighted the lack of formal procedures to report adverse events occurring during the conduct of a research study. It is a requirement of the Medicines for Human Use in Clinical Trial Regulations (2004) that such procedures are in place.  
Version 2.0 Review: An internal review of SAE processes undertaken in August 2013 revealed that revisions to the SAE form and reporting process were required. |
| Implementation and Monitoring: | To be implemented and monitored by Research and Development in response to national and Trust policies. Training to deliver the policy is incorporated into Good Clinical Practice training (Essential to role for Research) offered by the Trust. |
1.0 Introduction

The Medicines for Human Use (Clinical Trials) Regulations 2004 and Amendment 2006 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.

In studies that do not involve the trial of a medicinal product, any Serious Adverse Event that occurs in a participant that has possibly resulted from participation in the research must also be reported to the main Research Ethics Committee (REC).

Regardless of the identity of the Sponsor, the host organisation retains a responsibility to ensure the safety of its patients.

This policy sets out a consistent framework for the identification, evaluation and reporting of Adverse and Serious Adverse Events which may occur during clinical trials taking place in the NSFT, in compliance with latest regulations published by RECs and regulatory authorities. Current EU-wide safety reporting requirements are available here: http://ec.europa.eu/health/files/eudralex/vol-10/2011_c172_01/2011_c172_01_en.pdf

2.0 Purpose

This policy is for staff members of the Research and Development Department and Clinical Trials Research Teams who are involved in healthcare research taking place at the NSFT. The policy applies to all named research team members, regardless of whether their primary employer is the Trust or another institution.

3.0 Definitions and Abbreviations

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

An AE can be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporarily associated with the use of an investigational medicinal product (IMP), whether or not considered related to the IMP.

Adverse Reaction (AR)
Any untoward and unintended responses to an IMP related to any dose administered. All adverse events judged by either the reporting investigator or the sponsor as having a reasonable causal relationship to the IMP qualify as adverse reactions.

Clinical Trial of an Investigational Medicinal Product (CTIMP)
A Clinical Trial of an Investigational Medicinal Product (CTIMP) is defined in the Medicines for Human Use (Clinical Trial) Regulations 2004 as any investigation in human subjects, other than a non interventional trial intended:
• To discover or verify the clinical, pharmacological or other pharmocodynamic effects of one or more medicinal products
• To identify one or more adverse effects of these medicinal products
• To study absorption, excretion or distribution of medicinal products with a view of ascertaining the safety or efficacy of such products.

Since May 2004 when the Trial Regulations came into force, CTIMPs have been regulated by the Medicines and Healthcare Products Regulatory Agency (MHRA) who needs to give explicit authorisation for a CTIMP to be conducted in addition to the standard approvals required for clinical studies. This is termed “Clinical Trial Authorisation” or CTA.
Investigator’s Brochure (IB) and Summary of Product Characterisation (SmPC)

The Investigator’s Brochure (IB) is a comprehensive document that summarises the known information about an IMP prior to licensing/marketing. The purpose of the IB is to compile data relevant to studies of the IMP gathered during clinical trials and as described by ICH GCP “to provide the investigators and others involved in the trial with the information to facilitate their understanding of the rationale for, and their compliance with, many key features of the protocol, such as the dose, dose frequency/interval, methods of administration: and safety monitoring procedures. The IB also provides insight to support the clinical management of the study subjects during the course of the clinical trial.”

The Summary of Product Characterisation (SmPC) is a document that relates to a licensed/marketed medicinal product. It contains a description of the product’s properties and the conditions attached to its use. It provides information on the following criteria:
  - Name
  - Composition
  - Pharmaceutical form and strength
  - Holder of marketing authorisation
  - Licensed Indications
  - Adverse Reactions
  - Storage conditions

This document is important as it describes all known expected adverse reactions. The SmPC should be referenced in the case of an SAE to help classify the event. The holder of the marketing authorisation of the medicinal product will routinely update the SmPC based on receipt of new information.

A local Research Team should obtain and hold up to date copies of the IB or SmPC in the Trial Management File.

Independent Data Monitoring Committee (IDMC)

An independent data-monitoring committee that may be established by the sponsor to assess at intervals the progress of a clinical trial, the safety data, and the critical efficacy endpoints, and to recommend to the sponsor whether to continue, modify, or stop a trial.

Investigational Medicinal Product (IMP)

A pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorization but used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form. [EU 2011/C 172/01]

Non-CTIMPs:

Any trial which does not involve an IMP and is outside of the regulatory remit of the MHRA but still falls under the Research Governance Framework for Health and Social Care.

Non-CTIMPs encompass a variety of research involving the NHS and/or non-NHS settings, and may include NHS participants (e.g. patients, patient carers) and/or healthy volunteers. The type of studies that fall under the non-CTIMP categorisation include:
  - Research administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
  - Research involving qualitative methods only
• Research limited to working with human tissue samples and/or data
• Research using material from a Research Tissue Bank
• Imaging studies
• Mechanistic / physiological / experimental medicine studies involving healthy volunteers and/or patients

Serious Adverse Event/ Reaction (SAE/SAR)
Any adverse event or adverse reaction that at any dose or stage in the research participation of a study:

• results in death
• is life-threatening
• requires hospitalisation, or prolongation of existing inpatients’ hospitalisation.
• results in persistent or significant disability or incapacity
• is a congenital anomaly or birth defect

Life-threatening, in the definition of an SAE or SAR, refers to an event in which the subject was at risk of death at the time of event; it does not refer to an event which hypothetically might have caused death if it were more severe. Should a study participant become pregnant whilst undertaking a CTIMP, or aid in the conception of a child whilst they are participating in a CTIMP, the pregnancy and resulting child should be followed up for a period of no less than 18 months to verify whether a congenital anomaly or birth defect is present. This will be subject to guidance from the relevant pharmaceutical company.

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.

Severity: The term “severe” is used to describe the intensity (severity) of a specific event. This is not the same as “serious”, which is based on patient/event outcome or action criteria.

Suspected Serious Adverse Reaction (SSAR)
Any adverse reaction that is classed as serious and which is consistent with the information about the IMP listed in the SmPC or IB. The IB and SmPC should be reviewed regularly to ensure the most up to date version is in use, and if required a protocol review undertaken if required. The site file should be annotated to show that this check has been undertaken. Information on known adverse reactions can be found at http://emc.medicines.org.uk/ and should be described in the approved protocol.

Suspected Unexpected Serious Adverse Reaction (SUSAR)
Any adverse reaction that is classed as serious and is suspected to be caused by the IMP that is not consistent with the information about the IMP in either the IB or SmPC, i.e. it is suspected and unexpected. The trial protocol should include a list of known side effects for each drug in the study. This should be checked with each serious adverse event that occurs in terms of expectedness. If the event is not listed as expected, or has occurred in a more serious form than anticipated, this should be considered a SUSAR.
4.0 Duties and Responsibilities

The Chief Investigator (CI) on behalf of the Sponsor has overall responsibility for the conduct of the study. In a multi-site study, the CI has co-ordinating responsibility for reporting adverse events to the Sponsor, Medicines and Healthcare products Regulatory Agency (MHRA) and to the relevant Research Ethics Committee (REC). The CI also takes overall responsibility for the submission of Annual Safety Report forms to the Sponsor and REC and must ensure that all research team members are in possession of the current IB (or SmPC) safety information about the product.

The Principal Investigator (PI) has responsibility for the research at a local site where the study involves specified procedures requiring site-specific assessment. There should be one PI for each research site. In the case of a single-site study, the CI and the PI will normally be the same person. The PI is responsible for informing the CI, or the organising research team, of all SAEs that occur at their site following the guidelines below. The PI is also responsible for maintaining records of AEs, as specified in the study protocol.

CTIMPs: Any CI/PI who has agreed to undertake duties for pharmacovigilance delegated by the Sponsor must undertake both Investigator’s and Sponsor’s responsibilities as described throughout this document.

The Research and Development Office (R&D) has the responsibility of ensuring that the adverse event documentation and Annual safety reports are passed to the designated clinical reviewer (Medical Director) and collecting review outcomes from the Service Governance Committee meetings within the stated timelines. The R&D Office must also ensure that all investigators are aware of safety reporting procedures and timelines and provide training where deemed necessary. Acting of behalf of the Trust as sponsor, it is the responsibility of the R&D office to keep detailed records of all Investigator-reported adverse events.

5.0 Guidance to Good Practice

5.1 Recording Process of Serious Adverse Events

Recording of AEs SAEs in non- Clinical Trial of Investigational Medicinal Product (non-CTIMP) Studies: NSFT-Sponsored studies

All SAEs in non-IMP clinical studies should be reported to the NSFT R&D Office as soon as possible using the form in Appendix 1. This form should be completed and signed by the Responsible treating clinician and the reporting investigator of the research team.

The Sponsor and CI also have the responsibility of reporting SAEs to the main Research Ethics Committee (REC) which issued the approval for the study within 15 days of notification of the event.

Adverse Events should be recorded on the AE Record Sheet (Appendix 2) and periodically discussed by the study steering group committee as required. Any safety concerns arising from the team should be reported to the Research Office as soon as possible.

Recording of AEs and SAEs in non- Clinical Trial of Investigational Medicinal Product (non-CTIMP) Studies: Externally-Sponsored studies

AEs and SAEs in non-IMP clinical studies should be reported to the Sponsor by the CI using the guidance as described in the sponsor’s institutional policy and/or study protocol. It is the
responsibility of the CI to make local site team members aware of study safety-reporting procedures.

Recording of AE and SAEs in Clinical Trial of Investigational Medicinal Products (CTIMPs): Externally-Sponsored Studies

Before the Trial Starts

The management and reporting arrangements for SAEs should be in place for all trials.

All protocols should list known side effects and adverse reactions contained within the manufacturer’s product information. This 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. A detailed explanation of SAE reporting procedures should also be included in the protocol and patient safety/risk assessments made clear in Research Governance and Ethical documentation.

Recording of AE and SAEs

The CI will decide in advance how to record and report adverse events, whether expected or not. Adverse events are usually described on case report forms (CRFs), unless they are classified as serious, in which case, these should be reported on the sponsor’s SAE form. It should be clearly stated in the trial protocol and Trial Management File what will be recorded and how the reporting is to be managed. It may be decided that all, or only some, non-serious AEs are to be recorded. Whatever option is chosen, it must be consistent with the purpose of the trial and any known toxicity and efficacy end points.

Agreements at the beginning of the trial should be made for such SAEs that can be defined as disease-related and therefore not subject to expedited reporting. The procedures for managing and reporting SAEs must be clearly defined in the protocol.

For CTIMPs, it is recommended that an Independent Data Monitoring Committee (IDMC) is appointed in order to review safety data regularly throughout the trial and when necessary, recommend to the Sponsor whether to continue, modify or terminate the trial. Again, this procedure must be defined in the protocol. As with all recording and reporting, subject confidentiality and adherence to the Data Protection Act (1998) must be maintained on all reports.

During the Trial

Each AE must be evaluated for seriousness, causality, and expectedness. The responsibility for this evaluation can be shared between the CI and PIs. It may be most appropriate for the treating PI at each local site to evaluate each event, before reporting it to the CI. It must be stated in the clinical trial protocol and the local SOP who will take responsibility for the assessment and reporting of such events to the Sponsor and CI simultaneously. As expedited reporting may be required, this SOP assumes that responsibility of initial assessment and reporting to the CI lies with the PI. If the administered product is a comparator the event will be assessed for expectedness as per the SmPC or IB and if considered unexpected and related to the event then it will be subject to expedited reporting as a potential SUSAR.

Causality

Adverse reactions should be assessed for causality using the definitions below.
Relationship Description

<table>
<thead>
<tr>
<th>Relationship Description</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unrelated</strong></td>
<td>There is no evidence of any causal relationship</td>
</tr>
<tr>
<td><strong>Unlikely</strong></td>
<td>There is little evidence to suggest there is a causal relationship (e.g. the event did not occur within a reasonable time after administration of the trial medication). Or There is another reasonable explanation for the event (e.g. the patient’s clinical condition, other concomitant treatment).</td>
</tr>
<tr>
<td><strong>Possible</strong></td>
<td>There is some evidence to suggest a causal relationship (e.g. because the event occurs within a reasonable time after administration of the trial medication). However, the influence of other factors may have contributed to the event (e.g. the patient’s clinical condition, other concomitant treatments).</td>
</tr>
<tr>
<td><strong>Probable</strong></td>
<td>There is evidence to suggest a causal relationship and the influence of other factors is unlikely.</td>
</tr>
<tr>
<td><strong>Definitely</strong></td>
<td>There is clear evidence to suggest a causal relationship and other possible contributing factors can be ruled out.</td>
</tr>
<tr>
<td><strong>Not assessable</strong></td>
<td>There is insufficient or incomplete evidence to make a clinical judgement of the causal relationship.</td>
</tr>
</tbody>
</table>

If the AE is serious and unexpected, the **possible**, **probable** and **definitely** related should be notified to the MHRA, the relevant REC and the Sponsor as SUSARs.

### 5.2 CTIMP Reporting Guidelines

Once the CI/PI has evaluated the AE in terms of seriousness, causality and expectedness, the following guidelines should be followed.

**AEs**

AEs that are not considered serious should be included on the relevant case report forms (CRFs) as previously agreed by the CI prior to the start of the study. The completed form should be filed along with the other CRFs for the study and a copy provided to the Sponsor as agreed.

**SAEs**

*Procedure to be followed by Study CI in single site studies*

- **a)** An event is identified by the CI and assessed for seriousness.
- **b)** All non-serious AEs will be recorded in the participants CRF.
- **c)** An SAE Form (Appendix 1 or Sponsor SAE form) is completed by CI for all AEs considered to be serious. This role may be delegated to a member of the research team. However, the completed form must be signed by the CI. This form is sent as soon as possible to the Sponsor’s R&D Office.
- **d)** The completed SAE Form must contain records of the event with the CI’s assessment of causality and expectedness, which should allow classification of the event to SAE, SSAR or SUSAR.
- **e)** An entry of the details of the event and follow-up correspondence must be made in the study SAE log. This log should be available to the Monitor for review during monitoring visits.
f) The CI will perform appropriate regulatory reporting as delegated by the Sponsor. All logged events will be reported to Ethics and MHRA annually as a Safety report.

**g)** CI (or designee) will send a line-listing of all logged SAEs quarterly (from the date of R&D approval) to the sponsor’s R&D office. If there is nothing to report in a particular month, an email must be sent to R&D to confirm this.

**h)** The Study Trial Management Group must ensure that they regularly review SAEs, looking for possible trends etc. The review sessions must be minuted as having taken place, with a note of the attendees, and the SAEs that have been reviewed.

**Procedures for multi-centre studies.**

**Site reporting procedure**

**a)** Every adverse event identified by the local PI must be assessed for seriousness and reported to the CI as specified in protocol or trial management reporting arrangements.

**b)** All non-serious AEs will be recorded in the participant’s CRF.

**c)** The Study SAE Form is completed by PI for all AEs considered to be serious. This role may be delegated to a member of the research team. However, the completed form must be signed by the PI and sent to the Sponsor R&D Office as soon as possible.

**d)** The completed SAE Form must contain records of the event with the PI’s assessment of causality and expectedness, which will clearly support and justify the classification of the event as SAE, SSAR or SUSAR.

**e)** The PI **must** report the event to the CI **immediately or within 24 hours** of being made aware of the event. Where not all information is available while the SAE Form is being completed, the initial report must contain the following as a minimum:

- Identifiable Event
- Identifiable Patient
- Identifiable IMP
- Identifiable Reporter.

If the information available is less than the specified minimum or if the SAE Form is not available for completion and reporting to meet the 24-hours deadline an initial report can be made verbally but must be followed within 48hrs by a detailed, written report.

**f)** The PI must in addition ensure that all local safety policy rules are followed.

**g)** An entry of the event must be made in the study SAE log for the site.

**SUSARs**

Any AE that the PI evaluates as serious, is suspected of having a causal relationship to the trial medication and is unexpected, will require **expedited** reporting the sponsor R&D Office, MHRA, REC and to other organisations as required under the terms of the individual contracts.

If the CI, or Trial Management Group is not in agreement with the “expectedness” decision of the PI, the CI cannot overrule the PI’s decision. Both opinions should be recorded on the SAE form.

Sponsors are required to report SUSARs electronically via the MHRA eSUSAR system. Non-electronic reports are no longer accepted by the MHRA.

**Blinded CTIMPs in the event of a SUSAR:**

For blinded clinical trials, the blind should be maintained unless it is felt necessary to be broken in the interest of subject safety. It is recommended that the blind be broken by the Sponsor for all SUSARs before they are reported to the MHRA for that specific subject (even if the CI/PI remains blinded). If the CI has delegated responsibility by the Sponsor for pharmacovigilance management and reporting, then un-blinding should be performed by individuals who are not involved in every day data management (e.g. the IDMC).
The minimum data required for reporting SUSARs to the MHRA and REC are:

i) The suspected Investigational Medicinal Product (IMP)

ii) Subject trial Identification

iii) An adverse event assessed as serious and unexpected, and for which there is a reasonable suspected causal relationship

iv) An identifiable reporting source

**Unblinding Process for CTIMPs in the event of a SUSAR:**

Systems for SUSAR and SAR reporting should, as far as possible, maintain blinding of individual clinicians and of local trial staff involved in the day-to-day running of the trial. It is important that the details of the unblinding process are included in the trial protocol.

For blinded trials involving a placebo and an active drug, seriousness, causality and expectedness should be evaluated as though the patient was on active drug. Cases that are considered serious, unexpected and possibly, probably or definitely related (i.e. possible SUSARs) would have to be unblinded. Only those events occurring among patients on the active drug should be considered to be SUSARs requiring reporting to the sponsor, MHRA, RECs, R&D and pharmaceutical company (if required under the terms of the contract). It may be that individuals who are not directly involved in the management of the trial (e.g. pharmacist at site) could perform the unblinding.

### 5.3 Timeframes for expedited reporting

The CI must inform the sponsor R&D Office **immediately** when notified of any Serious Adverse Events (SAEs), whether they are deemed to be SUSARs or not. For NSFT-sponsored studies, reporting should be written and signed by hand using the form in Appendix 1. For externally-sponsored studies, including CTIMPs, the CI should use the agreed study SAE form or sponsor SAE form as appropriate.

**Non-CTIMP Studies: non fatal/life-threatening SUSARs and other SAEs**

All SAEs (SUSARs and SSARs) in non-IMP studies should be reported to the sponsor R&D Office **immediately**. The Sponsor/CI must inform the approving REC within 15 days of notification.

**CTIMP: Fatal/life threatening SUSARs**

Fatal or life-threatening SUSARs in CTIMP studies should be reported to the sponsor R&D Office **immediately**. The sponsor must inform the MHRA, approving REC, and relevant pharmaceutical companies (if required under the terms of the contract) of fatal or life threatening SUSARs **immediately**, but no later than **7 calendar days** after the CI has first knowledge of the minimum criteria for expedited reporting.

In each case, relevant follow-up information should be sought and a report completed as soon as possible. This should be sent by the sponsor within an **additional 8 calendar days**.

**CTIMP: Non- fatal and non-life threatening SUSARs**

Non-fatal or life-threatening SUSARs in CTIMP studies should be reported to the sponsor R&D Office **immediately**. The sponsor/CI must report all non-fatal and non-life threatening SUSARs to the MHRA, REC, and relevant pharmaceutical companies (if required under the terms of the contract) as soon as possible, but no later than **15 calendar days** after the CI has first knowledge of the minimum criteria for expedited reporting. Further relevant information should be given as soon as possible.

**Reporting to PIs involved in Study**

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Norfolk and Suffolk NHS Foundation Trust  
R&D016 Research Adverse Event and Safety Reporting Procedures  
Page 9 of 18
For multi-centre trials all PIs within the trial concerned must also be informed of the SUSAR, although this does not have to be within the 7/15-day deadline. All PIs should be sent a summary of SUSARs approximately every 3 months. This timeframe may vary between trials depending on the rates of recruitment and/or SUSARs. If the CI is informed of SUSARs from other trials by a pharmaceutical company, the CI should inform PIs as above.

5.4 CTIMPs: Annual Safety Reports

All SAEs should be reported annually to the sponsor’s R&D Office, MHRA, REC, and relevant pharmaceutical companies (if required under the terms of the contract) on the anniversary of the Clinical Trials Authorisation (CTA). The annual report may be done in conjunction with the IDMC.

Annual safety reports should be in the format for Development Safety Update Reports set out in the ICH E2F guideline (available at [http://ec.europa.eu/health/documents/eudralex/vol-10/index_en.htm](http://ec.europa.eu/health/documents/eudralex/vol-10/index_en.htm)). This guideline, which was adopted by the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) in September 2010 and came into effect on 1 September 2011, establishes a common standard for periodic reporting on drugs under development among the ICH regions. It meets the standards required for annual safety reports on CTIMPs undertaken in the EU.

Current guidelines state the format should be presented as below:

1. Title page
2. Executive Summary
3. Table of Contents
   1. Introduction
   2. Worldwide Marketing Approval Status
   3. Actions Taken in the Reporting Period for Safety Reasons
   4. Changes to Reference Safety Information
   5. Inventory of Clinical Trials Ongoing and Completed during the Reporting Period
   6. Estimated Cumulative Exposure
      1. Cumulative Subject Exposure in the Development Programme
      2. Patient Exposure from Marketing Experience
   7. Data in Line Listings and Summary Tabulations
      1. Reference Information
      2. Line Listings of Serious Adverse Reactions during the Reporting Period
      3. Cumulative Summary Tabulations of Serious Adverse Events
   8. Significant Findings from Clinical Trials during the Reporting Period
      1. Completed Clinical Trials
      2. Ongoing Clinical Trials
      3. Long-term Follow-up
      4. Other Therapeutic Use of Investigational Drug
      5. New Safety Data Related to Combination Therapies
   9. Safety Findings from Non-interventional Studies
10. Other Clinical Trial/Study Safety Information
11. Safety Findings from Marketing Experience
12. Non-clinical Data
13. Literature
14. Other DSURs
15. Lack of Efficacy
16. Region-Specific Information
17. Late-Breaking Information
18. Overall Safety Assessment
    1. Evaluation of the Risks
    2. Benefit-risk Considerations
5.5 Reporting SAEs within the Trust:

non-CTIMPs: Reporting SAEs in NSFT-sponsored Studies
Pharmacovigilance roles in non-CTIMP studies sponsored by the Trust are delegated to the study Chief Investigator. The NSFT R&D office, under the authority of the R&D Director and Trust Research Governance committee acts as the Sponsor’s representative for NSFT-sponsored studies.

The Chief Investigator must send all SAEs using the SAE form (Appendix 1) and within the timelines specified above to the R&D Department or Sponsor Representative.

CTIMPs and non-CTIMPs: Reporting SAEs in externally-sponsored Studies
For CTIMP studies and non-CTIMPs not sponsored by the NSFT, all SAEs notifications should be sent to the sponsor’s representative, whose contact information is found in the protocol and/or approval documentation.

The Chief Investigator must send all SAEs using the SAE form (Agreed Sponsor SAE form) and within the timelines specified above to the R&D Department or Sponsor Representative.

CTIMPs and non-CTIMPs: Annual Safety Reporting to NSFT R&D
a) Details of the SAE recorded on the appropriate form (Appendix 1 or study SAE form)
b) Quarterly Line-listing of all SAEs from the study.
c) (CTIMPs only) Copy of all safety reports (expedited and annual) sent to the regulatory authorities whether NSFT- or External-sponsored studies using the ICF E2F guidelines as above.

Sending Safety Reports to NSFT R&D Department
Send an email and attach a copy of all relevant documents to: RDOfficemailbox@nsft.nhs.uk specifying: “SAE Report: STUDY NAME, LOCAL STUDY REFERENCE NUMBER”

For documents that require the CI’s signature (e.g. annual safety reports), if an electronic copy of the signed document is not available for email, please follow up the email by sending a signed copy of the document by Post to: Research and Development, Norfolk and Suffolk NHS Foundation Trust, Hellesdon Hospital, Drayton High Road, Norwich, NR6 5BE

5.6 R&D Reporting and monitoring of SAEs within the Trust: NSFT Sponsored Studies
Upon receipt of an SAE form and supporting documentation, the Research and Development office will complete the final section of the SAE form before sending out to an independent Clinical Reviewer for review and authorisation. The Reviewer will consult with the Chief Investigator and/or relevant clinical colleagues if there are any outstanding concerns about the SAE, and will report the event to the Research Governance Committee or Service Governance Sub-Committee as required. Any immediate patient safety issues will be escalated as per Trust policy (Q11- Serious Incidents Requiring Investigation Policy). A list of SAEs and AEs will also be discussed and recorded in the Research Governance Committee meeting minutes on a monthly basis. The outcome of any discussions and actions resulting from the SAE review will be held by the R&D department in the study file and by the Research Team in patient files and the Trial Management file.
Appendix 1: SAE Report Form

Norfolk and Suffolk NHS Foundation Trust

NSFT RESEARCH SERIOUS ADVERSE EVENT (SAE) REPORTING FORM

Please Fax this form immediately to 01603 421282 or email signed copy via secure network to RDOfficemailbox@nhs.net UK FAQ: R&D Manager Research and Development

<table>
<thead>
<tr>
<th>Study Title/Acronym</th>
<th>Name/Role of Reporting Investigator</th>
<th>Date of Report (dd/mm/yyyy)</th>
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<tbody>
<tr>
<td></td>
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<table>
<thead>
<tr>
<th>Type of Report:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = First</td>
</tr>
<tr>
<td>2 = Follow-on</td>
</tr>
<tr>
<td>3 = Final</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name of Responsible Clinician:</th>
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<table>
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<tr>
<th>Reporting Institution:</th>
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1. Patient Details

<table>
<thead>
<tr>
<th>Patient Initials</th>
<th>Date of Birth (DD/MM/YYYY)</th>
<th>Patient Trial/Study Code</th>
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<tr>
<td></td>
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</table>

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<thead>
<tr>
<th>Patient NHS number</th>
<th>Patient Height: cm</th>
<th>Patient Weight: kg</th>
<th>Patient Sex:</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
<td>M</td>
</tr>
</tbody>
</table>

2. SAE details

<table>
<thead>
<tr>
<th>Classification of SAE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Resulted in Death</td>
</tr>
<tr>
<td>2. Life-Threatening</td>
</tr>
<tr>
<td>3. Required Inpatient Hospitalisation or prolongation of existing hospitalisation</td>
</tr>
<tr>
<td>4. Significant or persistent incapacity/ disability</td>
</tr>
<tr>
<td>5. Birth Defect/Congenital Abnormality</td>
</tr>
<tr>
<td>6. Other Important Medical condition, please specify</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Location where Main SAE occurred:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Hospital</td>
</tr>
<tr>
<td>2. Out-Patient Clinic</td>
</tr>
<tr>
<td>3. Home</td>
</tr>
<tr>
<td>4. Nursing/Care Home</td>
</tr>
<tr>
<td>5. Other Location, please specify</td>
</tr>
</tbody>
</table>

Details of SAE

<table>
<thead>
<tr>
<th>Main Diagnosis/Symptoms (Only 1 major event per form should be recorded. Symptoms associated with main event should be recorded here)</th>
<th>Date on Onset (dd/mm/yyyy)</th>
<th>SAE Status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1. Resolved</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Resolved with Sequelae</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. Ongoing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4. Worsened</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5. Fatal</td>
</tr>
</tbody>
</table>

Date Resolved (dd/mm/yyyy)

Signed By Responsible Clinician/staff member ………………… Date of Completion (dd/mm/yyyy) □ □ □ □ □ □ □ □ □

NSFT SAE reporting form v2.0 9th August 2013
### Describo Serious Adverse Event
(include manifestation and progression of event, any treatments given in response to the SAE, and any relevant tests and results of tests carried out for diagnostic or treatment purposes)

<table>
<thead>
<tr>
<th>Date of most recent administration/Session</th>
<th>Start Date of Trial Treatment</th>
<th>Causal relationship to SAE</th>
<th>Expectedness</th>
<th>Action Taken</th>
</tr>
</thead>
</table>

### Details of Trial Medication or other Research Treatment/Intervention Received

<table>
<thead>
<tr>
<th>Name of Trial Medication/Treatment</th>
<th>Actual Daily Dose</th>
<th>Route (Medication only)</th>
<th>Date of most recent administration/Session</th>
<th>Start Date of Trial Treatment</th>
<th>Causal relationship to SAE</th>
<th>Expectedness</th>
<th>Action Taken</th>
</tr>
</thead>
</table>

### Details of Non-Trial Medication or other Clinical Treatment
(Exclude therapy for management of SAE. Include concomitant medication, other clinical therapies, radiotherapy, surgery and palliative care. Continue on separate sheet if required)

<table>
<thead>
<tr>
<th>Name of Treatment</th>
<th>Total Daily Dose</th>
<th>Route (Medication only)</th>
<th>Start Data</th>
<th>Ongoing</th>
<th>End date</th>
<th>Causal relationship to SAE</th>
<th>Action Taken</th>
</tr>
</thead>
</table>

Signed By Responsible Clinician/staff member .......................... Date of Completion (dd/mm/yyyy) □□□□□□□□

NSFT SAE reporting form v2.0 9th August 2013
5. Is SAE likely to have been caused by anything other than the research treatments previously listed on this form?

☐ 0 = No
   1 = Yes. If yes, please specify: (include: medical history, drug or alcohol abuse, family history, findings from other investigations)

6. Authorisations

Signed by Responsible Clinician/Staff Member: ............................................

PRINT NAME ............................................

Contact Telephone Number ............................................

Date of Completion ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

R&D Office Use Only:

Date Received by RD office (dd/mm/yyyy) ............................................

Type of Event:

☐ SAE/R
☐ SUSAR – 7 day
☐ SUSAR – 15 day

In my position as Clinical Reviewer, I believe, based on the information provided, that the reported adverse event is:

☐ related ☐ unrelated to the conduct of the study and administration of research procedures.

☐ expected ☐ unexpected based on the study protocol.

And as such:

☐ Further ☐ no further action should be taken as a result of this event.

Date Completed by Clinical Reviewer: ............................................

Signature of Clinical Reviewer: ............................................

Name of Clinical Reviewer: ............................................

If related AND unexpected, date of notification sent to approving bodies: ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

Additional Comments: ............................................

Date Completed and Filed: ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ Name of R&D officer: ............................................

Signed By Responsible Clinician/staff member ......................... Date of Completion (dd/mm/yyyy) ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

NSFT SAE reporting form v2.0 9th August 2013
Appendix 2: Adverse Event Recording Sheet

**ADVERSE EVENT RECORD SHEET**

<table>
<thead>
<tr>
<th>Study Name/Acronym:</th>
<th>Participant study ID/Name:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Locality/Team:</td>
<td>R&amp;D/UDI/ACT/MHRA CTA no:</td>
</tr>
</tbody>
</table>

Please complete this sheet for all Adverse Events occurring from date of consent and throughout the duration of participation in the study.

<table>
<thead>
<tr>
<th>Date</th>
<th>Name of person completing form</th>
<th>Date of adverse</th>
<th>Description of Adverse Event</th>
<th>Actions/Outcomes</th>
<th>Signature</th>
</tr>
</thead>
<tbody>
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</table>

Version 1: 9th March 2012/Adverse Event Management Templates.

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<table>
<thead>
<tr>
<th>Date</th>
<th>Name of person completing form</th>
<th>Date of adverse</th>
<th>Description of Adverse Event</th>
<th>Actions/Outcomes</th>
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</tbody>
</table>

Version 1: 9th March 2012/Adverse Event Management Templates.
Appendix 3: AE reporting Pathway:
Adverse Event Occurs

CI and/or PI decides whether event is classified as: AE, SAE, SUSAR. PI to notify CI of event within 24 hours.

Adverse Event (AE)

Serious Adverse Event (SAE)

CTIMP

CI reports SAE to sponsor immediately using agreed SAE form

Non-CTIMP

CI Reports SAE to Sponsor as soon as possible using SAE form

Non-fatal SUSARs and all other SAEs

Recorded and Reported in accordance with study protocol and sponsor policy

Sponsor/CI reports to REC and MHRA immediately (no later than 15 days after notification)

Sponsor/CI reports to REC and MHRA immediately (no later than 7 days after notification)

Follow-up report within 8 days of initial report

Fatal/threatening SUSARs

Sponsor/CI reports to REC and MHRA immediately (no later than 7 days after notification)

Follow-up report within 8 days of initial report
## Monitoring Statement

<table>
<thead>
<tr>
<th>Aspects of the policy to be monitored</th>
<th>Monitoring method</th>
<th>Individual/Team responsible for monitoring</th>
<th>Frequency</th>
<th>Findings: Group/Committee that will receive the findings/monitoring report</th>
<th>Action: Group/Committee responsible for ensuring actions are completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timeline and reporting procedures to regulatory authorities</td>
<td>Changes to EU regulations and REC reporting to be monitored by R&amp;D in accordance with published guidance.</td>
<td>Research Manager (Research and Development)</td>
<td>Annually to be reviewed, changes monitored constantly in response to national publications.</td>
<td>Research Governance Committee</td>
<td>Research Governance Committee</td>
</tr>
</tbody>
</table>